SUNDAY – Posters 1–322/ Abstracts 1–322
1. GENETICS
a. Microarrays/genomics – human/animal 1–12/1–12

0001

EXOME SEQUENCING OF ILS AND ISS MOUSE STRAINS: DETECTION OF SEQUENCE VARIATION UNDERLYING ALCOHOL ACTION

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Sequence variation in the genomes of inbred mouse strains can have important phenotypic effects and may influence the risk of disease as well as drug response of individuals. Inbred long sleep (ILS) and inbred short sleep (ISS) mouse strains were selectively bred based upon differential sensitivities to alcohol. We propose that even slight differences in the genome sequences among these two inbred strains of mice may play a role in phenotypes related to alcohol metabolism. We have applied the Agilent SureSelect XT Mouse Exome Kit to enrich for the exome sequences of these two mouse strains. The Illumina HiSeq 200 was used, with an average coverage of 30X and 2x100bp paired-end reads, to determine the exome sequence of 8 mice (4 ILS mouse individuals and 4 ISS mouse individuals). We report here a number of sequence differences detected by exome sequencing. These results outline an important strategy as well as candidate genome sequences that could be key in determining genomic differences related to alcohol metabolism and alcoholism.

0002

HIGH DRINKING IN THE DARK (HDID) SELECTED LINES AND BRAIN GENE NETWORKS

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Replicate HDID selected lines have been formed from mouse heterogeneous stock (HS) founders (HS/NPT). Details of the selection phenotype are found in Crabbe et al. (2009 & 2010). HDID-1 (S_{22}), HDID-2 (S_{15}) and HS/NPT controls were used for brain gene expression analysis. Data (N=32 to 40 per line) were collected using the Illumina MouseRef 8 v2.0 arrays in both the ventral striatum (VS) and the occipital cortex (OC). Data were analyzed using both measures of differential gene expression and weighted gene covariance network analysis (WGCNA). All animals were genotyped using the Mouse Universal Genotyping Array (Geneseek). The genotyping data revealed evidence of significant genetic drift in both selected lines, with greater drift in the HDID-1 mice. The 9393 gene transcripts showing the greatest consensus variance in the selected lines and controls were used for the WGCNA. There were 21 sub-networks or modules that had significant connectivity and functional enrichment. Permutation testing (N=1000) was used to determine the significance of the differences in the gene modules between the HS/NPT controls and the selected lines. One module showed the largest and most consistent connectivity disruption across both selections; differential Z-scores were 7 or greater. Functional analysis of this module revealed a significant enrichment in genes associated with neurological system processes ($p< 5 \times 10^{-6}$), glutamate secretion ($p< 8 \times 10^{-6}$) and neurotransmitter transport ($p< 8 \times 10^{-6}$). Eleven gene transcripts within this module showed similar significant connectivity changes in both selections; the transcripts associated were *Dgkz, Fam13c, Fgf13, Isli, Npcd, Sh3rf1, Tpbg, Tuba8* and 3 putative genes of unknown function. No member of this module showed significant differential gene expression across both selections (eBayes, FDR < 0.05). There were however 133 transcripts outside of this module that showed significant and consistent differential expression; however, with few exceptions these changes were very small (< 10%). In the OC, the same module showed only modest and non-significant changes. The data suggest a targeted module and specific genes for manipulating ethanol drinking in the dark. We note these targets show almost no overlap with those associated with 2-bottle choice preference drinking. Supported in part by AA11034, 13484, AA 13519, AA10760, and AA020245 and the Department of Veterans Affairs.

0003

GENE EXPRESSION IN BRAIN AND LIVER PRODUCED BY THREE DIFFERENT REGIMENS OF ALCOHOL CONSUMPTION IN MICE: COMPARISON WITH IMMUNE ACTIVATION

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Three tests of alcohol consumption commonly used for neurobiological and pharmacological analysis of alcohol drinking are the traditional continuous two bottle choice (Chronic) and two newer tests, two bottle choice every other day (Chronic Intermittent, CI) and limited access one bottle (Drinking in the Dark, DID). However, little is known about the common effects of alcohol exposure by these tests on brain or liver function. Recent data (Blednov et al., 2011) show that immune activation (injection of lipopolysaccharide, LPS) increases alcohol drinking. To determine similarities and differences among the three alcohol tests and immune activation, we used microarrays to profile gene expression in prefrontal cortex (PFC) and liver of C57BL/6J mice chronically consuming alcohol or injected with LPS. LPS treatment produced marked changes in global gene expression in both liver and PFC, while changes in PFC produced by all three alcohol paradigms were more moderate. Changes produced by alcohol in liver were proportional to the total amount of alcohol consumed, with the DID paradigm resulting in fewer differentially expressed genes. Many of the gene changes were unique to each treatment and comparison of differentially regulated genes across treatments revealed various degrees of overlap in the two tissues. All treatment pairs showed significant overlap in liver, while in PFC only two pairs (CI-LPS and CI-Chronic) showed significant overlap, with the CI-LPS overlap being the most significant in both tissues. Ingenuity Pathway Analysis in PFC refined our search for common changes by detecting a neuron-related network of differentially regulated genes (e.g., *Drd1a, Drd2, Pdyn, Tac1, Fosb, Ppp1r1b* (DARPP-32)) that was highly over-represented in CI and also over-represented in the Chronic and LPS (but not DID) groups. Similar analysis in liver showed a CYP and GST centered metabolic network shared in part by all 4 treatments. In summary, all alcohol tests and LPS had similar effects on liver and the CI paradigm produced many of the same effects on gene expression in both tissues as did LPS, providing further evidence for some common mechanisms of chronic alcohol consumption and immune activation. Supported in part by grants from the NIH/NIAAA Integrated Neuroscience Initiative on Alcoholism (INIA-West; AA13520), NIH grant AA12404 and K award AA017234, to IP.

0004

ETHANOL REGULATION OF GSK3B IN PFC

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Alcohol dependence is a chronic neuropsychiatric disorder in which symptoms persist despite negative physical, mental and psychological consequences. We have previously shown using microarray analysis that glycogen synthase kinase 3β (GSK3β) is an ethanol responsive gene in mouse prefrontal cortex (PFC). Mice overexpressing GSK3β in the PFC exhibit a potentiation of ethanol drinking behavior (40% increase in 2-bottle choice drinking paradigm), an increase in alcohol withdrawal-induced anxiety and alterations in genes involved in synaptic transmission. Here, we have examined the effects of ethanol on GSK3β S9 phosphorylation levels in PFC. We found that acute ethanol treatment (2 g/Kg i.p.) of DBA2/J mice results in a significant induction in GSK3β expression in the PFC compared to saline treated mice using RT-PCR. We are currently assessing the effects of chronic intermittent ethanol exposure on GSK3β S9 phosphorylation levels in the PFC using western blot. We hypothesize that chronic ethanol exposure may result in a downregulation of GSK3β S9 phosphorylation levels and therefore an increase in GSK3β signaling, contributing to the potentiation of ethanol drinking behavior observed in mice overexpressing GSK3β. Unraveling the molecular and neuronal processes responsible for the development and persistence of these pathological behaviors might lead to the development of new strategies to treat alcohol dependence. This work was supported by NIAAA grant AA0106667 to MFM.

0005

ALTERATIONS TO THE SYNAPTIC TRANSCRIPTOME IN RESPONSE TO ETHANOL-INDUCED SENSITIZATION

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Characteristic behaviors associated with chronic drug use, such as sensitization, tolerance, craving and relapse, are thought to be caused by long-term molecular adaptations precipitated by the drug's continual administration. Ethanol-induced behavioral sensitization can provide a valid, testable model to study the neural plasticity that mediates chronic drug-related behavior. The lasting activity-dependent changes that underlie behavioral adaptation to chronic ethanol are thought to, in part, depend on new protein synthesis and remodeling at the synapses. It is well established that mRNA can be transported to neuronal distal processes, where it can undergo localized translation regulated in a spatially restricted manner in response to stimulation. These concepts have led to our hypothesis that behavioral sensitization to repeated ethanol exposure results, at least in part, from alterations in the trafficking of mRNAs to distal processes, contributing to synaptic remodeling and plasticity. To identify molecular targets involved in synaptic plasticity underlying ethanol behavioral sensitization, DBA/2J mice (n=16 per treatment) were subjected to a standard 14-day sensitization paradigm using 2.5g/kg i.p. ethanol. Four hours following the final treatment on day 14, frontal pole tissue was dissected and utilized for a synaptoneurosome preparation which concentrates synaptic mRNA encapsulated within vesicularized elements. Profiling of RNA obtained from these samples (Affymetrix® GeneChip® Mouse 1.0 ST Arrays) allowed for discrimination of expression changes in synaptically localized genes which may otherwise go undetected when studying the entire transcriptome. RMA expression data was analyzed to identify synaptically targeted genes differentially expressed as a result of ethanol treatment. Examination of gene expression patterns revealed a number of genes whose levels were altered in response to acute ethanol, but habituated in response to repeated, sensitizing treatment. Further investigation revealed enrichment for genes involved in the processes of synaptic transmission, kinase activity, and endoplasmic reticulum function. Further analysis of these data will focus on novel networks of genes whose alterations in synaptic transcript levels contribute to ethanol-induced behavioral sensitization. Supported by NIAAA grants F31AA021035 to MAO and AA016667 to MFM.

0006

IDENTIFICATION OF ALCOHOL-INDUCED MIRNOMES IN DISTINCT AREAS OF THE MOUSE BRAIN

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Background: The crucial role of microRNAs (miRNAs) in mediating pleiotropic effects of ethanol such as the development of tolerance, disruption of neural stem cell proliferation and differentiation during fetal brain development, and gut leakiness among others has been suggested. Our group recently identified consistent miRNA signatures in the frontal cortex of human alcoholics and ethanol-treated mice, which suggest an miRNA-mediated adaptive response targeting innate-immunity and synaptic signaling functions in brain tissue. Now we profiled miRNA expression levels in multiple brain areas of the mouse reward circuitry in order to identify additional signatures relevant to ethanol consumption.
Methods: F1 hybrid FVBxB6 mice were exposed to a high drinking in the dark protocol for 18 days. After this period, animals were sacrificed, brains dissected and snap-frozen in liquid nitrogen, and cryosectioned at 300 μm. Three different brain areas (Nucleus Accumbens, Amygdala, and Infralymbic/Prelymbic Cortex) were then dissected using micropunches. Total RNA was extracted and Exiqon's miRNA arrays (miRCURY LNA™ microRNA Array, 5th gen - hsa, mmu & rno) were used to assess miRNA expression levels in the micropunches . These arrays include 904 human, 710 mouse, and 388 rat probes as referenced by miRBase v.14, in addition to a number of proprietary probes. MiRNA microarray data analysis was implemented in R environment using the limma package from Bioconductor. Alcohol-treated animals were assessed against matched, untreated control group.
Results: We found miRNA signatures in multiple areas of the brain that reflect the effects of alcohol drinking in the mouse model. Based on the conservation of specific differential miRNA expression changes between alcohol-treated mouse and human alcoholics, a collection of miRNAs emerge as the most consistent and relevant to the human disease.
Conclusions: Our results add support for an important role of miRNAs in alcohol dependence and underscore the potential utility of our mouse model to conduct in-vivo manipulations of brain miRNAs with high relevance for medications development and treatment of human alcoholism.

0007

CHRONIC INTERMITTENT ETHANOL EXPOSURE ALTERS MICRO-RNA EXPRESSION IN VENTRAL TEGMENTAL AREA DA NEURONS—APPLICATION OF *LASER CAPTURE MICRODISSECTION*

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Excessive alcohol consumption over a prolonged period of time results in alcohol dependence, and one essential criterion in the diagnosis of alcohol dependence is the appearance of an alcohol withdrawal syndrome when alcohol consumption ceases. Increasing evidence indicates that repeated exposure and withdrawal from alcohol result in persistent molecular and cellular adaptations. However, the mechanisms of these adaptive alterations are not fully understood. MicroRNAs (miRNAs) have been recently identified as master regulators of gene expression through post-transcriptional regulation. Our previous studies with neuronal culture have implicated the role of miRNAs in ethanol withdrawal-related effects. This study was designed to investigate miRNA expression in a single neuronal population in ethanol dependent mice. Nine male tyrosine hydroxylase (TH)-GFP transgenic mice (C57BL/6 background), expressing GFP specifically in midbrain dopamine neurons, were used. Animals received two cycles of either alcohol vapor chamber exposure intermittently (EtOH) or room air control (Ctrl). Each cycle includes 10h ethanol and 14h room air exposure daily over a 9-day period, followed by 5 days of ethanol withdrawal (WD). Laser capture microdissection was used to isolate dopamine neurons of the ventral tegmental area (VTA) and followed by an optimized RNA isolation procedure from 500 captured neurons. The differential miRNA expression was examined using TaqMan Real-time PCR miRNA Array. Among 335 probed miRNAs, 96 were differentially expressed following ethanol exposure and/or withdrawal. Compared to control mice, 84 miRNAs were expressed differentially at the end of 9-day ethanol exposure, while 12 unique miRNAs were changed only after 5-days withdrawal (Fold Change>3). These results suggest that miRNAs may be involved in the regulation of neuronal adaptation in VTA dopamine neurons associated with ethanol treatment and its withdrawal. The potential role of these effects on miRNAs expression in the behavioral effects of ethanol remains to be determined. (This research is supported by NIAAA AA017362)

0008

THE ROLE OF SMALL RNA IN THE GENETIC PREDISPOSITION TO ALCOHOL CONSUMPTION

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Several genomic regions have been identified as having significant or suggestive associations with alcohol consumption in the recombinant inbred panel of HXB/BXH rats. One promising region on chromosome 1 is also syntenic with loci identified in human genome wide association studies for alcohol consumption. Based on the analysis of exon array data from the entire panel, our previous work has used the genetical genomics approach to focus on genes and the genetic control of gene expression modulated in these genomic regions of interest. In our analysis, we found candidate genes for alcohol consumption related to pathways linked to presynaptic GABA release, activation of dopamine neurons, and postsynaptic GABA receptor trafficking. We have now utilized the RNA-seq method to measure expression of protein-coding transcripts and non-coding (nc) RNAs, including small ncRNAs, in brains of the parental strains (SHR/Ola and BN-Lx/Cub) to obtain a comprehensive expression signature that can be used for a more detailed study of the alcohol consumption loci.
In this current work, we focus our analysis of the RNA-seq data to identify differentially regulated small ncRNA in the genomic regions associated with alcohol consumption. In particular, we examine previously annotated micro RNA (miRNA) and predict their gene targets, for which we have gene expression data on the same parental strains. These data allow us to not only identify differentially regulated miRNA but to also assess differential expression of their targets. In addition to genes found previously, our results suggest the role of small RNA and miRNA and their targets in the genetic predisposition for alcohol consumption. Supported by NIAAA (AA016922, AA013162, AA016663) and the Banbury Fund.

0009

SAME PATHWAY, DIFFERENT PERTURBATION: IDENTIFYING COMMON GENETIC THEMES ACROSS MULTIPLE RAT MODELS OF ALCOHOL CONSUMPTION

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Although the diagnosis of alcohol dependence does not include a quantitative criterion for alcohol consumption, heavy alcohol consumption is a necessary factor for becoming dependent. There also are many other societal and biological consequences to heavy alcohol consumption, even in the absence of dependence. This has led to the investigation of environmental and genetic factors that influence the quantity of alcohol consumed by animals and humans. We previously identified a genetically defined pathway related to predisposition to consume various amounts of alcohol and to GABA release and GABA receptor trafficking (Tabakoff et al 2009). We derived this pathway from quantitative transcriptome data and DNA sequence variation data from recombinant inbred rodents, and it represents randomly segregating genomic features that combine to predispose to a continuous spectrum of alcohol consumption levels in a free-choice, 24-hour access paradigm. We interrogated this pathway further to determine its relevance in rats, which were selectively bred to display extreme values in alcohol consumption. Using the Affymetrix Rat Exon Array, we generated exon-level brain transcriptome information on 6 pairs of selectively bred rat lines from 4 countries. We also generated detailed brain transcriptome data using RNA-Seq technology (Illumina HiSeq2000) on the two progenitor strains (BN-Lx/Cub and SHR/Ola) of the recombinant inbred panel (HXB/BXH) used in our previous study. With the RNA-Seq data, we reconstructed the rat brain transcriptome, identifying about 69,000 transcript-like units. We used this information to calculate transcript-level expression data from the exon array data from the selected rat lines. Although differential expression for individual transcripts within each of the 6 pairs had little concordance across pairs, each pair had at least one differentially expressed transcript relevant to our initial GABA-related pathway. In addition to identifying individual transcripts whose expression differs between high-consuming and low-consuming lines, we also used weighted gene co-expression networks and differential co-expression techniques to identify relationships between genes that differ between high-consuming and low-consuming animals. The results describe an integrated pathway of transcripts that can be perturbed in a variety of ways to produce similar phenotypes.
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0010

ALCOHOLISM TARGETS GAMMA-AMINOBUTYRIC ACID TYPE B RECEPTOR SUBUNIT 1 SPLICING IN HUMAN BRAIN

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Gamma-aminobutyric acid type B (GABAB) receptor agonists are used in the treatment of alcoholism, and previous microarray studies showed increased expression of GABAB1 subunit in brain following chronic alcohol exposure in humans. Chronic alcohol can change expression of specific splicing variants, and we asked if this occurs with GABAB1 transcripts. Given the complexity of these variants, we sequenced gene specific libraries as well as whole transcriptome libraries to maximize identification of GABAB1 specific splicing junctions from human prefrontal cortex. Using the splicing junction data, we found that the GABAB1 gene is at least 2 to 3 times longer than the known GABAB1 gene. Mapped reads and splicing junctions were also found from intronic and intergenic regions of the RefSeq Genes model. To examine these regions, we introduced new strategies, RPGM and RPJM, for gene expression and junction levels, respectively. GABAB1 exon and intron RPGM data showed low expression at the 5' end exons and exon grouping pattern. This indicated that there are more short splicing variants than just GABAB1a, the longest known major transcript containing all known exons. Comparing 14 alcoholics and 15 controls, chronic alcohol altered exon/intron and splicing junction expression in human brain. The majority of exon and intron changes could be explained based on changes in splicing junctions. Decreased expression at a GABA biding site, a transmembrane region (TM), and a miRNA binding site may decrease the population of normal GABAB1 transcripts and thereby decrease normal signal transduction. This suggests that the therapeutic benefit of GABAB receptor agonists used in treating alcoholism may be due to decreases in functional splice variants of brain GABAB transcripts in alcoholics. To the best of our knowledge, this is the first gene specific RNA-seq study and demonstrates the power of deep sequencing of a gene specific library to detect unexpected rare splicing junctions and splicing complexity from a single gene. In addition, we provide the first use of gene specific sequences to query human brain whole transcriptome sequences for changes in junctions and exon/intron usage in a psychiatric disease.
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0011

ALTERED EXPRESSION OF CYTOKINE SIGNALING PATHWAY GENES IN PERIPHERAL BLOOD CELLS OF ALCOHOL DEPENDENT SUBJECTS

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Background: Pre-clinical and clinical studies have implicated changes in cytokine and innate immune gene-expression in both the development of and end-organ damage resulting from alcohol dependence. However, these changes have not been systematically assessed on the basis of alcohol consumption in human subjects.
Methods: Illumina Sentrix Beadchip (Human-6v2) microarrays were used to measure levels of gene-expression in peripheral blood in 3 groups of subjects: those with alcohol dependence (AD, n=12), heavy drinkers (HD, defined as regular alcohol use over the past year of at least 8 standard drinks/week for women and at least 15 standard drinks/week for men, n=13), and moderate drinkers (MD, defined as up to 7 standard drinks/week for women and 14 standard drinks/week for men, n=17).
Results: 436 genes were differentially expressed among the three groups of subjects (FDR corrected p-value < 0.05). 291 genes differed between AD and MD subjects, 240 differed between AD and HD subjects, but only 6 differed between HD and MD subjects. Pathway analysis using DAVID and GeneGO Metacore software showed that the most affected pathways were those related to T-cell receptor and JAK-Stat (Janus kinase-Signal transducer and activator of transcription) signaling.
Conclusions: These results suggest the transition from heavy alcohol use to dependence is accompanied by changes in the expression of genes involved in regulation of the innate immune response. Such changes may underlie some of the previously described changes in immune function associated with chronic alcohol abuse. Early detection of these changes may allow individuals at high risk for dependence to be identified.

0012

BEHAVIORAL AND MOLECULAR EFFECTS OF ACUTE PRENATAL EXPOSURE TO ETHANOL ARE ALTERED BY SOCIAL ENRICHMENT

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Prenatal ethanol exposure is a risk factor for developmental disorders with abnormal social behaviors. Ethanol exposure on gestational day 12 alters social behavior of 28-, 42-, and 75-day-old rats; ethanol-exposed males show decreased social investigation and play fighting at all ages, and both sexes show social avoidance at postnatal day (P)42 and P75. Moreover, a form of social enrichment (housing ethanol-exposed rats with non-exposed control rats) normalized the social avoidance phenotype. The present study sought to test whether alterations in microRNA (miRNA) expression in the amygdala or ventral striatum could underlie the beneficial effects of social enrichment on reversing ethanol-induced social avoidance. We purified miRNA from the amygdala and ventral striatum of 72 male and female rats at P42. Samples were pooled and run on 48 Affymetrix miRNA Arrays using 3 arrays for each of 16 different conditions [2 treatments (Ethanol/Control), 2 social enrichment treatments (Enriched/Non), 2 brain areas (Amygdala/Ventral Striatum) and 2 sexes]. To identify miRNAs affected by prenatal ethanol exposure, we performed ANOVAs (exposure x brain area x sex) to reveal miRNAs with nominally significant changes due to prenatal ethanol exposure, but without any ethanol exposure x sex or ethanol exposure x area interactions. Next, we identified miRNAs affected by social enrichment, through ANOVAs (enrichment x brain area x sex) to reveal those miRNAs with a significant main effect of the social enrichment, but no significant enrichment x sex or enrichment x area interactions. Of the 600+ unique rat miRNAs interrogated, 55 showed nominally significant effects of ethanol and 297 showed nominally significant effects of enrichment. Additionally, we identified a small number of miRNAs with significant but opposing effects of ethanol and social enrichment, including rno-mir-30e (validated targets include p53, Synaptotagmin 4 and Activin receptor 1), rno-mir-301a (validated targets include Calpain 8), rno-mir-376b (top predicted targets include Ezrin and the GABA transporter Slc6a1), and rno-miR-30c-2 (top validated targets include Neurod1, Activin receptor 1, and Ctgf). We are currently validating the miRNA findings using qPCR, however, many of the gene targets of the altered microRNAs have previously been implicated in ethanol research. Thus, our data suggest a number of novel epigenetic mechanisms for social enrichment to reverse the effects of ethanol exposure.

0013

A HISTORY OF BINGE ALCOHOL DRINKING AUGMENTS HOMER2 EXPRESSION, AS WELL AS PI3K AND ERK SIGNALING, WITHIN THE BNST
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The extended amygdala is an interconnected group of brain structures that includes the shell subregion of the nucleus accumbens (NAC shell), the bed nucleus of the stria terminalis (BNST) and the central nucleus of the amygdala (CeA), all sharing cytoarchitectural and functional anatomical similarities. Our group has demonstrated previously that a month-long history of binge alcohol drinking under Drinking-in-the-Dark procedures (DID) procedures elevates signaling from Group1 mGluRs through both PI3K and PKC epsilon within the NAC shell and the CeA. Furthermore, functional studies have confirmed that the activation of these kinases upon Group1 mGluR stimulation within both the NAC shell and in the CeA are relevant for binge alcohol drinking. The present study continues, and extends to the BNST, our earlier line of inquiry regarding the role for mGluR5-Homer interactions in the manifestation of excessive, binge alcohol drinking. C57BL/6J mice were trained to drink 20% alcohol under DID procedures (2 hr access beginning at 3 hours into the dark phase of the circadian cycle) for 30 days. Control mice consumed water under identical procedures. Twenty-four hours following the last alcohol session, the BNST was excised and tissue homogenate immunoblotted for the following proteins: Homer1b/c, Homer2a/b, mGluR1, mGluR5, NR2a, NR2b, total PI3K, Akt, PKC epsilon and ERK, as well as phospho(Tyr458)-p85, phospho(Thr308/Ser473)-Akt, phospho(Ser729)-PKC epsilon and phospho(Tyr204)-ERK. As observed for the NAC shell and CeA, BNST levels of Homer2 were elevated in binge alcohol mice, as was the ratio of activated to total PI3K. However, in contrast to our earlier findings for the NAC shell and CeA, we failed to detect changes in glutamate receptor expression or in PKC epsilon activity within the BNST. While phospho-Akt levels were not changed following binge drinking, phospho-ERK levels were significantly elevated. These data support the working hypothesis of our laboratory that a history of binge alcohol drinking produces an increase in Homer2 expression throughout the extended amygdala and suggest that elevated PI3K and ERK signaling within the BNST may also contribute to maintaining excessive alcohol intake.
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0014

MOLECULAR SIGNALING MECHANISMS REGULATE FUNCTIONAL RESISTANCE OF THE NMDA RECEPTOR TO INHIBITION BY ACUTE ALCOHOL
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We previously reported that the N-methyl-D-aspartate receptor (NMDAR) on rat hippocampal CA1 neurons became resistant to inhibition by acute alcohol (80 mM) when neurons were first exposed to 45 mM alcohol for 3 hours *ex vivo*. The development of this adaptive resistance was mimicked by inhibition of Striatal Enriched protein tyrosine Phosphatase (STEP61) or activation of p38 mitogen-activated protein kinase (p38 MAPK), and is associated with an increase in NR2B subunit NMDAR activity. Here we report that the development of this adaptive resistance is regulated by calcium-calmodulin dependent protein kinase II (CaMKII), and also by the activity of metabotropic glutamate receptor type 1 mediated transient receptor potential channels (mGluR1-TRPC1). Rat brain slices were exposed to artificial cerebrospinal fluid (aCSF) or 45-mM alcohol in the presence or absence of various inhibitors for 3 hours. Whole-cell recording was performed to measure NMDAR-mediated excitatory postsynaptic currents (NMDAR EPSCs) in hippocampal CA1 pyramidal neurons. An acute application of 80 mM alcohol inhibited NMDAR EPSCs in control (aCSF-exposed) neurons by 34.8±2.9%, and by 1.4±2.0% in 45 mM alcohol-exposed neurons, showing an adaptive resistance of the NMDAR by the 3-hr alcohol treatment. Pre-treatment of the slices with BAPTA-AM (100 nM) blocked the adaptive resistance, indicating the involvement of synaptic Ca^{2+}-mediated mechanisms. Since increased Ca^{2+} can activate CaMKII, a major protein associated with postsynaptic density, we tested the effects of KN-93, a CaMKII inhibitor, and KN-92, an inactive control, on the development of this adaptive resistance. Unlike KN-92 (1 μM), KN-93 (1 μM) blocked the adaptive resistance, which supports an involvement of CaMKII. An increased synaptic Ca^{2+} concentration has also been shown to activate mGluR-TRPC1 channels, which in turn, enhanced NMDAR activity. Therefore, we pre-treated the neurons with CPCCoEt (30 μM), a potent mGluR1/mGluR5 antagonist, and found that CPCCoEt also blocked the adaptive resistance of the NMDAR, implicating TRPC1 in the alcohol-induced adaptive change of the NMDAR. These results suggest that the development of the adaptive resistance of the NMDAR in response to alcohol treatment is regulated by a cascade of signaling events involving the activity of the NR2B subunit, STEP61, p38 MAPK, CaMKII, and mGluR-TRPC1.
This study is supported by NIH grants AA018328, AA016548 and a VA Merit Review grant.

0015

LOOP 2 SEQUENCE PROFOUNDLY AFFECTS THE SENSITIVITY OF ALPHA 1 GLYCINE RECEPTORS (GLYRS) TO ETHANOL
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We previously demonstrated that replacing extracellular Loop 2 of α1 GlyR subunits with the Loop 2 residues from the highly ethanol sensitive δ $GABA_AR$ (δL2) reduced ethanol threshold and increased the degree of ethanol potentiation in GlyRs. Similarly, replacing Loop 2 of the γ subunit of $\alpha_1\beta_2\gamma_2$ $GABA_AR$ with δL2 shifted the ethanol threshold from 50mM in wildtype (WT) to approximately 1 mM in the dL2 mutant $GABA_AR$. In contrast, substituting the same residues from loop 2 of the γ $GABA_AR$ subunit did not alter ethanol sensitivity in GlyRs. These findings demonstrate that that the structure of Loop 2 can profoundly affect ethanol sensitivity in GlyRs and $GABA_ARs$ and suggested molecular models and mechanisms of ethanol action. In these studies, all of the non-conserved residues in Loop 2 of a1 GlyRs, and Loop 2 of the γ2 subunit in $GABA_ARs$, were mutated to those found in the GABA δ subunit. We do not know which combination of mutations causes the increased ethanol sensitivity of δL2 mutant GlyRs and $GABA_ARs$ or if the δL2 mutation produces the highest ethanol sensitivity receptor possible. Recently, we found that reverting the serine at position 52 (A52S) in δL2 back to alanine (δL2 A52) produced GlyRs that were ultrasensitive to ethanol—they had a greater magnitude of ethanol response and lower ethanol threshold (< 1mM)—compared to the δL2 mutant GlyRs. This finding suggests that other δL2 sub-sets may provide similar or higher ethanol sensitivity with fewer mutations of L2. To test this hypothesis, we reverted the mutations in δL2 at positions 57 (D57E) and 59 (R59T), back to the WT residue. This new mutant receptor (δL2 S50H, A52S, T54N, T55N) was similar in ethanol sensitivity to the δL2 A52 mutants. That is, it responded to 1 mM ethanol or less. We currently are testing other δL2 mutant combinations in GlyRs, are extending testing to lower ethanol concentrations and are determining if the findings extend to $GABA_ARs$. These and further studies that identify the minimal subset of δL2 mutations that are necessary and sufficient to produce receptors ultrasensitive and resistant to ethanol will provide important insight into the molecular structures and mechanisms of ethanol action, will facilitate development of knock in animals and may help identify polymorphisms that affect ethanol sensitivity in humans (Support: NIAAA/NIH AA3972, AA13378, AA13992, AA17243, LAB CTSI Grant 1UL1RR031986 and the USC School of Pharmacy).

0016

ACTIVITY-DEPENDENT PROCESSES UNDERLIE CHRONIC ETHANOL-INDUCED ENHANCEMENT OF SYNAPTOPODIN EXPRESSION IN HIPPOCAMPAL NEURONS
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Synaptopodin (SP) is a proline-rich actin-associated protein that regulates the activity of α-actinin, an actin crosslinking microfilament protein. SP is found in a subset of mature dendritic spines in hippocampal neurons where it is tightly associated with and regulates expression of the spine apparatus. Spines that contain SP have prolonged decay kinetics of intracellular Ca^{2+} transients and persistent activity-dependent increases in volume. Expression of SP is increased following induction of long-term potentiation (LTP) in hippocampus, and mice lacking SP exhibit decreased hippocampal LTP and more working memory errors on the radial arm maze task in comparison to wild-type mice. Chronic ethanol exposure is associated with enlargement of dendritic spines and altered synaptic plasticity in hippocampus. However, it is unknown if ethanol affects SP expression, and if so could this contribute to altered synaptic and morphological plasticity. To begin to address this, we examined changes in SP clustering in primary hippocampal neurons treated with chronic ethanol. Hippocampal neurons were co-stained with SP, phalloidin to label of F-actin-rich dendritic spines, and PSD-95, a postsynaptic density scaffolding protein. Confocal images of SP staining were acquired, and image analysis was performed using the Imaris 3D imaging program. As expected, we observed punctate SP clustering in the proximal and distal dendrites and the soma of hippocampal neurons. SP clusters were also observed in the head, neck and base of dendritic spines in ethanol-naïve neurons. Treatment of neurons with 50 mM ethanol for 4 d significantly increased SP cluster volume and density (n = 7–8 dishes/group; 640 total SP clusters). Because ethanol inhibits NMDA receptors and regulation of SP is thought to be activity-dependent, we treated neurons chronically with D-APV, an NMDA receptor antagonist. Similar to our findings with ethanol, prolonged inhibition of NMDA receptors with D-APV (50 μM) markedly enhanced SP cluster volume and density in comparison with untreated neurons (n = 7 dishes/group). These data suggest that the effects of chronic ethanol on SP expression are dependent upon ethanol inhibition of NMDA receptor activity. Thus, ethanol-induced changes in SP may be part of the homeostatic adaptive plasticity of dendritic spines and may contribute to aberrant synaptic and behavioral plasticity associated with chronic ethanol exposure.
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0017

CHRONIC ETHANOL EXPOSURE DECREASES KV4.2 CHANNEL AND KCHIP3 EXPRESSION IN THE HIPPOCAMPUS

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It is well documented that chronic ethanol exposure results in significant, long-term adaptations in neuronal homeostasis of glutamatergic synapses that alter cellular responses and signal transduction. However, it is unknown how chronic ethanol affects overall dendritic plasticity and ion channel surface expression at the synapse. Particularly, A-type K+ channels (Kv4.2) have an important role in determining neuronal firing properties and regulating neuronal excitability. Previous findings in our lab in ethanol-treated organotypic hippocampal slice cultures indicate an increase in backpropagating action potential amplitude, due to a decrease in transient A-type K+ current. Backpropagating action potentials may provide information on distance-dependent modulation of dendritic and synaptic plasticity. Additionally, an increase in phosphorylated Kv4.2 channels along with a decrease in Kv4.2 channel surface expression and Kv channel interacting proteins (KChIPs) were also observed. Kv channel interacting proteins are important for the formation and functional properties of Kv4.2 channels. Loss of KChIP3 in particular results in a decrease in A-type current densities. KChIP3 also serves as a negative regulator of NMDA surface expression. Chronic ethanol exposure increases NMDA surface expression with in vitro and in vivo models. In an in vivo model of chronic ethanol exposure, preliminary data using western blot also suggest a decrease in KChIP3 and Kv4.2 channel expression in the rat hippocampus. These decreases in Kv4.2 channel and KChIP3 expression, as well as increases in NMDA surface expression, may have important implications in the homeostatic adaptations at glutamatergic synapses during chronic ethanol exposure.

0018

COMMON AND DISTINCT MECHANISMS IN BK CHANNEL-MEDIATED RESPONSES OF CEREBRAL ARTERIES TO ALCOHOL AND CHOLESTEROL

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Hypercholesterolemia and binge alcohol (ethanol) drinking constitute independent risk factors for cerebrovascular disease and stroke. Moreover, *in vitro* alcohol levels obtained in circulation during binge drinking (20–60 mM) constrict cerebral arteries in several species, including humans. Artery constriction is negatively regulated by large conductance, Ca^{2+}- and voltage-gated K^+ (BK) channels in vascular myocytes (VSM). VSM BK channels are inhibited by cholesterol (CLR). Consistent with drug action on cerebral arteries, acute exposure to 50 mM alcohol inhibits VSM BK channels.Here, we used *in vitro* diameter determinations in pressurized cerebral arteries, patch-clamp and lipid bilayer electrophysiology to unveilmechanisms that mediate CLR and ethanol effects on cerebral arteries *via* VSM BK channel inhibition.

We applied 50 mMalcoholto BK made of channel-forming cbv1 (AY330293) and accessory β1 (FJ154955) subunits cloned from rat cerebral artery myocytes. Drug action was also evaluated on native VSM BK channels and cerebral arteries fromβ1-containing (C57BL/6)*vs.* β1-lacking (*KCNMB1* KO) mice.Data indicate that BK β1 is absolutely required for alcohol to evoke VSM BK channel inhibition and artery constriction. In addition, alcohol-induced channel inhibition was only observed at Ca^{2+}_{ic}>1 μM, this alcohol action being lost in absence of activating Ca^{2+}_{ic}.

Incorporation of cbv1 channels into CLR-free *vs.* CLR-enriched (33 mol%) lipid bilayers revealed that CLR inhibited channel activity. This CLR action, however, was unmodified by BK β1. In addition, CLR action was observed within a wide range of Ca^{2+}_{ic}levels, and sustained in Ca^{2+}-free solutions.

Remarkably, alcohol inhibition of cbv1+β1 channels in CLR-containing bilayers was significantly larger than the summation of alcohol and CLR individual effects. In addition, alcohol inhibition of cbv1+β1 was lost in CLR-free bilayers. Consistently, CLR depletion of rat cerebral artery VSMblunted alcohol inhibition of native channels. Finally, CLR-depletingtreatment of rat cerebral arteries ablated alcohol-induced constriction.

Our study indicates that the relative involvement of BK subunits and activating Ca^{2+}_{ic} in the inhibitory actions of alcohol and CLR differ. However, interacting mechanism(s) may operate at the VSM BK channel or its immediate environment to amplify CLR and alcohol actions when these modulators are applied together.

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0019

STRUCTURAL BASIS FOR ALCOHOL MODULATION OF A BACTERIAL LIGAND-GATED ION CHANNEL

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Despite its long history of use and abuse in human culture, the molecular basis for alcohol action in the brain is poorly understood. The recent determination of the atomic-scale structure of GLIC, a prokaryotic member of the pentameric ligand-gated ion channel (pLGIC) family, provides a unique opportunity to characterize the structural basis for modulation of these channels, many of which are alcohol targets in brain. We observed bimodal modulation of GLIC by n-alcohols, similar to some eukaryotic pLGICs: methanol and ethanol weakly potentiated proton-activated currents in GLIC, whereas n-alcohols larger than ethanol inhibited them. Mapping of residues important to alcohol modulation of ionotropic receptors for glycine, GABA, and acetylcholine onto GLIC revealed their proximity to transmembrane cavities that may accommodate one or more alcohol molecules. Site-directed mutations in the pore-lining M2 helix allowed the identification of four residues that influence alcohol potentiation, with the direction of their effects reflecting helical structure. At one of the potentiation-enhancing residues, decreased side chain volume converted GLIC into a highly ethanol-sensitive channel, comparable to its eukaryotic relatives. Covalent labeling of M2 positions with a methanethiosulfonate reagent further implicated residues at the extracellular end of the helix in alcohol binding. Molecular dynamics simulations elucidated the structural consequences of a potentiation-enhancing mutation and suggested a structural mechanism for alcohol potentiation via interaction with a transmembrane cavity at the subunit interface. These results provide a unique structural model for independent potentiating and inhibitory interactions of n-alcohols with a pLGIC family member. This work was supported by NIH/NIAAA postdoctoral fellowship F32 AA19875-01A1 and postdoctoral training grant fellowship T32 AA007471 (R.J.H.), NIH/NIAAA grants R01 AA06399 and R01 AA013378 (R.A.H.), and Swedish Research Council grant VR 2010-491 and European Research Council grant ERC 209825 (E.L.).

0020

BINDING OF ALCOHOL TO THE C1 DOMAIN OF PKC EPSILON

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PKC epsilon is a serine threonine kinase known to regulate the behavioral effects of alcohol. PKC epsilon knock out mouse consumes seventy five percent less alcohol compared to the wild type mice. To investigate if this regulation is by direct binding of alcohol molecule to the PKC epsilon, we previously studied the interaction of alcohols and the second cysteine rich regulatory subdomain (C1B) domain. Here we expressed, purified, characterized and studied the interaction of alcohols with a larger C1 domain which is the combination of the first (C1A) and the second (C1B) cysteine rich subdomains. Alcohols affect the energy transfer between the tryptophan residues of C1 domain and the fluorescent phorbol ester analog, SAPD and the diacylglycerol analog Dansyl-DAG. Although the effects are different for the two probes, these results indicate that alcohol interacts with both the subdomain C1A and C1B. Using photoactive azibutanol and azioctanol and mass spectrometry we identified Tyr-176 in the C1A and Tyr-250 in the C1B as the site of alcohol binding. The Tyr-250 was also identified earlier using isolated C1B domain. Molecular modeling showed that the two residues are at a distance of 35.7Å. To study the cellular significance of the interaction between C1 domain and alcohols, effects of alcohols on PKC epsilon C1 expressed in HEK293 cells is under investigation. The present studies indicate that PKC epsilon C1 has more than one binding site(s) for alcohols.

0021

ALCOHOL DEPENDENCE PRODUCES ALLOSTATIC SHIFTS IN NEUROPEPTIDE Y (NPY) LEVELS IN THE EXTENDED AMYGDALA OF RATS

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Neuropeptide Y (NPY) in the central amygdala (CeA) mediates excessive alcohol-drinking behaviors in rodents, and chronic alcohol exposure affects NPY levels in CeA. Less is known about the effects of chronic high-dose alcohol and withdrawal on NPY in the bed nucleus of stria terminalis (BNST) and nucleus accumbens (NAc), the two other major regions of the extended amygdala, both with important roles in emotion and reward. The purpose of this study was to examine changes in NPY expression in extended amygdala (i.e. BNST and NAc) during the development of alcohol dependence and during withdrawal. To induce alcohol dependence, male Wistar rats were exposed to chronic intermittent (14 hrs on/10 hrs off daily) ethanol vapor inhalation for various periods of time. Four groups of rats (n=6/group) were exposed to alcohol vapor and sacrificed at the following time points following start of vapor exposure: 14 hrs, 14 days, 28 days, or 28 days + 10 hrs withdrawal. Four separate control groups of rats were exposed to ambient air for the same periods of time. Upon sacrifice, rats were intracardially perfused with 4% paraformaldehyde, brains extracted, stored in paraformaldehyde until transfer into 30% sucrose overnight, snap-frozen in isopentane and stored at -80°C. After collection, brains were coronally sectioned (30mm) on a cryostat, stored in phosphate-buffered saline (PBS), then stained with a primary antibody for NPY, followed by processing with horseradish ABC kit and diaminobenzidine (DAB) kit. Slices were mounted, cover slipped, and photomicrographs were taken with a Zeiss Axiophot microscope at multiple rostral-caudal depths for each region of interest. Density of NPY staining was measured using NIH Image J. Blood-alcohol levels were maintained in the 175–250 mg% range during chronic alcohol vapor exposure. Density of NPY staining in BNST and NAc was not affected by 14 hrs or 14 days of alcohol vapor when rats were sacrificed at the end of the 14-hr intoxication period. Following 28 days of alcohol vapor, rats exhibited a robust increase in NPY immunoreactivity in BNST and NAc that was reversed by 10 hrs alcohol withdrawal. These data suggest that four weeks of chronic intermittent alcohol vapor inhalation, previously shown to produce alcohol dependence in rats, is sufficient to produce an allostatic shift in NPY content in BNST and NAc, similar to what has been previously shown in the amygdala. This work was supported by NIH grants AA016436 and AA018400.

0022

ASSESSING THE ROLE OF PKA IN ETHANOL ACTION IN ADOLESCENT SPRAGUE-DAWLEY RATS

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Adolescents display reduced sensitivity to many ethanol-related behavioral measures including motor-ataxic and sedative-hypnotic effects; however, the neurobiological differences for these responses remain unknown. The cAMP dependent protein kinase (PKA) pathway has been implicated in ethanol-related behaviors. Previous studies have shown that inhibiting PKA activity or ablating the PKA RII$\beta\varepsilon\tau\alpha$ subunit in adults decreases ethanol-induced righting reflex, analogous to adolescents. However, the effects of PKA on ethanol-related effects during adolescence are currently not known. In the current set of studies, we sought to determine whether the PKA pathway contributes to reduced ethanol-related effects in adolescents. Ontogenetic, expression of PKA subunits RII$\alpha\lambda\pi\eta\alpha$ and RII$\beta\varepsilon\tau\alpha$ were examined in whole cell homogenates of cortical tissue from adolescent and adult male Sprague–Dawley rats (postnatal days 28, 35, 42, and 75) by Western blot analysis. Ethanol induced effects on PKA subunit expression were analyzed in cortical P2 synaptosomal fractions at various time points following a single 3.5 g/kg ethanol exposure by Western blots. PKA involvement in ethanol-related behavioral effects were assessed by administering the PKA activator Sp-cAMP (100nmol) intracerebroventricular (i.c.v.) prior to ethanol for loss of righting reflex. Small but significant increases and decreases, respectively, were observed in RII$\alpha\lambda\pi\eta\alpha$ and RII$\beta\varepsilon\tau\alpha$ subunit expression in adolescent compared to adults. Interestingly, adolescent PKA subunit expression was unchanged 30 and 60 minutes following a 3.5 g/kg ethanol exposure. This is in contrast to previous studies indicating ethanol increases in adults. Moreover, while RIIalpha and RII$\beta\varepsilon\tau\alpha$ were increased at 24 hours following ethanol exposure, no effect was observed in adolescents. Behaviorally, i.c.v. administration of Sp-cAMP increased ethanol-induced loss of righting reflex in adolescents. Overall, these data suggest that PKA regulation in the P2 synaptosomal fraction is not altered in adolescents compared to adults and may reflect ontogenetic differences in PKA activity. Current studies are directly assessing ontogenetic PKA activity as well as determining whether dose-dependent ethanol-induced effects in P2 PKA expression exist. Studies are also assessing the PKA inhibitor Rp-cAMP (100nmol) in ethanol-induced loss of righting reflex in adolescents and adults. [Supported by grants P30 AA019367].

0023

INVESTIGATION OF PKC IN ADOLESCENT ETHANOL-ACTION IN SPRAGUE-DAWLEY RATS

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Ethanol is one of the most commonly used and abused drugs in the United States. However, much remains unknown about alcohol's molecular mechanism of action in the developing brain. Adolescents display differential behavioral sensitivity to ethanol. For instance, adolescents are less sensitive to ethanol's motor-ataxic and sedative/hypnotic effects, but are more sensitive to its memory-impairing effects. The protein kinase C (PKC) pathway has been implicated in mediating many behavioral responses in adults, however little is known about PKC in ethanol-related behaviors in adolescence; especially since PKC modulates many neurotransmitter systems involved in ethanol action. Previous studies have implicated four major isoforms of PKC involved in ethanol-related behaviors- β, ε, γ and δ. The goal of the current study was to fully characterize PKC isoforms during adolescence as well as assess its involvement in ethanol related behaviors. Western Blot analysis assessed PKC isoforms in whole cell homogenates of cortical tissue, from Sprague-Dawley rats ages P28 35, 42 and 75, as well as in P2 synaptosomal fractions. In order to assess the effects of PKC on ethanol-induced loss of righting reflex (LORR), a non-selective PKC inhibitor calphostin C (CalC, (500 pmol/rat) or activator phorbol-12,13-dibutyrate (PDBu, (100 pmol/rat) were injected intracerebroventricularly followed by co-administration of ethanol (4.0 g/kg). Initial results indicate that basal levels of PKCε and PKCδ isoforms were significantly increased while PKCγ was decreased in animals at P35 compared to P75. No ontogenetic differences were observed for PKCβ between the two ages. Behaviorally, inhibiting PKC activity in adolescents significantly increased ethanol-induced sleep time in adolescents, whereas activating PKC did not have any effect. Conversely, in adults, the exact opposite effects were observed. Overall, these data suggest that differences in basal PKC levels during ontogeny may contribute to variances in ethanol related behaviors. Current studies are comparing ethanol-induced effects on PKC isoform expression in adult and adolescents following acute ethanol exposure. [Supported by grants P30 AA019367, AA17823].

0024

BINGE ALCOHOL CONSUMPTION PRODUCES SEX-DEPENDENT ALTERATIONS IN PI3K-ASSOCIATED SIGNALING MOLECULES WITHIN THE NUCLEUS ACCUMBENS OF MICE

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Binge alcohol consumption produces a blood alcohol concentration of 80mg% or higher. To achieve this level of intoxication, men on average consume more alcoholic beverages in a two-hour period compared to women (5 for men; 4 for women). Despite this difference, men are twice as likely to participate in binge drinking. However, knowledge of sex-differences in response to binge alcohol consumption is underdeveloped. As previous studies from our laboratory and others have indicated that phosphoinositide 3-kinase (PI3K)-associated signaling in the nucleus accumbens is impacted by binge alcohol consumption, the purpose of the present study sought to examine whether binge drinking impacts these signaling molecules in the nucleus accumbens in a sex-dependent manner. C57BL/6J mice (males and females, 8 week old adults and 4 week old adolescents) were single-housed and introduced to the Scheduled High Alcohol Consumption paradigm. In this paradigm the animals receive intermittent (every 3rd day) access to 5% alcohol for 30 minutes which is sufficient to elicit blood alcohol concentrations that averaged 150mg%. Following 24-hour withdrawal from the seventh binge session, the nucleus accumbens was collected and homogenized. Western blotting was then conducted for the following proteins: metabotropic glutamate receptor 1 (mGluR1), mGluR5, PI3K, phosphoinositide-dependent protein kinase 1 (PDK1), mammalian target of rapamycin (mTOR), 4E binding protein 1 (4E-BP1), p70 ribosomal S6 kinase (p70S6K), and extracellular signal-regulated kinase 1/2 (ERK1/2). Following binge alcohol consumption, no parallel changes in protein levels or phosphorylation were found between males and females. In females, alcohol decreased the levels of mGluR5 and increased the activation index of p70S6K without impacting indices of any of the other molecules. Conversely, male mice had no alterations in the levels of mGluR1 or mGluR5 while having a consistent alcohol-induced decrease in indices of PDK1, mTOR, 4E-BP1, and p70S6K activation. Together these data suggest that males show a strong inhibition of PI3K-associated signaling while females selectively target p70S6K to increase activation. These data suggest that binge alcohol consumption produces sex-specific alterations in the PI3K-associated signaling cascade. These findings may prove critical in the development of pharmacotherapeutics, suggesting that different treatments for men and women may be prudent.

0025

ACUTE ETOH-INDUCED ALTERATIONS IN CENTRAL CYTOKINES IN RATS WITH A HISTORY OF LONG-TERM MODERATE ETHANOL CONSUMPTION

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Alcohol-induced alterations in expression of inflammatory cytokines are a potential mechanism by which alcohol exposure exerts changes in behavior, stress- and physiological-related processes. Recently, we and others have shown that exposure to a large bolus of ethanol (EtOH) results in changes in both peripheral and central cytokine expression. To our knowledge, however, no one has yet examined how a long-term history of moderate voluntary EtOH consumption would influence these alterations. In this study, therefore, male Sprague-Dawely rats (N = 24) were given 24 hr continuous access to a 2-bottle choice between water and an unsweetened EtOH solution (20% v/v) every other day, with 8 additional animals given access only to water throughout the experiment. Two days following the final (30^{th}) EtOH exposure, rats were given an acute intragastric intubation of either: EtOH (4 g/kg, 20% v/v); EtOH plus minocycline, a microglial inhibitor (60 mg/kg in 4 g/kg EtOH); or tap water (isovolumetric) and then killed 3 hours later. Results showed that, by the final exposure, rats were drinking approximately 3.5 g/kg of EtOH during the 24 hr exposure and 0.7 g/kg during the first 30 min of EtOH presentation. Three hours after the acute EtOH gavage, BECs were not significantly different in rats with or without a history of EtOH consumption. Assessment of brain cytokine levels demonstrated that IL-1 mRNA expression in both the PVN and amygdala were significantly suppressed by acute EtOH, and a history of EtOH intake did not impact this effect. In contrast, expression of IL-6 mRNA was significantly increased in both the PVN and amygdala following the acute EtOH bolus and a long-term history of EtOH intake resulted in tolerance to this enhancement of IL-6. Administration of minocycline in combination with the EtOH bolus did not impact expression of these cytokines. Taken together, the results of this experiment corroborate previous results from our laboratory demonstrating that acute EtOH significantly alters expression of several central cytokines in brain regions intimately involved in inflammation and stress-related processes. Furthermore, while a history of chronic EtOH intake may lead to tolerance to some of these cytokine changes, not all are changed, indicating that the effects of EtOH on inflammatory processes are quite complex and that history of EtOH exposure is a critical determinant of cytokine changes evoked by alcohol challenge in rodent models.

0026

BINGE EXPERIENCE ALTERS NUCLEUS ACCUMBENS AND HIPPOCAMPAL GENE EXPRESSION IN ADOLESCENT AND ADULT MICE

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Alcohol abuse among adolescents can have lasting implications into adulthood. Adolescents are more vulnerable to the pharmacological effects of alcohol and across many species, adolescents will voluntarily drink higher amounts of ethanol (EtOH) and sustain higher levels of drinking into adulthood if exposed to binge levels of alcohol during adolescence. Much of the literature points to the hippocampus and the nucleus accumbens (NaC) as important components of the drug reward circuit. With these results in mind, both male and female adolescent and adult C57BL/6J mice were tested in the Scheduled High Alcohol Consumption paradigm. EtOH-naïve male and female mice were single-housed and exposed to either water or 7 EtOH binges (30-min; every 3^{rd} day) over 21 days. Following 24-hr withdrawal, brain tissue was processed for quantitative RT-PCR, and mRNA expression of genes involved in the glutamatergic and PI3K signaling cascades were assessed. In the hippocampus, EtOH exposure decreased expression of metabotropic glutamate receptor 1 (mGluR1) (↓28% vs. water controls) in female, but not in male mice. Hippocampal PDK-1, which is downstream of PI3K in the signaling cascade, was decreased by EtOH exposure in male and female mice (↓20% and↓16%, respectively). Male adolescent mice were particularly sensitive to this effect (↓37% vs. control). The nucleus accumbens revealed an opposite effect of EtOH exposure between male and female mice. In the NaC of female mice, expression of mGluR1 and mGluR5 was unchanged by EtOH exposure, but EtOH exposure decreased (↓45% vs. control) expression of PDK-1. Conversely, in the NaC of male mice, PDK-1 expression was unchanged by EtOH exposure, but EtOH exposure decreased (↓26% vs. control) expression of mGluR1, and male adolescent mice were particularly sensitive to this effect (↓35% vs. H2O). EtOH exposure also decreased (↓35% vs. H2O) expression of mGluR5 in the NaC of male mice. To summarize, hippcampal gene expression was inhibited by ethanol exposure in female mice, and nucleus accumbens gene expression was inhibited by ethanol exposure in male mice. Taken together, these data indicate that binge-like intake of EtOH alters the expression of genes in the PI3K pathway associated with alcohol addiction and can inform future treatment strategies.

0027

ACUPUNCTURE REDUCES ALCOHOL INTAKE BY DOWN REGULATING FOSB/ΔFOSB IN THE CORTEX

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Our goal is to understand the molecular mechanisms underlying the effects of acupuncture on alcohol abuse. FosB and FosB are members of the Fos family of transcription factors that are implicated in neural plasticity in addiction. Accumulating evidence indicates that electroacupuncture (EA) may be beneficial for the abusers of various drugs, including alcohol. Although we and other have shown previously that EA reduced alcohol intake, the underlying mechanisms have not been fully elucidated.
Methods: Male adult Sprague–Dawley rats were trained to self-administrate a 20% ethanol solution under a modified intermittent access two-bottle choice procedure, in which 5% sucrose was added in the first three drinking sessions. This procedure rapidly and sharply accelerated ethanol intake. At about one month after the initiation of the training, when rats achieved a stable high level of alcohol consumption, EA was applied at the bilateral acupoint Zusanli (ST36) or the tail (sham EA) for 6 consecutive days. The expression of FosB/ΔFosB was assessed by immunohistochemistry assay in multiple cortical areas including prelimbic cortex (PrL), infralimbic cortex (IL) and orbitofrontal cortex (OFC).
Results: High (100 Hz) but not low frequency (2 Hz) EA applied at the bilateral ST36, but not at the tail for 6 consecutive days, significantly reduced the intake of and preference for alcohol. The reduction maintained for at least 72 h after the last EA treatment. Moreover, chronic alcohol consumption robustly increased expression of FosB/ΔFosB in PrL and OFC, but not in IL. Multiple administrations of 100 Hz EA significantly reduced the expression of FosB/ΔFosB in the PrL, OFC, and also in IL. Conversely, EA treatment did not alter the intake of and preference for sucrose, the natural rewarding agent.
Conclusion: The data indicate that multiple administrations of high frequency EA at ST36 is effective in reducing the intake of and the preference for alcohol in rats that chronically drink large quantities of ethanol. The reduction by EA may be mediated by down-regulation of FosB/ΔFosB in the cortical area. This result provides new evidence for the molecular basis for the beneficial effect of EA for alcoholic or alcoholism.

3. PHARMACOLOGY C.N.S.

0028

ACTIVATION OF β3 ADRENOCEPTORS IN THE BASOLATERAL AMYGDALA REDUCES ETHANOL DRINKING BEHAVIORS IN MALE LONG EVANS RATS

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A growing body of evidence suggests that the interaction between ethanol and anxiety may play an integral role in the development and maintenance of alcoholism. While acute ethanol exposure decreases a broad spectrum of anxiety-related behaviors, withdrawal from chronic ethanol is associated with profound increases in measures of anxiety. Withdrawal-induced anxiogenesis also likely contributes to the negative affective state that is often associated with alcohol use disorders. Not surprisingly, many medications in pre-clinical or clinical trials for the treatment of alcoholism share anxiolytic properties. However, these drugs typically have untoward side effects, such as sedation or impairment of motor function, that may limit their clinical use. We have recently demonstrated that BRL 37344 (BRL), a selective β3-adrenoceptor agonist enhances a discrete population of GABAergic synapses in the basolateral amygdala (BLA) that mediate feedforward inhibition from lateral paracapsular (LPC) GABAergic interneurons onto BLA pyramidal cells. Behavioral studies revealed that intra-BLA infusion of BRL significantly reduced measures of unconditioned anxiety-like behavior without any locomotor depressant effects. Here we tested the effect of BRL on ethanol self-administration using an intermittent home cage two-bottle choice procedure and a limited access operant paradigm. Intra-BLA infusion of BRL significantly decreased ethanol intake in the first 30 min of intermittent drinking sessions and this effect was greatest in animals exhibiting the highest levels of ethanol intake. Using an operant procedure that permits the discrete assessment of appetitive (seeking) and consummatory measures of ethanol self-administration, in which rats are trained to complete 16 lever presses to gain access to a 10% ethanol solution for a 20 minute drinking session, BRL selectively reduced measures of ethanol seeking but had no effect on consummatory behaviors. Together, these data suggest that intra-BLA infusion of BRL significantly reduces motivation to consume ethanol and provide initial evidence that β3-ARs and LPC GABAergic synapses may represent promising targets for the development of novel pharmacotherapies for the treatment of alcoholism.
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0029

EFFICACIOUS KAPPA ANTAGONISTS FOR DECREASING ALCOHOL SELF-ADMINISTRATION

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Several series of substituted aryl amide derivatives of 6-naltrexamine showing kappa opioid receptor antagonism were synthesized and tested in vitro and in vivo. SG-II-39 and SG-II-49 were designed to be metabolically stable and non-hepatotoxic without the long residence time of currently available kappa antagonists. Binding assays showed that SG-II-39 (like SG-II-49) had subnanomolar K_i values for μ and κ opioid receptors. Functional assays for stimulation of [^{35}S]GTPγS binding showed the compounds acted as partial or inverse agonists and antagonists of the, μ, δ, κ opioid or NOP receptors. The compounds showed considerable stability in the presence of rat, mouse or human liver preparations and NADPH and only modest inhibition of CYP3A4, CYP2C9 and CYP2C19 was observed. To test the most potent compound (SG-II-39) *in vivo*, we utilized 2 models of ethanol intake in the rat: oral operant self-administration in dependent and non-dependent P rats and "binge drinking" in both P rats and outbred Sprague-Dawley rats. Results from testing SG-II-39 in dependent and non-dependent P rats revealed that P rats showed a significant reduction in ethanol intake at doses of 0.00625, and 0.0125 mg/kg in both vapor conditions. In the "binge drinking" model, similar results were observed with both P rats and Sprague-Dawley rats showing significant reductions in ethanol intake at 0.00625 and 0.0125 mg/kg. These results suggest that SG-II-39 might be an effective treatment for alcoholism. Supported by NIH Grant R44 AA018066

0030

EFFECTS OF DUTASTERIDE ON ALCOHOL RESPONSES IN A LABORATORY SETTING AND ON DRINKING IN THE NATURAL ENVIRONMENT

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Introduction: Pre-clinical studies support the hypothesis that endogenous neuroactive steroids mediate some of the behavioral and electrophysiological effects of alcohol. We examined the effect of dutasteride inhibition of 5α-reduced neuroactive steroid production on subjective responses to acute alcohol in humans.
Methods: Using a within-subjects, factorial design, 70 healthy men completed 4 randomly ordered monthly sessions in which pre-treatment with dutasteride (4 mg) or placebo was paired with a moderate dose of alcohol (0.8 gr/kg) or placebo alcohol. Self-reports of alcohol effects were obtained at 40-min intervals for 3 hr following alcohol administration using the Biphasic Alcohol Effects Scale (BAES) and the Alcohol Sensation Scale (SS). We used linear mixed models to examine the effects of dutasteride and alcohol administration on BAES and SS responses. The pharmacologic effect of dutasteride was measured by assay of serum androstanediol glucuronide as a measure of 5-alpha-reductase inhibition. We also measured drinking between laboratory sessions both for safety and to examine whether exposure to dutasteride influenced drinking in the 3 weeks following each lab session.
Results: A single 4-mg dose of dutasteride produced a 70% (SD=14%) reduction in androstanediol glucuronide. Dutasteride pretreatment reduced alcohol effects on the BAES sedation ($F_{(1,1325)}$=12.6, p<0.001), SS anesthesia ($F_{(1,1325)}$=10.6, p=0.001), and SS impaired subscales ($F_{(1,1325)}$=7.3, p=0.007). Moderate drinkers (n=29, mean of 14 standard drinks/week) had fewer heavy drinking days during the first and second week following dutasteride sessions (paired t-test vs. baseline, week 1 t= -4.15, p<0.001; week 2 t= -2.29, p=0.028) and in the total number of drinks per week in the first week after dutasteride (t= -3.12, p=0.003). There was no such effect following placebo medication sessions. No significant effect on drinking was seen for low-intensity drinkers (n=33, mean of 14 standard drinks/week), perhaps because of a floor effect for this group.
Conclusion: These results provide evidence that neuroactive steroids mediate some of the sedative effects of alcohol in humans and that dutasteride may warrant further study for reduction of alcohol use. Supported by NIH grants R01 AA015606, M01 RR06192 and K24 AA13736.

0031

NALTREXONE PLUS PRAZOSIN DECREASES ALCOHOL DRINKING MORE EFFECTIVELY THAN DOES EITHER DRUG ALONE IN A RODENT MODEL OF HIGH ALCOHOL DRINKING

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Naltrexone, a nonspecific opioid receptor antagonist, decreases alcohol drinking in both rats and humans and is one of only three medications that are FDA approved for the treatment of alcoholism. Currently, naltrexone is under-utilized in clinical treatment settings because the efficacy of naltrexone is modest, it is not effective for all alcoholics and, when it is effective, some alcoholics fail to maintain initial treatment gains and relapse to heavy drinking. We have previously demonstrated that prazosin, an α_1-adrenergic receptor antagonist, also decreases alcohol drinking in rats under a variety of conditions. A recent clinical study has demonstrated that prazosin also decreases alcohol drinking in alcohol dependent men. In the current study we examined whether combining prazosin with naltrexone in a single medication would more effectively reduce alcohol drinking than would administration of either drug alone. Male rats selectively bred for high voluntary alcohol drinking (alcohol preferring or "P" rats) were given 24-hour access to food and water and scheduled access to a 15% (v/v) alcohol solution for 2 hours a day, which constitutes a daily 2-hour free-choice between alcohol and water. Naltrexone (10.0 mg/kg BW) or prazosin (2.0 mg/kg BW), alone or in combination, or vehicle, were dissolved in a jello/gelatin mixture and apportioned into molds with dosage based on body weight and were fed to the rats at 45 min prior to onset of the daily 2-hour alcohol access period for 3 weeks. During the first week of treatment neither prazosin nor naltrexone, when administered alone, reduced alcohol drinking when compared with alcohol intake in the vehicle-treated control group. During weeks 2 and 3 prazosin alone became effective in decreasing alcohol drinking (p<0.01 and p<0.05, respectively) but naltrexone alone did not. In contrast, the combined medication (naltrexone + prazosin) significantly reduced alcohol drinking during the first week of treatment and continued to significantly reduce alcohol drinking throughout 3 weeks of daily treatment when compared with alcohol intake in the vehicle-treated controls (p<0.01). Supported by AA018604 (Froehlich and Rasmussen), AA007611 (Froehlich), and AA010567 (Rasmussen).

0032

PRAZOSIN, AN α_1-ADRENERGIC RECEPTOR ANTAGONIST, BLOCKS THE EXPRESSION OF A GENETIC PREDISPOSITION TOWARD HIGH VOLUNTARY ALCOHOL DRINKING

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We have previously demonstrated that prazosin, an α_1-adrenergic receptor antagonist that suppresses central noradrenergic signaling, decreases alcohol intake in an animal model of high alcohol drinking when it is administered either acutely, via IP injection, or chronically, via voluntary ingestion. In the current study we investigated whether prazosin treatment during initial exposure to alcohol can block the acquisition of alcohol drinking in rats selectively bred for high voluntary alcohol intake (alcohol preferring or "P" rats). Male P rats were given 24-hour access to food and water and scheduled access to a 15% (v/v) alcohol solution for 2 hours a day, which constitutes a 2-hour free-choice between alcohol and water. Prazosin (1.0 or 2.0 mg/kg BW) or vehicle was dissolved in a jello/gelatin mixture, apportioned into molds with dosage based on body weight, and fed to the rats at 45 minutes prior to onset of access to alcohol. In one group, prazosin or vehicle was fed daily for 2 weeks prior to onset of access to alcohol (15% v/v) and throughout 3 weeks of daily alcohol access. In another group, prazosin or vehicle was fed, for the first time, concomitantly with the first opportunity to drink alcohol and throughout 3 weeks of alcohol access. When prazosin was administered beginning with the first opportunity to drink alcohol, both doses completely abolished alcohol drinking in P rats. When P rats were pretreated with prazosin for 2 weeks prior to initiation of alcohol access, both doses of prazosin suppressed, but did not abolish, acquisition of alcohol drinking. It appears that prazosin may "devalue" alcohol when given together with the initial drinking experience. The fact that prazosin treatment was able to block the expression of a genetic predisposition toward high alcohol drinking suggests that it may be a useful prophylactic approach for individuals with a family history of alcoholism. Supported by AA018604 (Froehlich and Rasmussen), AA007611 (Froehlich), and AA13881 (Rasmussen).

0033

VARENICLINE DOES NOT ATTENUATE THE EXPRESSION OF ETHANOL-INDUCED CPP OR THE DEVELOPMENT OF ETHANOL-INDUCED SENSITIZATION IN DBA/2J MICE

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There are limited pharmaceutical options for the treatment of alcohol dependence. One promising new drug varenicline (VAR), with FDA approval as a smoking cessation aid, has also been found to reduce ethanol (EtOH) consumption in humans and rodent models. There has been limited research on the effects of VAR on other behaviors relevant to alcohol abuse, which would provide a better understanding of its clinical usefulness for the treatment of alcohol dependence. For example, VAR could attenuate the conditioned rewarding effects of EtOH or alter neuroadaptive responses to EtOH. The ability of VAR to attenuate the expression of an established EtOH-induced conditioned place preference (CPP) was examined. DBA/2J (D2) mice were conditioned with 2 g/kg EtOH and saline on 8 alternating days, each paired with a distinct floor type, and then examined for their place preference after pretreatment with saline or VAR (0.5, 1 or 1.5mg/kg). The pretreatment was given 15 min prior to the 30-min preference test. All pretreatment groups exhibited preference for the EtOH-paired floor, but there was no significant effect of VAR on floor preference. The 1 and 1.5 mg/kg doses of VAR significantly reduced locomotor activity levels on the preference test day. Due to the lack of effects of one time VAR treatment on the expression of EtOH-induced CPP, our initial study of neuroadaptation examined the ability of VAR to block the development of locomotor sensitization. On days 3-12 mice were pretreated with saline or VAR (0.5, 1 or 2 mg/kg), 15 min before treatment with saline or 2 g/kg EtOH. Activity was assessed every third day. On day 13, all mice received a 2 g/kg challenge dose of EtOH. On the EtOH challenge day, mice that had been repeatedly treated with EtOH exhibited a sensitized response, compared to mice that had been repeatedly injected with saline. However, VAR did not disrupt the acquisition of EtOH-induced behavioral sensitization. A study in progress is examining the effect of VAR on the expression of EtOH-induced sensitization. The current results indicate that VAR may not be effective at reducing the preference for environmental cues that have been previously paired with EtOH and that are thought to influence relapse. Further, the partial agonist effects of VAR at $\alpha4\beta2$ nicotinic acetylcholine receptors do not appear to influence the development of locomotor sensitization to EtOH. Support: Department of Veterans Affairs, P60AA010760, R24AA020245 and T32AA007468.

0034

VARENICLINE REGULATES ETHANOL CONSUMPTION IN RATS BY ACTIONS IN THE NUCLEUS ACCUMBENS

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Varenicline, a nicotinic acetylcholine receptor (nAchR) partial agonist, is currently being investigated in clinical trials to evaluate its utility in treating Alcohol Use Disorders. Our lab has previously reported that varenicline decreases ethanol consumption in rodents; however, the mechanism of action and brain loci responsible for the effect remains to be elucidated. In order to answer these questions, we utilized a number of different techniques to conduct experiments in male, Wistar rats following long-term ethanol (20%) exposure in the intermittent-access two-bottle choice paradigm. To investigate the brain regions mediating the effects of varenicline on ethanol consumption, varenicline (0, 1, and 2 ug) was microinfused directly into the ventral tegmental area (VTA) and the nucleus accumbens (NAc) 10 min prior to ethanol access. Results from these experiments show microinfusion of varenicline into the NAc significantly reduces ethanol consumption; in contrast, intra-VTA infusions did not alter voluntary ethanol intake. Next, we used two different techniques, *in vivo* microdialysis and fast scan cyclic voltammetry (FSCV) on *in vitro* slice preparations, to determine the mechanism by which varenicline is acting in NAc to reduce ethanol consumption. Following long-term ethanol consumption, microdialysis was performed on freely moving rats that received injections of varenicline (0 or 1 mg/kg, s.c.) and a second injection of ethanol (0 or 2.5 mg/kg, i.p.) 40 mins later. Results showed a significant increase in accumbal dopamine (DA) following varenicline and ethanol treatments, with the greatest enhancement observed in rats that were co-administered varenicline and ethanol. FSCV was performed on slices of the NAc to measure DA release evoked by stimuli mimicking reward-related phasic activity and nonreward-related tonic activity. First, baseline measures were established with ACSF then varenicline (1 or 10 uM) was bath applied to the slice. Slices that showed similar DA release to tonic and phasic activity during ACSF application exhibited a significant increase in the ratio of tonic-to-phasic DA signals during varenicline application, indicating the drug modulates DA transmission through pre-synaptic nAchRs. Overall these data demonstrate varenicline enhances extracellular DA in the NAc which is likely a major contributing factor in its ability to decrease ethanol consumption.

0035

ANTI-INFLAMMATORY PROPERTIES OF SPECIFIC FLAVONOIDS IS MEDIATED THROUGH ALPHA7 NICOTINIC RECEPTORS: IMPLICATIONS FOR ALCOHOL INDUCED NEURODEGENERATION

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Alcohol induced neurodegeneration is characterized by a plethora of etiologies which makes the identification of a single therapeutic target difficult. However, recent work has shown that chronic ethanol enhances neuroinflammation which contributes to neuronal toxicity. Alpha7 nicotinic acetylcholine receptors (nAChRs) have recently been found to be involved in inflammation and indirect evidence suggests that they are involved in alcohol mediated neuroinflammation. Indeed, ethanol inhibits alpha7 nAChRs in neurons and we have found that acute ethanol (50mM) inhibits the anti-inflammatory effects of choline, an alpha7 nAChR selective agonist, in microglia. Therefore, alpha7 nAChR selective agonists may reverse ethanol mediated neuroinflammation. As reported previously, extracts of Solidago nemoralis (gray goldenrod) were identified by high throughput screening to contain alpha7 nAChR agonist activity and to exert anti-inflammatory properties. Very surprisingly the active compounds appear to be methoxylated flavonoids. To evaluate the contribution of this activity to the anti-inflammatory effects we compared a flavonoid that binds to alpha7 nAChRs (rhamnetin) with a structurally similar flavonoid that does not (sakuranetin) on LPS-induced release of inflammatory mediators from BV2 microglia. Rhamnetin was not only more potent than sakuranetin but its dose response also exhibited a Hill coefficient of 2.0. This is indicative of either 2 anti-inflammatory mechanisms or functional positive cooperativity. On the contrary, the dose response for sakuranetin exhibited a Hill coefficient of 1.0. Thus we hypothesised that the responses exhibited by flavonoids that bind alpha7 nAChRs is mediated through both a nicotinic mechanisms as well as a nicotinic-independent mechanism. MLA, an alpha7 nAChR selective antagonist, was found to inhibit positive cooperativity of rhamnetin (Hill slope = 1.0) and had no effect on sakuranetin. Therefore, rhamnetin mediates its anti-inflammatory effect partly via alpha7 nAChRs. Furthermore, a concentration of nicotine that did not produce an effect by itself (1uM) was found to produce positive cooperativity on the sakuranetin dose response (Hill slope = 2.0). Therefore, flavonols with alpha7 nAChR activity benefit from cooperative anti-inflammatory mechanisms. These qualities, along with the known free radical scavenging properties could have great therapeutic potential for the treatment of alcohol induced neuroinflammation.

0036

WITHDRAWN

0037

PRECLINICAL TESTING OF A NOVEL DRUG THERAPY FOR ALCOHOL USE DISORDERS
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Alcohol use disorders (AUDs) are a major national and global problem affecting both adolescents and adults. AUDs are associated with tremendous psychosocial impact and billions of dollars in health-care expenditures and lost revenues. Unfortunately, current pharmacologic treatments for AUDs are only modestly effective, highlighting the need for developing new therapeutic approaches for the treatment of AUDs. Our lab recently reported that acute administration of the widely used anti-parasitic drug ivermectin (IVM –1.25 to 10.0 mg/kg) significantly reduced 1) ethanol intake using a 24-h access two-bottle choice model; 2) reduced anxiety but 3) did not cause any overt signs of IVM toxicity across a wide range of well-validated behavioral assessments of sensory, motor and cognitive competence. Notably, the same IVM doses did not exert rewarding properties, indicating that the anti-alcohol benefits of IVM are free of addiction potential. Collectively, our initial murine data point to IVM as a safe, tolerable, and effective agent for the treatment of AUDs. However, AUDs are chronic in nature. Hence, effective treatments would require longer term dosing strategies. The current study investigates the utility of IVM for use as an anti-alcohol agent by testing the effects of IVM (1.25mg/kg/day) administered daily for 7 days (i.p.) on ethanol (10%v/v – 10E) intake and preference in C57BL/6J mice using a 24-h access two-bottle choice model. Previous work determined that 1.25 mg/kg was the lowest dose of IVM to significantly reduce 10E intake. In support of longer term use of IVM, we found that IVM administered for 7 days significantly reduced 10E intake and that the degree of 10E intake did not significantly differ from day to day (reduction ranged from 11–27%). Importantly, no overt changes in behavior, food intake or water intake were observed during the 7 day IVM administration. We are currently extending our investigation to higher doses of IVM. Taken together, our findings indicate that IVM has potential to serve as a platform for further development of novel treatments for AUDs. Given that IVM is already FDA approved for use in humans, its repurposing would provide a new treatment for AUDs that could be implemented in a shorter time frame and at lower cost than required for the development of entirely new chemical entities.
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0038

ENDOCANNABINOIDS MEDIATE NEUROTOXICITY AND NEUROPROTECTION IN AN IN VITRO MODEL OF ETHANOL-INDUCED NEUROTOXICITY
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Excessive alcohol consumption produces neurodegeneration which may lead to cognitive deficits. Understanding the mechanisms that lead to neurodegeneration may open new therapeutic avenues to treat alcohol use disorders. The endocannabinoids are one such avenue, as targeting this system affords neuroprotection in other disease models. We hypothesized that targeting the endocannabinoid system by inhibiting anandamide catabolism would attenuate neuronal cell death induced by ethanol withdrawal (EWD). To test this hypothesis, organotypic hippocampal slice cultures were allowed to mature *in vitro* for 5 days before being exposed to either control media or 50 mM ethanol (EtOH) media for 10 days. Cultures were then withdrawn for 24hr in the presence of 5 μM NMDA, respective drug treatment and 2.5 μg/mL Propidium Iodide (to assess cell damage). Each experimental group contained ~54 cultures pooled from three separate rat litters. As shown previously, 10 days of EtOH exposure significantly potentiated NMDA toxicity in the CA1 and CA3 subfields after 24 hours of EWD (CA1, $p<0.001$; CA3 $p<0.05$). Interestingly, application of 50.0 nM URB597, a fatty acid amide hydrolase (FAAH) inhibitor, completely reversed EWD potentiation of NMDA toxicity, but had no effect on NMDA treatment alone. To determine if CB1 receptor activation was involved in the neuroprotection effect of FAAH inhibition, we applied the CB1 antagonist SR141716 (0.1 to 100.0 μM). Surprisingly, SR141716 attenuated EWD potentiation of NMDA neuronal damage in a U-shaped dose-response curve. After these unexpected results, we tested the hypothesis that CB1 antagonism was mediated though increased GABA neurotransmission, as GABA tone and release are, in part, under control of CB1 receptors in hippocampal networks. 10 μM Bicuculine (a GABAaR antagonist) was applied with the highest effective dose of SR141716 to determine the involvement of GABAaR. Our results showed that elevation of GABAaR activity is not necessary for the observed neuroprotection by SR141716 as its antagonism did not prevent SR141716 mediate neuroprotection. In conclusion, we have shown that the endocannabinoid system is sensitive to ethanol exposure in hippocampal slice cultures and that manipulation of this system affords neuroprotection against EWD-induced excitotoxicity. These results suggest that ethanol causes neuroadaptations in the endocannabinoid system that can be targeted with specificity. Funded by NIAAA R01AA016959 & F31AA019853

0039

CHRONIC ALCOHOL EXPOSURE INCREASES SELF-ADMINISTRATION OF ALCOHOL AND KAPPA-OPIOID RECEPTOR AGONIST-STIMULATED G-PROTEIN SIGNALING IN RAT AMYGDALA
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Previous evidence has shown that the endogenous ligand for kappa-opioid receptors (KOR), dynorphin (DYN), is upregulated in alcohol dependent animals and implicated KORs in the excessive alcohol self-administration that accompanies withdrawal in alcohol-dependent animals. However, the effect of chronic alcohol exposure on kappa-opioid receptors (KOR) function is undetermined. The present study examined the effect of chronic intermittent alcohol vapor exposure on KOR-mediated G-protein signaling in the amygdala (AMYG) of Wistar rats using a [^{35}S]GTPγS assay. The assay was optimized using tissue from the AMYG of alcohol-naïve rats. The initial results indicated that DYN A, DAMGO (mu-opioid receptor agonist) and DADLE (delta-opioid receptor agonist) stimulated GTPγS coupling in a concentration-dependent manner and DYN A-stimulated signaling was KOR antagonist reversible; providing support for the use of this assay to measure KOR signaling with a high degree of specificity. Subsequently, male Wistar rats 1) were trained to self-administer 10% alcohol (w/v), 2) exposed to air or intermittent alcohol vapor for three months and 3) confirmed to display the characteristic escalation of self-administration when dependent for at least two-weeks prior to brain extraction which occurred during acute withdrawal (6–8 hrs into withdrawal). AMYG tissue was dissected and homogenates incubated with [^{35}S]GTPγS in the presence of DYN A, DAMGO or DADLE prior to liquid scintillation spectrophotometry. DYN A, DAMGO and DADLE produced concentration-dependent increases in GTPγS coupling in the AMYG of non-dependent and alcohol-dependent rats. While there were no differences between non-dependent and alcohol-dependent animals in DAMGO- or DADLE-stimulated GTPγS coupling, DYN A-stimulated GTPγS coupling was significantly elevated in the alcohol-dependent group compared to non-dependent controls. Increased signaling via the KOR is consistent with previous evidence showing increased mRNA for KORs following repeated alcohol exposure, but this is the first functional demonstration of increased KOR signaling following chronic alcohol exposure. In conjunction with evidence indicating increased DYN A concentrations in the central AMYG of alcohol vapor-exposed rats, a role for DYN / KOR systems in the regulation of excessive alcohol consumption continues to emerge. Most importantly, the present results have identified a novel therapeutic target for the treatment of alcohol dependence.

0040

THE EVOLUTION OF PLANT METABOLITES FOR SMOKING CESSATION IN ALCOHOLICS
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The majority of alcohol dependent individuals also smoke cigarettes, and smoking-related diseases claim the lives of more alcoholics than alcohol-related illnesses. Alcoholics also display higher levels of nicotine dependence and experience more difficulty with smoking cessation. This may be due to the complex interplay of both ethanol and nicotine with nicotinic receptors (nAchRs) and monoamine transporters (MATs). Our research is aimed at identifying compounds active at both targets as potential leads for the treatment of alcohol and nicotine co-dependence. Plants represent a source of such molecules, because they have evolved molecules targeting nAchRs and MATs as a means of defense against herbivorous insects. From an evolutionary perspective, targeting multiple neurotransmitter systems for defense is a more effective strategy. Screening of extracts from ~1,000 plant species native to the SE USA for these characteristics identified *Lobelia cardinalis* as possessing a multifunctional alkaloid, lobinaline. Lobinaline inhibits the dopamine transporter (DAT) (IC_{50}=11.95μM) and displaces the non-subtype selective nAChR ligand, epibatidine, from nAchRs (IC_{50}=17.3μM). Both activities are likely important for defense, targeting nAChRs and MATs in the insect CNS. If lobinaline biosynthesis evolved via natural selection, it should be possible to direct the evolution of *L. cardinalis* to produce higher levels of lobinaline, or congeners with similar activity. To do so, we have expressed DAT in plant cells of *L. cardinalis*. This increases susceptibility to the DAT transported neurotoxin MPP+ ~20X above non-transgenic cultures, and toxicity is attenuated by the selective DAT inhibitor GBR12909. A population of transgenic DAT cultures with random gain-of-function mutations is now being selected on medium containing MPP+. Mutants overproducing inhibitors of DAT, preventing intracellular accumulation of MPP+, should have a survival advantage under these conditions. Thus, MPP+ resistant mutants should be enriched with inhibitors of DAT. Since activity at DAT and nAchRs reside in the same molecule in wild-type plants, novel molecules active at DAT in resistant mutants are also likely to be active at nAchRs. These characteristics are of potential value in treating alcohol and/or nicotine dependence. Therefore, this natural product drug discovery platform may be capable of "evolving" natural products with optimal molecular pharmacological activity for this therapeutic use.

0041

COMBINED INHIBITION OF REWARD AND CONDITIONING PREVENTS RELAPSE IN AN ANIMAL MODEL OF ALCOHOL DEPENDENCE

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Ethanol ingestion leads to reward and reinforcement while the cues associated with drug acquisition are conditioned reinforcers. We investigated whether reward and conditioning are responsible for (a) the development of dependence and (b) relapse, and whether the inhibition of both synergistically reduces ethanol self-administration. Ethanol administration leads to dopamine release in nucleus accumbens. Intracerebral administration of acetaldehyde also releases dopamine, and animals self-administer acetaldehyde into brain dopaminergic (VTA) areas. Since systemic acetaldehyde is degraded by blood-brain barrier cells, this metabolite must be generated in the brain itself, primarily by the action of brain catalase. Wistar-derived UChB rats allowed to drink 10% ethanol and water consume the equivalent of 500g ethanol/70kg per day. In naive rats, a single intracerebral (VTA) administration of a lentiviral vector coding for an shRNA anticatalase inhibits (85–95% $p<0.001$) their voluntary alcohol consumption for over two months. Thus, reward and reinforcement generated by alcohol are blocked if catalase gene expression is inhibited. Animals that have consumed ethanol on a 24-hour basis for 2 months continue to unabatedly drink high levels of ethanol, even after the intracerebral administration of the anticatalase shRNA vector. Data indicate that drinking in dependent animals no longer depends on the reward generated by the metabolism of ethanol into acetaldehyde, while strongly suggesting that it is maintained by conditioning (cues such as ethanol taste/smell). If these animals are submitted to 4-week alcohol deprivation to reduce alcohol-cue response and are again offered ethanol, a marked reduction (50% $p<0.01$) of ethanol intake by the anticatalase vector is again observed. A near maximal reduction of alcohol-cue conditioning occurs if the ethanol cues are altered by addition of a foreign taste (0.01% quinine) to the solution. In this condition, ethanol intake of animals treated with the anticatalase lentiviral vector is inhibited by >80% ($p<0.01$) versus intake of lentiviral controls. Propranolol, which blunts conditioning, markedly reduces ethanol intake (75–80%; $p<0001$) if the reward is abolished by shRNA anticatalase. The studies indicate that inhibition of ethanol reward potentiates conditioning blunting leading to near abstinence in alcohol dependent animals.

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NEUROPROTECTIVE EFFECTS OF LOW ALCOHOL CONCENTRATION AGAINST LPS-INDUCED TOXICITY IN CULTURED CELLS

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Detrimental effects of high alcohol consumption including possible neurotoxic effects are well established. On the other hand, epidemiological as well as preclinical studies suggest positive effects of low alcohol concentrations. We have observed antidepressant as well as protective effects of low alcohol levels using animal models and cell cultures, respectively. The protective effects of alcohol were observed in cultured neuroblastoma-derived (SH-SY5Y) cells that were exposed to salsolinol, an endogenous neurotoxin resembling MPTP. Since inflammation may be involved in both depressive-like behavior and neurodegenerative diseases, we were curious to determine whether low alcohol concentration may also provide protection against lipopolysaccharide (LPS)-induced toxicity. LPS, a chemical expressed on the outer membrane of gram-negative bacteria, has been shown to cause neuroinflammation and death of neurons. Exposure of SH-SY5Y cells to LPS for 72 h resulted in dose-dependent toxicity with maximal effect achieved by 200 ug/ml LPS (approximately 35% cell death). Treatment with ethanol (0.1–50 mM) resulted in dose-dependent protection with maximal protection (100%) at 50 mM ethanol. None of the alcohol concentrations on their own resulted in any cellular toxicity. These preliminary results suggest protective effects of low alcohol concentrations against inflammatory mediated neurotoxicity. Further verification of the anti-inflammatory effects of low ethanol concentrations and elucidation of its mechanism of action may provide therapeutic potential in inflammatory-mediated diseases.

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0043

INVESTIGATING THE ROLE OF SEROTONIN IN IMPULSIVE CHOICE WITH TRYPTOPHAN DEPLETION

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The tendency to favor smaller, immediate rewards over larger, delayed rewards (i.e., impulsive choice) is an intermediate phenotype of alcohol use disorders and may be a key neurocognitive factor in sustaining these disorders. Despite its clinical relevance, we know little about the neuropharmacological regulation of impulsive choice in humans, with the majority of studies to date focusing on the role of dopamine. Other work has investigated serotonin's role and shown that consuming an amino acid beverage deficient in tryptophan (serotonin's precursor) does not consistently alter impulsive choice across subjects (Crean et al., 2002; Clark et al., 2010). Here we tested whether certain individual differences, including sex, could account for variation in the effect of tryptophan depletion on impulsive choice. To do so, we used a double-blind placebo-controlled randomized crossover design and measured discounting of delayed rewards in each session. Adult participants (22–40 years old; n=23) consumed a balanced amino acid (control) beverage or a tryptophan-depleted beverage on two separate visits. To measure impulsive choice, participants completed a delay-discounting task, and we calculated the ratio of immediate choices:total choices (impulsive choice ratio; ICR). Consistent with published data, we found no significant main effect of beverage on ICR [$F(1,21)=0.4$; $p=0.52$]. We also found no significant main effect of sex on ICR [$F(1,21)=0.8$; $p=0.37$]; however, we did find a significant beverage×sex interaction [$F(1,21)=5.3$; $p=0.031$]. This interaction was driven by differences in the direction of tryptophan depletion effects between sexes. There was a trend toward decreased ICR among females following tryptophan-depletion [$t(7)=2.4$; $p=0.26$], while males showed a trend toward increased ICR following tryptophan-depletion [$t(14)=2.1$; $p=0.15$]. Thus, tryptophan-depletion appears to affect impulsive choice differently in men and women. Future work will test whether specific genetic polymorphisms in the serotonin system also influence the effect of tryptophan depletion on impulsive choice in humans.

0044

ETHANOL ATTENUATES CAPSAICIN INDUCED HAYPERALGESIA

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Many of the acute and chronic behavioral effects of ethanol are believed to be mediated through its actions as a N-methyl-d-aspartate (NMDA) glutamate receptor antagonist. NMDA antagonists, such as ketamine, have proven efficacious in preventing and attenuating hyperalgesia, the heightened pain response resulting when the spinal cord dorsal horn neurons become hypersensitized following a sustained afferent barrage. The objective of this study was to determine whether ethanol's NMDA antagonist activity would exhibit an anti-hyperalgesic effect in a capsaicin induced hyperalgesia pain model.
Healthy volunteer subjects between the ages of 21–30 yrs were recruited following an IRB approved protocol. Following intake screening, subjects were scheduled for three separate test days at least 3 days apart in a randomized order under double-blind conditions. Test days included an ethanol high concentration (targeted breathalyzer = 0.100 g/dl), ethanol low concentration (targeted breathalyzer = 0.040 g/dl) or placebo. Prior to the alcohol infusion, subjects received intradermal capsaicin injection (250ug in 25ul) to the volar surface of the forearm and the hyperalgesic field was mapped using a 20.9g von Frey filament. A second capsaicin injection was administered 60 minutes after the alcohol infusion was clamped.
18 subjects (10 females, 8 males with mean age 20 years) participated in the trial. There was a significant attenuation of hyperalgesic area with high dose ethanol compared to placebo. Using a capsaicin pain model in healthy volunteers we observed ethanol at the targeted concentration of 0.100 g/dl to exhibit an anti-hyperalgesic effect compared to placebo. These results provide support that in clinically relevant concentrations ethanol acts as a potent NMDA antagonist and suggest capsaicin pain responses as a potential tool in ethanol research.

0045

SUBJECTIVE EFFECTS OF THIOPENTAL IN YOUNG ADULTS WITH AND WITHOUT A FAMILY HISTORY OF ALCOHOLISM

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The development of alcohol use disorders is genetically influenced, and may be mediated through differences in the subjective response to alcohol. There is some evidence to suggest that response differences to alcohol could be conveyed by heritable differences in $GABA_A$ receptors. The purpose of this study was to investigate whether individuals with a family history positive (FHP) for alcohol dependence would experience alterations in response to the $GABA_A$ receptor agonist thiopental, in comparison to family history negative (FHN) subjects. 73 subjects (24 FHP & 49 FHN) between the ages of 21 and 30 years were administered sub-anesthetic doses of the $GABA_A$ receptor agonist thiopental and placebo on two separate test days. Various alcohol-related measures were administered, including those examining subjective effects, coordination, and cognition.
Sub-anesthetic doses of thiopental produced alcohol-like subjective effects, as well as alcohol-like impaired coordination and cognition in healthy subjects. While there were no significant main effects in subjective, coordination, or cognitive effects between FHP and FHN individuals, secondary analyses suggested FHP had blunted sedative, but not stimulant, effects compared to FHN.
Thiopental produced alcohol-like effects and perceived similarities to alcohol in healthy individuals. Subtle differences in sedative effects are consistent with reports of blunted FHP response to the negative but not stimulant effects of alcohol. These findings highlight the potential importance of $GABA_A$ receptors in human alcohol intoxication. Future studies are needed to better understand how this insight informs our understanding of the heritable risk for alcoholism and the treatment of alcohol use disorders.

0046

PRAZOSIN, AN α1-ADRENERGIC RECEPTOR ANTAGONIST, DECREASES VOLUNTARY ALCOHOL INTAKE BY WISTAR RATS IN THE INTERMITTENT ACCESS TO ALCOHOL (IAA) MODEL

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We have previously demonstrated that a CNS-active α1-adrenergic receptor antagonist, prazosin, reduces alcohol withdrawal-induced increased operant alcohol intake in Wistar rats and also reduces voluntary alcohol drinking in selectively bred alcohol-preferring (P) rats under varied conditions. We hypothesized that prazosin would be similarly effective in another useful model of alcohol drinking, intermittent access to alcohol (IAA). Individually housed young adult male Wistar rats (Simonsen Labs, Gilroy, CA) received 24-h 2-bottle choice of 20% alcohol *vs* water on 3 days (M, W, F) each week (i.e., IAA) to achieve stable 24-h alcohol intakes in two separate experiments. In the first experiment, rats then received alcohol for only 2 h on each of 3 days (M, W, F). Basal alcohol intake was 0.82±0.09 g/kg/2 h on day 1. On days 2 and 3, prazosin (1 or 1.5 mg/kg, IP) or vehicle (11–12 rats/treatment) were administered 30 min before the 2-h alcohol access. Alcohol intake was suppressed by 1.0 and 1.5 mg prazosin/kg (both $p<0.01$ relative to vehicle; main effect of treatment, no day X treatment interaction), with most - or all - alcohol drinking occurring during the first 15 min. In the second experiment, we confirmed this response with a different adaptation of the IAA model. After establishing stable IAA alcohol drinking, alcohol intake was measured for the first 2 h of each 24 h alcohol access on 6 consecutive alcohol access days (M,W,F,M,W,F). Alcohol intake on the first 2 days was 0.81±0.09 g/kg/24 h (total n=33 rats). Prazosin treatment (1 mg/kg, IP, 30 min before alcohol access, n=20) on days 3 and 4 suppressed alcohol intake relative to alcohol intake by vehicle-treated rats (n=13) ($p<0.001$; main effect of treatment, no treatment X day interaction). The results of these two experiments demonstrate that prazosin is effective in decreasing voluntary alcohol intake by Wistar rats during IAA, in doses comparable to those in our studies with P rats and in our studies with alcohol-dependent Wistar rats during acute withdrawal. Efficacy of prazosin in suppressing alcohol drinking in such varied rat models suggests that noradrenergic activation has an important central role in excessive alcohol drinking, consistent with a report that prazosin decreases alcohol drinking in alcohol dependent men. Supported by resources from VA Puget Sound Health Care System, VISN 20 MIRECC and NIH AA017839, AA010567.

0047

ESTROGEN AND BENZODIAZEPINE FOR BIOENERGETICS OF ETHANOL WITHDRAWAL

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We investigated whether acute estrogen co-treatment confers mitochondrial bioenergetic advantages over benzodiazepine alone during abrupt ethanol withdrawal (EW). HT22 cells were exposed to ethanol (0–100 mM) for 3 days and withdrawn for 4 hours. Cells were treated with 17β-estradiol, benzodiazepine (Lorazepam), or the combination of both drugs during the 4 hours of EW. Cells were then collected at the end of the EW for the assessment of mitochondrial respiration using XF Real-time respirometry. Mitochondrial respiration was suppressed during EW and further so by benzodiazepine treatment. By comparison, cells treated with 17β-estradiol + benzodiazepine showed a greater mitochondrial respiration during EW than EW alone cells or EW cells treated with either drug alone. Benzodiazepine alone treatment to non-ethanol cells showed a dose-dependent suppression of mitochondrial respiration. These results suggest that acute estrogen provides bioenergetic protection, absent with benzodiazepine. Therefore, the combination of acute estrogen with benzodiazepine may confer a superior protection against EW than benzodiazepine alone at the bioenergetic level (supported by NIAAA 018747 and 015982).

0048

THE EFFECT OF ACUTE ESTROGEN ON VENTILATORY RESPONSE DURING ALCOHOL WITHDRAWAL

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We investigated whether acute estrogen treatment is beneficial for the management of EW at the level of ventilatory response. Young adult male rats received a control dextrin diet or a 30-day ethanol diet with repeated withdrawal. Animals were injected with 17β-estradiol (100 or 300 μmol, s.c.) 5 hours after the last ethanol diet. Another set of animals were injected with Rotenone (inhibitor of mitochondrial respiration) in addition to estrogen injection. Ventilatory response was measured using pulse-oxymetry, three hours and 20 hours after the drug injection. Although statistically not significant, EW showed a tendency of ventilatory suppression. Animals injected with estrogen at 300 μmol abolished this effect of EW and improved ventilatory response to the control level. Intriguingly, Rotenone blunted the protective effect of estrogen on ventilatory response during EW. These results suggest that acute estrogen provides ventilatory tolerance in the face of EW stress, perhaps through bioenergetic protection (supported by NIAAA 018747 and 015982).

4. ANIMAL BEHAVIOR

0049

INDIVIDUAL DIFFERENCES IN ETHANOL BEHAVIORAL SENSITIZATION ARE ASSOCIATED WITH D1 RECEPTOR INTRA-CELLULAR SIGNALING OF DARPP-32 IN NUCLEUS ACCUMBENS

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There are clear individual differences in Swiss Webster mice regarding the development of behavioral sensitization to ethanol, a progressive potentiation of drugs' stimulant effects. Variability in the behavioral responses to ethanol has been suggested as a marker for alcohol preference. Here we investigated if, in the NAc - a brain region known to play a role in drug reinforcement, the functionally hyperresponsive D1 receptors observed in ethanol sensitized mice lead to an increased activation of DARPP-32, a central regulatory protein in medium spiny neurons. Swiss Webster mice received i.p. ethanol (2.2 g/kg/day) or saline for 21 days. Ethanol treated mice were classified as sensitized or non-sensitized. Different groups of mice received intra-NAc administrations of saline and, 48h later, SKF 0.1 or 1 μg/side (SKF-38393, D1 receptor agonist). We observed an increased locomotor activity in the sensitized mice when compared to the non-sensitized or saline control. Other groups of mice received systemic saline or SKF 10 mg/kg two weeks after the ethanol treatment, 20 min before the euthanasia. The NAc were dissected for the Western Blot analyses of total DARPP-32 and phospho-Thr34-DARPP-32 expression. D1 receptor activation induced higher phospho-Thr34-DARPP-32 expression in sensitized mice than in non-sensitized or saline. The functionally hyperresponsiveness of D1 receptors in the NAc is associated with an increase of phospho-Thr34-DARPP-32 expression after D1 receptor activation. In fact, these data suggest that an enduring increase in the dopamine D1 receptor intracellular pathway sensitivity may represent a neurobiological correlate associated with the development of sensitization to ethanol.
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0050

IDENTIFICATION OF SPECIFIC STRIATAL MOLECULAR TARGETS INVOLVED IN THE INHIBITORY EFFECT OF SODIUM BUTYRATE ON ETHANOL-INDUCED BEHAVIORAL SENSITIZATION

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Ethanol-induced behavioral sensitization (EIBS) is a commonly used model of neuroadaptations occurring during the initiation and the recurring steps of alcohol dependence. EIBS is characterised by a progressive and long-lasting increase of locomotor activity after chronic ethanol treatment, mirroring the sensitization of the dopaminergic reward circuitry. There is growing evidence of an involvement of epigenetic mechanisms in the induction and the persistence of ethanol-related behaviors, such as ethanol withdrawal-induced anxiety or rapid ethanol tolerance. Thus we focused on the involvement of histone acetylation in EIBS using sodium butyrate (NaB), a histone deacetylase inhibitor (HDACi). We injected female DBA/2J mice, a strain chosen for its sensitivity to ethanol locomotor effects, for 10 consecutive days with ethanol at 3 different doses: a non sensitizing dose of 0.5 g/kg and two sensitizing doses of 1.0 and 2.0 g/kg. In a first protocol, NaB was injected before each ethanol injection. Very interestingly, NaB did not alter locomotor activity of mice repeatedly injected with ethanol 0.5 or 2.0 g/kg but specifically blocked the 1.0 g/kg-EIBS induction. In a second protocol, NaB was administered during abstinence once mice were sensitized and an ethanol challenge was performed at day 17. NaB reversed 1.0 g/kg-EIBS but not 2.0 g/kg-EIBS.
Several brain structures were isolated to identify modifications in both genes (by PCR arrays targeting neurotransmitters, chromatin remodelling enzymes or transduction pathways) and proteins expression associated with sensitization development or with its inhibition by NaB. These experiments led us to identify BDNF as a key protein involved in the blockade of EIBS. These data led us to several relevant observations. The neuroadaptations occurring during the induction of ethanol sensitization are different depending of the ethanol dose. The induction and expression of EIBS with a low dose of ethanol (1 g/kg) may involve chromatin remodelling mechanisms. Our findings also suggest that BDNF could play a crucial role in the development and inhibition of EIBS. Finally, the interest of studying HDACi in alcohol addiction is increased by our results showing the reversion of sensitization by NaB.

0051

ANXIETY-LIKE BEHAVIOR AND BDNF LEVELS AS MARKERS OF VULNERABILITY TO ETHANOL-INDUCED BEHAVIORAL SENSITIZATION

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Clinical and preclinical data show that most alcohol users do not develop alcohol addiction, thus demonstrating a vulnerable phenotype. Identification of markers that could predict individual's propensity to addiction represents a crucial issue regarding intervention and prevention. Here, we focused on the characterization of predictive factors of vulnerability to develop ethanol-induced behavioral sensitization (EIBS) in mice. EIBS is defined as a progressive enhancement of locomotor activity following chronic ethanol treatment and is proposed as a relevant process in the initial and recurring stages of addiction. Anxiety is one of the various contributing factor that may predispose individuals to ethanol responsiveness, we thus focused on one major question: do anxiety traits influence the subsequent development of EIBS in mice?
First, ethanol-naïve mice were submitted to anxiety-like behavioral tests. Then, during 10 days, mice were injected once daily with ethanol immediately followed by locomotor activity measurement. Mice were classified into two groups (resistant or sensitized) based on their sensitization score. A retrospective analysis highlighted a strong negative correlation between the sensitization score and the basal anxiety profile. Furthermore, the high-anxiety mice (resistant mice) maintained their profile all along the sensitization induction and during expression at day 17, after an ethanol challenge (''trait'' anxiety). Mice were then sacrified to isolate several brain structures involved in addiction, such as striatum and amygdala. We then employed pathway focused real-time PCR arrays targeting genes involved in transduction pathways to elucidate some of the neuroadaptations underlying EIBS. Among the 84 genes screened, we identified putative anxiety-related genes differentially regulated between resistant and sensitized mice (crf, creb and bdnf). Based on basal anxiety levels, we demonstrated that anxiety predicts the propensity to develop EIBS and identified bdnf as a crucial molecular marker of this susceptibility.
In summary, we confirmed a strong relationship between behavioral sensitization and anxiety trait and identified bdnf as a marker of vulnerability.

0052

EFFECT OF EARLY-ADOLESCENT ALCOHOL AND MK801 EXPOSURE ON DEVELOPMENT OF QUINPIROLE-INDUCED BEHAVIORAL SENSITIZATION IN MALE WISTAR RATS

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Emerging literature indicates neurobiological differences exist between the developmental phases of adolescence and adulthood, which may play a critical role in altered propensity for alcohol addiction between the two age groups. For example, while dopamine D2-receptor (D2R) density is reportedly increased prior to puberty, a progressive loss of D2R expression occurs in the transition to adulthood, leading possibly to differing degrees of brain vulnerability to neuroplastic changes induced by dopamine acting drugs at the different ages. This study investigated the functional (behavioral) consequence of the reported loss of D2R levels on measures of locomotor sensitization after repeated administration of the selective D2-like agonist quinpirole (QNP). Rats were administered QNP (0.06, 0.25, or 0.50 mg/kg, s.c.) twice per week for a total of 7 injections, beginning either in their stage of early-adolescence or as matured adults (postnatal days 29–33 and 69–77, respectively, on day 1). A separate group of adolescent and adult rats received saline injections during this time and behavior was assessed in an open field at 15 min post injection. Results show a marked biphasic effect of acute QNP administration on motor activity in adolescent rats but not adult animals. Thus, adolescent rats treated with QNP, as compared to their age-matched saline controls, exhibit a transient depression in motor activity, which is followed by significant motor activation in a dose-dependent manner over a 70 min recording period. Responses are consistent across treatment days with no apparent locomotor sensitization on the last vs. first QNP injection in the adolescent group. In contrast, QNP-treated adult rats show a lasting motor depression relative to their age-matched saline controls, which is not overcome by behavior activation during week 1 of QNP injections. Rather, the motor activating effects of QNP are increased progressively in adult rats, resulting in significant locomotor sensitization on the last vs. first QNP injection in the older group. Interestingly, combined exposure to MK801 (0.2 mg/kg, s.c.) and alcohol via vapor inhalation (~300 mg/dL in blood) in adolescence results in a blunted adult sensitization phenotype at the 0.25 mg/kg of QNP tested. Results thus point to a lasting impact of chronic NMDA-R blockade in adolescence on the observed age-related difference in neuroplasticity as revealed by D2R agonist induced sensitization.
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0053

CHRONIC INTRAGASTRIC ETHANOL EXPOSURE IN ADOLESCENCE OR ADULTHOOD: ASSESSMENT OF TOLERANCE TO ETHANOL-INDUCED MOTOR IMPAIRMENT AND VOLUNTARY INTAKE

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Chronic tolerance may permit increased consumption of ethanol; however, ontogenetic differences in chronic ethanol tolerance development are not well understood. The purpose of the current study was to examine age-related differences in chronic tolerance development and subsequent voluntary ethanol intake after intragastric (i.g.) ethanol (EtOH) administration. Sprague-Dawley rats of both sexes were given a total of six exposures to 4 g/kg EtOH or water every other day starting on postnatal day (P)28 for adolescents and P70 for adults, or were left unmanipulated. On the final EtOH exposure day, tolerance to the motor impairing effects of 4 g/kg i.g. ethanol was assessed using a stationary inclined plane, and tail blood samples were collected for determination of blood EtOH concentrations (BECs) upon recovery. Seventy two hours later, voluntary intake of ethanol (10% EtOH in supersac) was measured in a limited 30 min access paradigm (1 bottle intake procedure) every other day for a total of 6 drinking days. In non-manipulated animals, male adolescents recovered from ethanol-induced motor impairment more quickly than adult males, whereas age differences were not evident in females. A significant portion of chronic ethanol-exposed females at both ages, as well as adolescent females chronically exposed to water did not show motor impairment at test, seemingly reflecting decreased ethanol sensitivity in females after chronic exposure. Males at both ages chronically exposed to EtOH showed faster recovery from EtOH-induced motor impairment along with significantly lower BECs at recovery relative to controls. These data appear to reflect not only development of metabolic tolerance, but also an apparent increase in behavioral sensitivity to the motor impairing effects of EtOH in males. Despite evidence of changes in EtOH sensitivity after chronic EtOH gavage, this exposure regimen did not influence voluntary EtOH intake among animals of either age or sex. Together, these results suggest that males and females may be differentially influenced by chronic intragastric EtOH exposure as assessed by sensitivity to EtOH-induced motor impairment.

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0054

ACUTE ALCOHOL PRODUCES PROFOUND ATAXIC AND COGNITIVE EFFECTS IN AGED ANIMALS

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Aging in humans is thought to accompany physiological changes that might increase biological sensitivity to ethanol intoxication. However, it is not yet known if similar increases in the biological sensitivity to ethanol intoxication can be successfully modeled in rodents. For this reason, we sought to investigate if ethanol produces differential effects on ataxia and spatial cognition in adult and aged rats.

Male adult (Postnatal Day 70–72) and aged (~ 18 months) Sprague-Dawley rats were tested on two motor tasks: the accelerating rotarod (RR) and the aerial righting reflex (ARR). Animals were given 5 training trials on the RR, the last 3 of which were averaged to reflect a stable measure of baseline performance. No significant difference was found between adult and aged rats ($F(1,30) = 0.003$, $p > 0.05$) during training. Twenty-four hours later, animals were given an i.p. injection of 1.0, 1.5, or 2.0 g/kg ethanol prior to RR testing. Data revealed significant main effects of both age ($F(1, 25) = 5.55$, $p < 0.05$) and dose ($F(2, 25) = 4.23$, $p < 0.05$). No significant interaction was found. For the ARR task, baseline analysis indicated no age difference (animals all righted at the lowest amount). However, a profound ataxic impairment was found when subjects were administered 2.0 g/kg ethanol i.p., prior to being released from an inverted position. Specifically, successful righting, in which 3 out of 4 paws made contact, was assessed at 10, 30, 50, 70, and 90 minutes following the ethanol injection. A significant main effect of time ($F(4, 14) = 13.01$, $p < 0.05$) and age ($F(1, 14) = 379.2$, $p < 0.05$) was demonstrated. Preliminary cognitive data from the Morris water maze further indicates an age-dependent effect of ethanol such that aged rats are more profoundly impacted than adult rats.

Our findings are the first to demonstrate that aged rats are more adversely affected by ethanol than adult rats in tasks of motor and spatial cognitive performance and that these deficits are exacerbated with increasingly high ethanol doses. Interestingly, blood ethanol levels from the RR revealed no significant difference between ages; although aged animals demonstrate significantly higher performance deficits, these are not attributable to increased BECs. Future research should investigate the physiological changes that produce this increased sensitivity to ethanol during aging.

0055

FREE-CHOICE ETHANOL ACCESS AND DAILY ETHANOL INJECTIONS DO NOT ALTER LOCOMOTOR RESPONSE IN CROSSED HIGH-ALCOHOL PREFERRING MICE

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An increase in the acute locomotor stimulant effects of a drug following repeated administration is often linked to the ''incentive salience'' theory of drug addiction. Development of this phenomenon, known as locomotor sensitization, is believed to be associated with high alcohol consumption. Crossed High Alcohol Preferring (cHAP) mice are bred for their exceptionally high voluntary ethanol intake and were therefore used in the current study to observe the stimulant effects of voluntary ethanol consumption and ethanol injections in a locomotor sensitization paradigm. In Experiment 1, male and female cHAP mice were given either free-choice access to a 10% ethanol solution and water or only water for thirteen days in the home cage. Mice reached high levels of ethanol intake, consuming 25.0 ± 2.4 g/kg by day 6 and 26.2 ± 1.4 g/kg by day 13. Five days after removal of the ethanol bottles each mouse was given a 2.0 g/kg injection of ethanol and placed in a testing apparatus to assess locomotor activity. In Experiment 2, the same mice from Experiment 1 were split into ethanol or saline injection groups so that half of the ethanol-water and water-water free-choice animals received 2.0 g/kg ethanol injections while the other half received saline injections every day for 11 days. Locomotion was assessed on Days 1, 5, and 9. Forty-eight hours after the injection on Day 11 all mice were given a 2.0 g/kg ethanol injection and locomotion was assessed. In Experiment 1 free-choice ethanol access did not alter locomotor response to an ethanol injection. In Experiment 2, previous voluntary ethanol consumption did not alter locomotor response in animals injected with ethanol or saline compared to animals that were only given water access. There was also no difference in locomotor response on the ethanol test day between animals that had received chronic ethanol or saline injections. These data are not consistent with many of the previous studies that have shown an increase in locomotor activity through voluntary experience with ethanol and ethanol injections. They thereby contradict many of the popular theories of ethanol sensitization including those of Hunt & Lands (1992), Newlin & Thomson (1991), and Robinson & Berridge (1993).

0056

CIRCADIAN MODULATION OF ACUTE ALCOHOL SENSITIVITY IN DROSOPHILA MELANOGASTER REQUIRES CAMP SIGNALING

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With its well-characterized circadian clock, *Drosophila melanogaster* represents an outstanding system for investigating the molecular mechanisms through which the circadian clock modulates alcohol sensitivity at the behavioral and cellular levels. Stereotypical behaviors following alcohol exposure, including the loss of motor control, the development of tolerance and addiction to alcohol, appear to be remarkably similar from *Drosophila* to humans (Scholz et al., 2000; Wolf et al., 2002; Devineni and Heberlein 2010). Previously, we found that the circadian clock modulates the acute loss of motor control in flies using the loss-of-righting reflex (LoRR) assay. Flies exhibit a circadian rhythm in the LoRR with the greatest sensitivity to alcohol occurring from mid- to late night during light-dark cycles and under constant conditions (van der Linde and Lyons, 2011). Sedation also appears regulated by the circadian clock with a greater percentage of flies sedated by alcohol exposure at CT 17 (mid-night) compared to CT 5 (mid-subjective day). In circadian mutants, no time of day differences were observed in behavioral responses to alcohol. The circadian rhythm in behavioral sensitivity to alcohol was not correlated with absorbance indicating that the circadian clock regulates alcohol physiology downstream of initial exposure. Taking advantage of the extensive genetic mutants available in *Drosophila*, we are investigating the molecular mechanisms through which the circadian clock modulates the LoRR following alcohol exposure. We found that the cAMP signaling pathway appears necessary for circadian regulation of acute alcohol sensitivity. Flies containing a mutation in either adenylyl cyclase (*rutabaga* mutants) or cAMP phosphodiesterase (*dunce* mutants) demonstrated no time of day differences in the LoRR, whereas these flies demonstrated robust circadian rhythms in locomotor activity. Although previously implicated in alcohol sensitivity, transmission of circadian information to the cAMP pathway does not require the PACAP-like neuropeptide as *amnesiac* mutants display significant circadian rhythms in the LoRR. In contrast, flies with mutations in either the neuropeptide PDF or its receptor exhibit significantly altered rhythms in the LoRR on the first day of constant conditions. These results suggest that circadian information is transmitted via the circadian neuropeptide PDF to the cAMP pathway to modulate acute behavioral responses to alcohol exposure.

0057

ROLE OF ADRENAL GLUCOCORTICOID SIGNALING IN PREFRONTAL CORTEX GENE EXPRESSION AND ACUTE BEHAVIORAL RESPONSES TO ETHANOL

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Adrenal glucocorticoid hormones, the final step in activation of the hypothalamic-pituitary-adrenal (HPA) axis, modulate acute and chronic behavioral and molecular responses to drugs of abuse including psychostimulants and opioids. There is growing evidence that glucocorticoids might also modulate behavioral responses to ethanol. Acute ethanol activates the HPA axis, causing glucocorticoid hormone release. Our prior genomic studies suggest glucocorticoids play a role in regulating gene expression in the prefrontal cortex (PFC) of DBA2/J (D2) mice following acute ethanol administration. However, little work has been done regarding HPA axis regulation of gene expression and glucocorticoid regulation of behavioral responses to ethanol. Such work could be significant, given the predictive value for level of response to acute ethanol in the risk for alcoholism. We studied whether the glucocorticoid receptor (GR) antagonist, RU-486, or adrenalectomy (ADX) altered male D2 behavioral responses to acute (locomotor activation, anxiolysis or loss-of-righting reflex (LORR)) or repeated (sensitization) ethanol treatment. Whole genome microarray analysis and bioinformatics approaches were used to identify candidate genes that may be responsible for altered behavioral responses to ethanol following ADX. We show that ADX and RU-486 both impair acute ethanol (2 g/kg) induced locomotor activation in D2 mice without affecting basal locomotor activity. However, neither ADX nor RU-486 alter initiation of ethanol sensitization, ethanol-induced anxiolysis or LORR. We also show differing expression of previously identified ethanol-responsive genes in the PFC of SHAM vs. ADX mice. *Fkbp5* was significantly decreased and *Gpr6* was significantly increased basally in ADX mice. Our studies suggest that ethanol's activation of adrenal glucocorticoid release and subsequent GR activation may partially mediate ethanol's acute locomotor activating properties in male D2 mice. In addition, adrenal glucocorticoid basal tone can regulate PFC gene expression. This suggests that glucocorticoid regulated PFC gene expression may be an important factor modulating acute behavioral responses to ethanol. This work was supported in part by NIAAA grants F31 AA20141-0 to BNC and AA016667 to MFM.

0058

EFFECT OF PARTIAL SLEEP-DEPRIVATION ON ALCOHOL-INDUCED LOCOMOTOR ACTIVATION IN ADOLESCENT AND ADULT MICE

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Sleep deprivation has been hypothesized to contribute to the development of alcohol abuse and alcoholism. Partial sleep-deprivation, defined as less than 6 hours of sleep, is a common problem particularly in the adolescent population. However, it is currently unknown whether there is an interaction between partial sleep-deprivation and responses to chronic alcohol exposure. The purpose of this study was to determine 1) whether partial sleep deprivation alters the response to chronic alcohol exposure, and 2) whether there are age-related differences in this response between adolescents and adults. A total of 66 male and female Balb/C mice were used. Four groups of mice were studied: 1) adolescent (approximately 30 days at the start of testing) non-sleep-deprived, 2) adolescent sleep-deprived, 3) adult (60–90 days of age) non-sleep-deprived, and 4) adult sleep-deprived. Mice were given saline baseline testing followed by 13 days of alcohol exposure at 1.5 g/kg. Mice were partially sleep-deprived by handling between 6am and noon. Locomotor activation was assessed using the activity chamber and mice were tested at baseline and on days 1, 2, 4, 12 and 13 of the alcohol exposure. Consistent with previous results, ethanol exposure caused sensitization in all groups of mice as shown by enhanced locomotor activity on the last days of testing. In adult animals, sleep deprivation had no effect on alcohol-induced locomotor activation. In contrast, adolescent mice showed enhanced sensitization following partial sleep deprivation. Thus, sleep deprivation alters alcohol-induced responses in an age-related manner. Similar to what has been observed for other phenotypes, the adolescent mice were more sensitive to the interaction between partial sleep-deprivation and alcohol-induced locomotor activation. These results suggest that partial sleep deprivation could contribute to the effects of ethanol and ultimately alcohol abuse and addiction.

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0059

THE EFFECTS OF BINGE ALCOHOL AT THE TIME OF TRUAMATIC BRAIN INJURY ON FUNCTIONAL SENSORIMOTOR RECOVERY

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Approximately 1.4 million Americans suffer a traumatic brain injury (TBI) every year. 30–50% of emergency room patients have a blood alcohol level above the legal limit at the time of admittance. The degree to which alcohol affects subtle sensorimotor function has not been fully explored. To this end we trained adult, male, Sprague-Dawley rats on the skilled reaching task, a sensitive test measuring sensorimotor function. Animals were given a binge paradigm of 2gm/kg ethanol or saline i.p. for 3 consecutive days. One hour after the final injection rats were subjected to a controlled cortical impact injury (a well characterized model of TBI). Following the injury, rats were tested daily on the skilled reaching task for 8 weeks. At all time points, the average score in the alcohol treated group was worse than the average score of the saline treated group. However, a repeated measures ANOVA revealed no significant difference between groups. The results of this study will be important for understanding the effects of binge alcohol drinking on sensorimotor recovery following brain injury.

0060

CHRONIC ETHANOL CONSUMPTION INCREASES THE SENSITIVITY OF THE POSTERIOR VENTRAL TEGMENTAL AREA (PVTA) TO THE REINFORCING PROPERTIES OF NICOTINE

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There is evidence for a genetic association between alcoholism and nicotine dependence. Ethanol (EtOH) drinking has been shown to increase the sensitivity of the pVTA to the reinforcing effects of EtOH. There is also evidence that prior exposure to nicotine can increase the sensitivity of the pVTA to the stimulating actions of EtOH. The current study examined the effects of chronic EtOH consumption on the self-administration of nicotine directly into the pVTA. Adult alcohol-preferring (P) rats were allowed to consume water only or 15% EtOH and water for 10 consecutive weeks. Following a two week EtOH abstinence period, rats were tested in standard 2-lever operant chambers (active and inactive) for the self-administration of nicotine directly into the pVTA. Rats were randomly assigned to one of four groups (n = 4–6/group) that self-infused (FR1 schedule) artificial CSF (aCSF), or 1, 3 or 10 μM nicotine in a volume of 100 nl/infusion for sessions 1–4; only aCSF for sessions 5 and 6, and the original infusate for session 7. EtOH naïve P rats failed to self-administer either 1 or 3 μM nicotine, but did self-administer 10 μM nicotine (25 ± 4 infusions/session). In contrast, P rats that chronically consumed EtOH self-administered all concentrations of nicotine (e.g., 33 ± 6 infusions/session for 1 μM nicotine) into the pVTA. In addition, P rats with chronic EtOH experience received more self-infusions of 10 μM nicotine than naïve P rats (44 ± 5 vs 25 ± 4 infusions/session). The current data indicate that chronic EtOH consumption increased the reinforcing properties of nicotine within the pVTA, and suggest that cross-sensitization can occur to the reinforcing effects of EtOH and nicotine in this region, which can persist in the absence of EtOH. AA019366, AA07611

0061

NUCLEUS ACCUMBENS PKC EPSILON REGULATES ALCOHOL AND NICOTINE CONSUMPTION IN MICE

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Alcohol and nicotine addiction often occur together, and our recent work suggests that protein kinase C epsilon (PKCε) contributes to both disorders. Thus, mice that lack PKCε (*Prkce* $^{-/-}$ mice) drink less ethanol and nicotine, and show reduced conditioned place preference for ethanol and nicotine compared with wild-type mice. These behaviors are associated with reduced α_6 and β_3 nicotinic acetylcholine receptor (nAChR) subunit transcripts in the ventral midbrain and striatum of *Prkce* $^{-/-}$ mice. The α_6-containing nAChRs are mainly found on dopamine neuron somata in the ventral tegmental area (VTA) and their projections in the nucleus accumbens (NAc). In the NAc, α_6-containing nAChRs modulate local dopamine release, and using fast scan cyclic voltammetry we found reduced regulation of dopamine release by α_6-containing nAChRs in the NAc of *Prkce* $^{-/-}$ mice. Since these results point to a key role for NAc PKCε in regulating dopaminergic signaling, we investigated if PKCε activity in the NAc is also important for regulating alcohol and nicotine consumption. We used lentivirus delivered short hairpin RNA (shRNA) against *Prkce* transcripts to specifically reduce PKCε levels in the NAc of wild-type mice. In a preliminary experiment, mice that received shRNA against PKCε showed reduced ethanol consumption in a 24-hour two-bottle choice paradigm compared with mice that received an inactive control shRNA (F_{siRNA} (4,88)=4.244, P=0.05, N=11 controls, N= 13 PKCε shRNA). After three weeks of water consumption, these same mice were tested for nicotine consumption in a 24-hour two-bottle choice test. Mice that received active shRNA also showed reduced average weekly nicotine consumption (F_{siRNA} (1,66)=4.177, P=0.05). These results support our hypothesis that PKCε activity within the NAc regulates both alcohol and nicotine consumption.

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0062

NUCLEUS ACCUMBENS CORE ADAPTATIONS THAT PROMOTE PATHOLOGICAL ETHANOL INTAKE IN RATS

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Background: Alcoholism imposes a tremendous social and economic burden. There are relatively few pharmacological treatments for alcoholism, with only moderate efficacy, and there is considerable interest in identifying additional therapeutic options. Alcohol exposure can alter SK-type potassium channel (SK) function [1,2] and glutamate receptor function in limbic brain regions. Thus, we used in vitro patch-clamp electrophysiology as well as optogenetic methods in vitro and in vivo to understand the possible functional role of alcohol-intake-related ion channel and glutamate receptor adaptations in the Nucleus Accumbens core (NAcore) on alcohol intake.

Methods: We used in vitro electrophysiology and optogenetics to determine whether the function of SK channels and AMPAR- and NMDAR-type glutamate receptors was altered in the NAcore of adult, male Wistar rats after at least 3 months of intermittent intake of 20% alcohol. For optogenetics, channelrhodopsin (ChR2) is injected into one of several cortical areas or the BLA, and glutamatergic currents representing a particular glutamatergic input to the NAcore are elicited through LED light activation in vitro. We also performed in vivo intra-NAcore pharmacological manipulations and optogenetic inhibition of selective glutamatergic inputs to the NAcore to understand how different inputs to the NAcore and functional adaptations within the NAcore could regulate alcohol intake that is aversion-resistant (i.e., that persists despite pairing with aversive consequences like quinine taste or intermittent footshock).

Results: While the FDA-approved SK inhibitor chlorzoxazone inhibits regular alcohol intake (i.e., without overt pairing with an aversive consequence) [1,2], NMDAR antagonists only reduced alcohol intake when consumption was paired with an aversive consequence. Similar selectivity for aversion-resistant intake was observed after halorhodopsin inhibition of cortical inputs to the NAcore in vivo. These results also concur with increased NMDAR function under cortical inputs to the NAcore of alcohol-drinking rats seen in vitro.

Conclusions: Different neural circuits and molecular mechanisms may mediate alcohol intake in the presence versus absence of overt pairing of alcohol intake with an aversive consequence. In addition, different alcohol-related adaptations within the NAcore may critically facilitate regular and aversion-resistant alcohol intake.

[1] Hopf et al., Neuron, 65:682, 2010.
[2] Hopf et al., Biol Psych, 69:618, 2011.

0063

NEURAL BASIS OF DIFFERENTIAL PERSISTENCE OF REINSTATEMENT BY STIMULI CONDITIONED TO ETHANOL VS. CONVENTIONAL REWARD

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Previous findings from this lab revealed that cue-induced reinstatement of alcohol seeking is highly persistent. The purpose of this study was (i) to investigate whether this effect extends to behavior induced by stimuli conditioned to potent natural reward, and (ii) to identify brain regions that are activated by stimuli conditioned to EtOH vs. natural reward. Separate groups of rats were trained to associate distinct olfactory discriminative stimuli with self-administration of 10% (w/v) EtOH or a potent non-drug reinforcer, 3.0%/0.125% (w/v) glucose/saccharin (SuperSac) (S+) vs. non-reward (S-). Following extinction during a subsequent reinstatement phase, rats were exposed to S+, and the degree of conditioned reinstatement was determined in 30-min sessions, conducted every 3rd day for a total of 4 test sessions. After the 1st and 4th reinstatement tests, rats were euthanized and their brains processed for Fos neural mapping. The number of Fos-positive cells was quantified in nucleus accumbens (NAC) as neural activity in NAC is known in mediating drug-related learned behavior.

Following extinction, presentation of the EtOH or SuperSac S+ (but not the respective S- cues) both produced robust reinstatement. Subsequent tests, conducted every 3rd day, showed that reinstating effects of the SuperSac S+ returned to extinction levels during the 3rd and 4th tests. In contrast, the EtOH S+ elicited identical high levels of reinstatement across the 4 test sessions. Rats exposed to EtOH or SuperSac S+ on reinstatement day 1 showed significantly increased number of Fos positive cells within NAC compared to extinction control. While Fos counts were similar on reinstatement day 4 vs. day 1 in rats exposed to the EtOH S+, Fos counts decreased on reinstatement day 4 vs. day 1 in rats exposed to SuperSac S+. In addition, Fos counts differed significantly in rats exposed to the EtOH vs. SuperSac S+ on reinstatement day 4.

The results confirm that contextual stimuli conditioned to alcohol, but not cues conditioned to potent conventional reward produce persistent, compulsive-like seeking behavior. The findings also suggest a possible regulatory role of NAC in these differential behavioral effects. Neural mapping of other brain regions is underway to identify additional sites that may participate in mediating the differential persistence of behavior induced by stimuli conditioned to ethanol vs. potent natural reward. Supported by NIH/NIAAA AA 018010 (FW).

0064

BIOCHEMICAL ADAPTATIONS IN THE DORSOLATERAL STRIATUM ASSOCIATED WITH ESCALATION OF VOLUNTARY ALCOHOL CONSUMPTION IN RODENTS

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It is thought that a fundamental switch from goal-directed behavior, governed by the medial prefrontal cortex (mPFC) to habitual behavior, mediated by the dorsolateral striatum (DLS), contributes to high rates of consumption in individuals with alcohol use disorders. Repeated episodes of ethanol exposure and withdrawal are associated with enhanced relapse vulnerability, possibly contributing to this switch. Similarly, rats will develop a preference for ethanol and escalate their drinking if given ethanol in an intermittent alcohol access (IAA) paradigm. Studies have shown that IAA reduces the ability of small conductance potassium (SK) channels to regulate firing in the nucleus accumbens (NAc), another key brain region associated with the alcohol circuitry. Here, we examined the underlying biochemical adaptations associated with the escalation of voluntary drinking, specifically in regions relating to goal-directed and addictive behavior. Long-Evans rats were given intermittent access to ethanol under a two-bottle choice (20% ethanol or water) model. We measured ethanol consumption and drinking patterns with a lickometer system for 9 weeks. After one week of withdrawal from IAA consumption, we assessed changes in glutamate receptor and SK channel expression levels in PSD-enriched fractions. As expected, rats demonstrated an escalation in drinking from 2.2 g/kg to 4.1 g/kg after 9 sessions of IAA exposure. This level of drinking remained stable for an additional 17 sessions, with rats showing a slight preference for ethanol over water. We found a strong, positive correlation between g/kg ethanol consumed and number of licks in the first four drinking sessions (R^2 = 0.716) and after the rats reached their baseline drinking level (R^2 = 0.931). The rats consumed ethanol in discrete episodes every 2–3 hours during the dark cycle, with some rats also showing an isolated episode of drinking 1–2 hours before the onset of the light cycle. Western blot analysis indicated a significant decrease of SK3 expression in the DLS of IAA rats compared with control rats. No significant differences in the expression of glutamate receptor subunits or SK channels were observed in either the mPFC or NAc. The reduction in SK3 channels by IAA may contribute to enhanced glutamatergic activity reported in the DLS. Thus, these data suggests a possible role for SK3 channels in the DLS in regulating escalation of habitual alcohol consumption. This work was supported by NIH grants AA019722 and AA007474.

0065

DIFFERNTIAL CONDITIONED APPROACH BEHAVIOR TO REWARDS; INDICATION OF DIFFERENCES IN CUE SENSITVITY IN ALCOHOL PREFERRING P RATS AND WISTARS

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Hypersensitivity to environmental stimuli associated with rewarding substances is hypothesized to be a mediating factor in binge or relapse behaviors observed in substance abusing individuals. The current study describes a novel model of stimuli-paired cue sensitivity using selectively bred alcohol preferring (P) rats and outbred Wistars. Animals were first exposed to an intermittent drinking paradigm that established a drinking history for either 20% ethanol or 2% sucrose in both lines. To examine approach behavior, a two-compartment operant chamber with stimulus lights, retractable sippers, and IR photocells in each compartment was used. Cue-evoked approach to the retractable sipper containing either ethanol or sucrose (US) paired with a light stimulus (CS) was quantified. The availability of either liquid (US) was signaled via 2 sec illumination of the stimulus light (CS) prior to the insertion of the sipper in the chamber. Initially, CS/US pairings were presented on the same side of the chamber then on opposite sides; with a CS on the left indicating a US would appear on the right and vice versa to further determine the associative strength of the CS. Consistent differences in rat strain were observed for both the sucrose and ethanol groups. Specifically, P rats in both groups consumed greater amounts of their respective US substance, approached both sucrose and ethanol CS sooner, and remained at the US longer than Wistar rats. Differences in approach behavior observed in P rats suggest that phenotypic differences may underlie cue hypersensitivity previously observed in addicts and warrant further examination of the biological basis of these apparent behavioral differences. These data establish a novel method to examine the pathology of reward paired cues as predictive factors for reward which may also influence seeking and consumption of addictive substances for individuals disposed to substance use or dependence. Human imaging studies have demonstrated pronounced differences in prefrontal activation in the presence of reward predictive cues in numerous addicted populations including heavy drinkers. Our prospective work will include an analysis of neural firing and oscillatory activity in the PFC of animals engaged in this paradigm to further explore both physiological and behavioral differences in cue sensitivity.

0066

VOLUNTARY ALCOHOL INTAKE INCREASES THE REWARDING ACTION OF COCAINE

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The goal of this study was to examine whether voluntary ethanol intake would be associated with reward or could increase the rewarding action of cocaine. On day 1, mice were tested for baseline place preference, in which each mouse was placed in the central neutral chamber of a 3-chambered conditioned place preference (CPP) apparatus and allowed to freely explore the CPP chambers for 15 min. The amount of time that mice spent in each chamber was recorded. On days 2–5, mice received a 15-min conditioning session in the morning and another session in the afternoon. To promote water and ethanol consumption during the conditioning sessions, mice were kept water-deprived overnight. During the conditioning sessions (days 2–5), mice had free access to water or alcohol (4%) from a bottle mounted on one of the corners of the conditioning chambers. Following the conditioning sessions, mice were tested for place preference on day 8, as described above for day 1. On day 9, mice received a single saline/cocaine (20 mg/kg) or cocaine/saline conditioning for 30 min and were tested for cocaine CPP on the following day. Our results revealed that water-deprivation increased water and ethanol consumption but the increase in ethanol or water consumption was not associated with CPP. However, such an increase in voluntary ethanol intake increased the motivational valence of contextual cues leading to cocaine CPP. Overall, the present results suggest that initial alcohol exposure can enhance the rewarding action of cocaine and possibly its addictive properties. Furthermore, these results may have implication in the pathogenesis of poly-drug use and abuse and suggest that alcohol could be a gateway drug.

0067

PHASIC NEURAL ACTIVITY IN THE DORSOMEDIAL AND DORSOLATERAL STRIATUM DURING EXTINCTION AND REINSTATEMENT IN GOAL-DIRECTED AND HABIT-TRAINED RATS

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Depending on the history of reinforcement, the execution of an instrumentally trained response can be goal-directed and tied to expectations of outcome value or a habitual response to a stimulus that is largely independent of outcome value. Recent lesion work has demonstrated that goal-directed behavior relies heavily on the dorsomedial striatum (DMS) while habitual, outcome-independent behavior depends heavily on the dorsolateral striatum (DLS). We investigated this anatomical-behavioral distinction during extinction and reinstatement with single-unit electrophysiology in the DMS and DLS of rats trained to press levers for sucrose or ethanol reward under variable interval (VI) or fixed ratio (FR) schedules of reinforcement. Across repeated days of extinction, VI rats were slower to cease pressing behavior than FR rats, indicating that the behavior of the VI rats was habitual relative to the FR rats. Furthermore, and in line with lesion work, phasic changes in neural firing during unrewarded lever presses are more prevalent in the DMS of goal-directed FR-schedule rats (33% and 18% of neurons in DMS and DLS, respectively), while phasic changes are more prevalent in the DLS of habit-like VI-schedule rats (19% and 37% in the DMS and DLS, respectively). People with alcohol use disorders frequently describe ''habitual'' alcohol seeking that occurs despite the expectation of negative outcomes and the ease of reinstatement of alcohol seeking after periods of prolonged abstinence. Thus, future work will examine differential striatal neural activity in rats trained to seek alcohol versus sucrose during reinstatement of reward-seeking behavior.

0068

ENHANCED EXTINCTION LEARNING OF ALCOHOL CUES IS ASSOCIATED WITH PLASTIC CHANGES IN AREAS OF THE PRELIMBIC CORTEX

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Relapse is one of the most difficult components to treat in alcoholism. Alcohol cues, formed through basic classical- and operant-conditioning principles, elicit craving in alcoholics and often lead to relapse. However, the use of learning and memory principles, particularly extinction learning, have not proven very effective in the treatment of alcohol addiction. Our laboratory has shown that treatment with the mGluR5 positive allosteric modulator (PAM) CDPPB can enhance the extinction learning of alcohol-associated cues in rats. The purpose of this study was to assess changes in neuronal plasticity in brains areas thought to mediate extinction in rats that displayed facilitated extinction learning. A secondary aim was to examine the impact of CDPPB on relapse-like behavior. Male Wistar rats were trained to self-administer a 10% alcohol solution using a modified sucrose fading technique. Active lever presses were accompanied by light/tone complex stimulus. Rats were then exposed to an extinction training or forced abstinence procedure and were given either an injection of CDPPB (30 mg/kg s.c.) or vehicle (10% Tween 80) 20 minutes prior to each session. Lever pressing behavior was monitored until extinction criteria were met. We then utilized a diolistic-labeling technique combined with 3D image analysis to assess changes in dendritic spines in areas of the prelimbic cortex and nucleus accumbens after extinction learning. To examine the impact of CDPPB treatment on relapse-like behavior, a separate group of rats were trained to self-administer alcohol, treated with CDPBB, and subsequently exposed to a cue-induced reinstatement session. The results indicated the CDPPB treatment facilitated the extinction of cue-induced alcohol-seeking behavior. Rats that showed enhanced extinction learning also had significantly increased overall dendritic spine density in the prelimbic and infralimbic cortices. Additionally, these animals also had significant changes spine class morphology in these brain regions. These results indicate that the mGluR5 PAM could serve as a novel pharmacological intervention to aid in the treatment of alcoholism through exposure therapy, possibly due to plastic changes in the prefrontal cortex. The enhancement of extinction learning should ultimately reduce the propensity for relapse and data are currently being examined to determine if CDPPB treatment during extinction training attenuates the reinstatement of alcohol-seeking behavior.

0069

ADOLESCENT BUT NOT ADULT ALCOHOL INITIATION INFLUENCE ALCOHOL CONSUMPTION AFTER A SHORT PERIOD OF DEPRIVATION

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Background: It has been suggested that the earlier the onset of alcohol use – which usually occurs during adolescence – the greater the likelihood of later alcohol problems. We recently observed heightened alcohol consumption in adolescent rats that had been exposed to alcohol (5 or 2 intubations given every other day, dose: 2.5 g/kg) during early adolescence. The aim of the present study was to further explore the permissive effect of passive alcohol exposure on later alcohol intake and analyze if this effect is also observed during adulthood.
Methods: A total of 32 adolescent (postnatal day 28 at the beginning of the procedures, PD 28; n=8 per group) and 28 (PD70; =7 per group) adult male Wistar rats were given intragastric (i.g.) administrations every other day. They received either 5 [5-day exposure group, ethanol on PDs 28, 30, 32, 34 and 36 (adolescents); or ethanol in PDs 70, 72, 74, 76, 78 (adults)], 2 [2-day exposure group: ethanol on PD 28 and 32, vehicle on PD 30, 24 and 36 (adolescents); or ethanol on PDs 70 and 74 and vehicle on 72, 76 and 78 (adults)] or 0 [control group treated with vehicle on PDs 28- 36 (adolescent); or 70–78 (adults)] administrations of 2.5 g/kg ethanol. Voluntary alcohol consumption was subsequently measured through a 24h, 2-bottle choice test (concentration: 5.6% alcohol, vehicle: 1% sucrose; ad-libitum food) at PDs 39-42 (adolescents) or PDs 80 to 83 (adults); and after a short period of alcohol recess at PD 50 or PD 91 (for adolescents and adults, respectively). We also tested anxiety response through a light/dark box test before commencement of self-administration and in the last day of alcohol recess.
Results: Alcohol-initiated adolescent, but not adult, rats showed significantly greater alcohol consumption after a period of alcohol recess (PD50) than non-initiated animals. This facilitative effect of early exposure to alcohol was fairly similar in adolescents given 2 or 5 alcohol intubations. These results do not seem to be associated with an ethanol-induced exacerbated anxiety response, as there were no treatment differences in the dark/light box test at any developmental stage.
Conclusions: Altogether, these results highlight the permissive role that alcohol exposure exerts on later alcohol intake. At least under the present experimental circumstances, this phenomenon seemed to be an early debut effect that occurred only when alcohol initiation begun at adolescence.

0070

MODELLING THE COMORBIDITY ALCOHOL USE DISORDERS - SCHIZOPHRENIA : CRITICAL ROLE FOR THE ADOLESCENCE PERIOD

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Alcohol use and abuse disorders (AUDs) occur in about 10% of the population in Western countries and usually have dramatic consequences. Interestingly in schizophrenic patients, the proportion of individuals with AUDs can reach 50% and even more. AUDs and schizophrenia show several similarities. The age of onset of schizophrenia – late adolescence – corresponds to a window of vulnerability to alcohol. Moreover the brain structures involved in both pathologies are very similar: the ventral tegmental area, the nucleus accumbens, the prefrontal cortex and the hippocampus. The two major neurotransmitters implicated in these particular brain regions are dopamine and glutamate which are known to be involved in AUDs and schizophrenia.
The aim of this study was to establish an animal model of comorbidity AUDs – schizophrenia. We choose to use the NVHL (Neonatal Ventral Hippocampus Lesion) model to observe a schizophrenia-like phenotype and the 20% intermittent access paradigm (20% IA) to induce alcohol (EtOH) consumption.
In a first experiment, rats (NVHL and sham operated) were exposed to EtOH at the age of 90 days in a 20% IA paradigm. No difference in EtOH consumed was observed between both groups over a period of 5 weeks. Since adolescence is a critical period for both AUDs and schizophrenia we decided to pre-expose rats to EtOH for 2 weeks during the adolescence (day 28 to day 45). During these 2 weeks rats had free continuous access to 2 bottles (water *vs.* 10% EtOH). No difference in EtOH consumption was observed during this period and levels consumed were relatively low (1–2 g/kg/day). Then at adulthood rats were submitted to the 20% IA paradigm as in the first experiment. NVHL rats pre-exposed to EtOH during adolescence showed an escalation in EtOH consumption while sham-operated rats do not. The amount of EtOH consumed reaches 4–5 g/kg/24 hrs and preference for EtOH approaches the limit of 50% defining the alcohol-preferring rats. No difference in sucrose consumption was observed between the NVHL and control rats.
For the first time a phenotype of loss of control of EtOH consumption associated to a schizophrenia-like phenotype was observed. Pre-exposure to EtOH even at moderate doses during adolescence seems to be a critical event for the occurrence of this comorbidity. These results open the way to genetic, molecular and cellular studies aiming at the identification of the underlying mechanisms responsible for the comorbidity AUDs – schizophrenia.

0071

SEX DIFFERENCES IN ETHANOL DRINKING AND BEHAVIORAL RESPONSES TO CHRONIC INTERMITTENT ETHANOL EXPOSURE

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Male C57BL/6J mice exposed to chronic intermittent ethanol (CIE) show increases in ethanol intake in subsequent two bottle choice tests as well as increased anxiety-like responses following stressor exposure. While female C57BL/6J mice drink more ethanol than male mice under various conditions, it is not clear whether they show these same changes following CIE exposure. Baseline two hour two-bottle choice ethanol drinking was determined in male and female C57BL/6J mice, they each were then assigned to an ethanol vapor group (3 days, 16 hr per day) or control group, and then two bottle choice ethanol drinking was reexamined following 3 days of abstinence. This entire cycle was repeated 2 additional times (for a total of 3 cycles). The week following the final drinking test the mice were assessed for anxiety-like behavior following stressor exposure (30 min restraint) in the light/dark transfer test. One week later all mice were tested in the fear conditioning procedure in order to examine cognition relevant to emotional processing. Finally, all mice were tested in the forced swim test in order to examine helpless-like behavior. Blood alcohol levels during the 3 cycles of vapor exposure averaged about 200 mg% with no sex differences at any sample time. Overall there were significant sex differences independent of group in ethanol drinking (f>m) and forced swim immobility (f<m). Male mice exposed to CIE showed significantly increased ethanol drinking following the 3rd vapor cycle, increased anxiety-like behavior following mild stressor exposure, a non-significant trend for a deficit in cued fear conditioning, and no change in immobility in the forced swim test relative to control male mice. Female mice showed a non-significant trend toward increased ethanol drinking following the 2nd vapor cycle (which was gone following the 3rd cycle), no effect on anxiety-like behavior, a significant deficit in contextual fear conditioning and a trend toward a deficit in cued fear conditioning, and a trend toward a decrease in immobility in the forced swim test. These data suggest that CIE exposure producing equivalent blood alcohol levels results in different behavioral outcomes in male and female mice. Male mice appear more sensitive to increased ethanol drinking and anxiety-like behavior, while female mice appear more sensitive to cognitive disruptions produced by CIE. Supported by the Integrated Neuroscience Initiative on Alcoholism (INIA)-West, 1U01 AA020893.

0072

THE INFLUENCE OF ALCOHOL AND CAFFEINE INTAKE ON THE ETHANOL PREFERENCE FORMING IN RATS: SEX DIFFERENCES

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The goal of the study was the investigation of ethanol and caffeine influence on the alcohol preference formation and behavior in male and female rats under the conditions of long-term experiment.
The study was conducted on 60 adult Wistar rats: 30 males and 30 females. The animals were kept on a standard diet. Rats were divided into four groups. Within 6 months of the experiment the first group had access only to a solution containing 10% ethanol and 0.4 g / l of caffeine, the second group - only 10% alcohol solution, and the third - to a solution containing 0.4 g / l caffeine, the fourth (control) - only to water. Alcohol preference was measured using a standard ''two bottle'' test before the experiment and each subsequent month during the whole experiment after a 24 hours deprivation. Behavior parameters were estimated before and every month of the experiment using ''Open field''. After 6 months of the experiment the anxiety and behavioral activity were investigated in the ''Suok test''.
It was found that a long-time intake of caffeine, ethanol and their combination has led to the increase of alcohol preference both in male and female rats. Alcohol preference was higher in female rats consuming caffeine with ethanol and pure ethanol solution compared to male rats. Alcohol preference was formed earlier in rats consumed combination of caffeine with ethanol, later on in rats consumed ethanol. In animals consumed caffeine the strong alcohol preference did not form up to the end of the experiment. Behavioral activity significantly increased in female consumed caffeine and caffeine with ethanol, compared to animals received ethanol and controls. Similar tendency was observed in male rats. The anxiety level was significantly higher in females rats in all experimental groups compared to controls, while males did not demonstrate increased anxiety.

0073

AN ETHANOL VAPOR CHAMBER FOR SMALL ANIMALS

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Introduction: Ethanol vapor chambers have been widely utilized in alcohol research since 1971. A six-chamber system for rats was designed with backup air pumps, with features designed for simplicity, ease of use, and low cost.
Methods: The air flow was used to adjust ethanol vapor levels on the basis of flow velocity and dilution, without the use of a heater or fans. Multiple pumps ensure animal survival in the case of failure of the primary air pump. Measurements of ethanol vapor concentrations were done with a factory-calibrated breathalyzer, using room air to dilute the vapor chamber output into the range of the breathalyzer. The ethanol vapor measurement was rapid (around 1 minute for measurement and 2 minutes for recovery based on the measured ethanol concentration) and efficient, at a parts cost of approximately $4,000. The vapor chamber system allowed a range of ethanol vapor concentrations (16mg/L to 26mg/L), adjusted with different volumes of ethanol in the flask, verifying the ability to select from a broad range of levels. Vapor levels were stable for long time with the changes of pure ethanol. To adjust the concentration easily, a valve was introduced to dilute the high concentration to a lower value by mixing with room air. To evaluate mechanisms to control the vapor level, the influence of different parameters was investigated. The parameters included ethanol temperature, water content, pump rate, and the presence of bedding and food. To generate a steady state vapor concentration of 23 mg/L, a temperature of 14oC and 200 proof ethanol yielded the most stable results. The system was tested with three rats to assess comfort and elevation of blood ethanol.
Results and Conclusions: The rats showed no signs of discomfort but did show blood ethanol levels of 168.8 ± 22.3 mg/dL. The system has a relatively low cost, ease of use, convenient and inexpensive measurement of ethanol vapor concentrations, and no need for a heater or other electrical components that could come into contact with ethanol. The chamber's parameters can easily be modified to achieve other alcohol concentrations and be used for other small animals.

5. PATHOLOGY: HUMAN/ANIMAL

0074

DIFFERENTIAL EXPRESSION OF GENES AND TRANSCRIPTION FACTORS RELATED TO ALCOHOLIC HEPATIC STEATOSIS IN THREE STRAINS OF RATS

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Alcohol consumption results in alcoholic liver disease (ALD), starting with reversible stage of hepatic steatosis and can progress to steatohepatitis, fibrosis, cirrhosis and in certain cases to hepatocellular carcinoma. To determine if transcription factors have a role in hepatic steatosis, 6–7 weeks old male Wistar, Sprague-Dawley (SD) and Fischer-344 rats were pair fed for 6 weeks with or without 5% alcohol via Lieber-DeCarli diet. Hepatic steatosis was observed in all three strains of rats with predominance in Wistar followed by SD and Fischer rats. To elucidate the mechanisms of steatosis, we analyzed genes and transcription factors involved in lipid metabolism by quantitative real-time PCR (RT-qPCR) using their primers. Genes involved in fatty acid synthesis, acetyl-CoA carboxylase alpha, malonyl-CoA decarboxylase, fatty acid synthase and stearoyl-CoA desaturase were up-regulated in Wistar rats while down-regulated in SD and Fischer rats. Diglyceride acyltransferase O-acyltransferase and peroxisome proliferator-activated receptor gamma involved in trigyceride synthesis were up-regulated in Wistar and Fischer rats and down-regulated in SD rats. Low expression of betaine-homocysteine S-methyltransferase (BHMT) and phosphatidylethanolamine *N*-methyltransferase (PEMT) was observed in Wistar rats. In SD rats low BHMT and high PEMTs level were observed, while in Fischer rats both BHMT and PEMT levels were elevated. The expressions of sterol regulatory element-binding protein involved in lipid synthesis, carnitine palmitoyltransferase I-a involved in transportation of long chain fatty acids, acetyl CoA carboxylase beta and peroxisome proliferator-activated receptor alpha involved in fatty acid oxidation remained unchanged in all the three strains. In conclusion, increased expression of genes involved in fatty acid and triglyceride synthesis supports increased steatosis in Wistar rats compared to SD and Fischer rats.

0075

DEFICIENCY OF CD36 PROTECTS AGAINST ETHANOL-INDUCED HEPATOMEGALY AND OTHER COMPLICATIONS

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CD36 is a receptor with multiple ligands including long chain fatty acids (LCFAs). It is ubiquitously expressed and plays an important role in LCFA uptake in the heart, skeletal muscle and adipose tissue. Although the role of CD36 in the liver is not clear, the expression of CD36 in the liver is upregulated by ethanol feeding. We hypothesized that CD36 plays a role in ethanol-induced fatty liver development. To test the hypothesis, age-matched male CD36 knockout (KO) of C57BL/6 background (n=14) and wild-type (WT) C57BL/6 mice (n=20) were studied. We have previously shown that 4 weeks of 6.4% ethanol feeding significantly increased hepatic triglyceride (TG) accumulation in C57BL/6 mice (*J Lipid Res* 52:2021-2031, 2011) using a standard Liber-DeCarli diet (35.9% fat calories). To minimize the contribution of high fat-induced TG accumulation, we fed one group of mice from each genotypic group with a low fat Liber-DeCarli diet (12.5% fat calories) containing 6.4% ethanol and the other group (per genotype) with an isocaloric Liber-DeCarli control diet without ethanol. Unexpectedly, a significant percentage (80%) of WT mice died only 11 days after 6.4% ethanol consumption. In contrast, none of the CD36 KO mice was affected by the ethanol feeding ($p<0.001$ vs. ethanol-fed WT mice) even though blood alcohol contents were similar for the 2 groups. Despite the short duration of feeding, ethanol significantly increased liver weights in WT mice (control vs. ethanol: 1.07±0.12 vs. 1.67±0.05 g, $p<0.001$), but not in CD36 KO mice (1.13±0.10 vs. 1.07±0.07 g, $p=0.2$). The ratio of liver weight/body weight was also lower ($p<0.05$) in the ethanol-fed CD36 KO mice (0.044±0.005) compared to that in ethanol-fed WT mice (0.057±0.003). Oil Red O staining of liver sections showed the most intense staining for neutral lipids in ethanol-fed WT mice amongst the 4 groups. In summary, CD36 deficiency protected against ethanol-induced hepatomegaly, neutral lipid accumulation and ethanol-induced complications. These results raise the possibility that fat content may affect adverse complications associated with chronic ethanol consumption. The mechanisms underlying these observations are currently under investigation. (Supported by NIH Grants R21 AA020561 and RC2 AA019413)

0076

ALTERED FATTY ACYL COMPOSITION OF RETINYL ESTER IS AN EARLY EFFECT OF ALCOHOL CONSUMPTION

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Retinoids (vitamin A, and its metabolites) are essential nutrients that are required for normal cell proliferation, differentiation, and apoptosis. Alcohol consumption has profound effects on retinoid homeostasis; as Leo and Lieber (NEJM 307, 597-601 (1982)) demonstrated in alcoholics, hepatic retinoid content is progressively depleted with advancing stages of alcoholic liver disease. The research in our laboratory is focused upon the interactions between alcohol and retinoid metabolism, and resultant effects on disease development. Data from C57BL/6 mice chronically fed alcohol, as a component of the Lieber-DeCarli liquid diet, reveals a progressive decline in hepatic retinoid levels. Interestingly though, prior to this decrease we have observed a pronounced change in the fatty acyl (FA) composition of hepatic retinyl esters. Specifically, we observed lower levels of retinyl palmitate (C16:0) which are offset by increases in other retinyl ester species, primarily retinyl oleate (C18:1). This highly reproducible change in retinyl ester FA composition has been observed after as little as two weeks of alcohol consumption, and has been confirmed in three different rodent models of alcohol feeding. Based on these observations, we believe that an alteration in the fatty acyl composition of retinyl ester is an early effect of alcohol consumption. Continuing research in our laboratory is focused upon the mechanism through which alcohol consumption exerts its effect on retinyl ester FA composition, as well as the implications of this change with regard to alcoholic liver disease. The changes observed evoke a model whereby alcohol stimulates the hydrolysis of stored retinyl ester. The retinol generated by this reaction is then re-esterified with a different FA moiety. We hypothesize, and are interested in establishing, whether the change in FA group used for the synthesis of retinyl ester in alcohol consuming mice reflects changes in membrane phsophatidylcholine, which provides FA substrate for retinyl ester synthesis. In summary, alcohol consumption leads to a rapid and marked change in the FA composition of hepatic retinyl esters, indicating that this is an early effect following alcohol exposure, and may prove useful as a biomarker of alcohol consumption (Supported by NIAAA grants RC2 AA019413 and R21 AA020561).

0077

A PROTECTIVE ROLE FOR ADIPONECTIN IN LIVER DAMAGE IN RESPONSE TO ACUTE ALCOHOL FEEDING IN THE MOUSE

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Hepatostestosis and inflammation are thought to be major contributors to pathogenesis associated with chronic alcohol intake. The adipokine adiponectin has been the subject of interest in alcohol research because it antagonizes inflammatory processes and induces lipid oxidation in the liver. Many studies have demonstrated a correlation between adiponectin levels and protection of the liver in response to acute alcohol injury in mice and rats. Our study was designed to test directly the effects of chronic alcohol feeding in adiponectin knockout mice and congenic controls (wild type, WT). The liquid Reyes chocolate diet was fed ad libitum to animals, and with alcohol accounting for 22% of calories in week 1, 27% in week 2 and 34% for week 3 of feeding. Alcoholic mice were isocalorically pair-fed with carbohydrate controls. We found that 34% but not 27% alcohol feeding significantly increased circulating adiponectin levels in WT mice, and that 34% but not 27% alcohol led to significant changes in the liver/body weight ratio, indicative of hepatomegaly. Histological examination in WT mice revealed small amounts of hepatosteatosis in response to alcohol treatment relative to controls. Adiponectin KO mice on the same alcohol diet consumed alcohol at rates equivalent to WT mice, but exhibited hepatosteatosis at consistently higher levels. Adiponectin KO mice also had a significant increase in liver weight to body weight ratio that was significantly higher than that found in WT mice on the same feeding regimen. Biochemical analyis showed decreased levels of total AMPK protein in livers in both adiponectin KO and control animals, with no significant differences observed in phosphorylation levels. Also, there was no difference detected by western blot between mitochondrial oxidative phosphorylation components. Significantly higher levels of PEPCK protein were detected in alcohol-fed adiponectin KO mice relative to WT controls, indicating a higher gluconeogenic state in adiponectin KO mice. Taken together, our data suggest that 34% alcohol leads to hepatomegaly in both WT and adiponectin KO mice, but it is more severe in the absence of adiponectin. Increases in circulating adiponectin levels in WT mice may have a protective effect. Our data also indicate that there may be a link between metabolic regulation and the pathology observed in response to alcohol treatment.

0078

ALCOHOL-INDUCED miR-132 AND ALCOHOL-INDUCED INTESTINAL HYPERPERMEABILITY

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Circadian rhythm disruption promotes alcohol-induced gut leakiness but it is not clear how this occurs. Our previous studies indicated that alcohol-induced miRNAs contribute to alcohol-induced intestinal permeability by inhibiting tight junction gene expression in intestinal epithelial cells. Recent studies discovered that two circadian miRNAs, miR-132 and miR-219 are expressed in a rhythmic fashion to modulate the intrinsic pacemaker activity in the suprachiasmatic nuclei, the master circadian clock in mammals. miR-132 is induced by photic entrainment cues via a MAPK/CREB-dependent mechanism, modulates clock gene expression, and attenuates light entrainment. miR-219 is a target of the CLOCK/BMAL1 complex and exhibits robust circadian rhythms of expression in suprachiasmatic nucleus. We hypothesize that alcohol-induced circadian miRNAs play an important role in the alcohol-induced circadian desynchrony through fine-tuning the expression of target genes in the intestinal epithelium. To test this hypothesis, we used Caco-2 cells and an animal model of alcohol-induced hyperpermeability. Caco-2 cells were incubated with 0.2% alcohol for 1h, 2h, 4h, 6h, and 24h, and then harvested for analysis. Trans-epithelial resistance was chosen as a marker of tight junction permeability for Caco-2 monolayers. The miR-132 and miR-219 expression levels were assayed by real-time PCR. Alcohol time-dependently induced hyperpermeability of Caco-2 cell monolayers and this increase in hyperpermeability was associated with a significant increase in miR-132 expression (40 fold) compared with control at 24h after alcohol treatment. The expression of miR-219 was low in the Caco-2 cells and not changed by alcohol. To determine if the same phenomenon is observed *in vivo*, we fed mice an alcohol containing diet (28% of total daily calories from alcohol) for 4 weeks. The intestinal permeability of mice fed with alcohol was significantly increased by 4 fold compared with control. miR-132 expression was also increased (6 fold) in the colon of alcohol-fed mice. These data suggest that alcohol-induced miR-132 over-expression plays an important role in the alcohol-induced circadian disruption and alcohol-induced intestinal hyperpermeability. Our studies indicate that miR-132 is a novel mechanism for alcohol-induced gut leakiness, and is a potential therapeutic target for preventing the leaky gut in patients with alcoholic liver disease. Studies were supported by R21AA018729 and R01AA020216.

0079

THE ROLE OF MIR-21 IN THE SUPPRESSION OF LIVER REGENERATION IN CHRONIC ETHANOL TREATED RAT

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miR-21 has been identified as a pro-proliferative miRNA. It is over-expressed in many cancer types. As reported by others, we find miR-21 expression to increase during liver regeneration following partial hepatectomy (PHx) in the rat in seeming agreement with this pro-proliferative role. However, chronic ethanol treated animals with impaired liver regeneration have even stronger up-regulation of mir-21 expression than their corresponding pair-fed calorie-matched controls were fed diet in which ethanol calories were replaced by carbohydrate. Global gene expression data was used to predicted potential targets for miR-21 in our experimental model. To further elucidate the role of mir-21 in liver regeneration, we treated rats with oligonucleotide designed to inhibit mir-21. Injection of mir-21 inhibitor 72 h prior to PHx followed by the second injection immediately after the surgery suppressed expression of mir-21 by more than 90% in the regenerating rat liver. Control saline and scrambled oligo injections did not significantly affect mir-21 expression levels.
The effects of anti-mir-21 treatments on the expression levels of multiple cell cycle related genes and both validated and predicted mir-21 targets 24 and 48 h after PHx were analyzed using BioMark Dynamic Array. This analysis shows that suppression of mir-21 results in up-regulation of expression of such validated mir-21 targets as Hipk3, Pan3, Sox5 and Tagln. Cell cycle genes required for progression through G1 phase and for G1/S transition are not affected by mir-21 inhibitor. mir-21 inhibitor treatment does have an effect on later stages of the cell cycle; Ccnb1, Ccnb2 and Cdc20 were suppressed by mir-21 inhibition.
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0080

BETA-ENDORPHIN NEURONAL TRANSPLANTATION ATTENUATES CHRONIC ALCOHOL INDUCED HISTOLOGICAL AND INFLAMMATORY RESPONSES

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Alcoholic liver disease (ALD) is a serious health problem among alcoholics, characterized by the development of fibrosis and cirrhosis coupled with a state of chronic, low-grade inflammation. These changes negatively affect normal function of both parenchymal and non-parenchymal cells resident in the liver, as well as the recruitment of additional cell types to the liver in response to damage and inflammation. It is well known that the multiple levels of the neuroaxis, including the paraventricular nucleus (PVN) of the hypothalamus, are involved in regulation of efferent sympathetic nerve discharge to various organs and modulate many pathophysiological processes. Our previous research shown that a set of hormone secreting nerve cells in the hypothalamus, called beta-endorphin (BEP) neurons, plays a role in regulating stress response and immune function. Recently, retrograde tracing has provided evidence for an influence of BEP neurons on the liver. In order to better understand the influence of these neurons on liver functions, we evaluated the effects of transplantation of *in vitro* differentiated BEP neurons into the PVN in alcohol induced histological and inflammatory responses of the liver. Male Fischer rats (100–150g) were transplanted with either BEP neurons or cortical neurons (control) and randomly assigned to treatment of feeding alcohol-containing (AF) liquid diet or pair-feeding control liquid diet (PF) for 8 weeks. The animals were sacrificed, and their livers dissected and used for histopathological, determination of the degree of fibrotic changes and inflammation. Alcohol-fed, but not pair-fed animals, demonstrated histopathological changes such as prominent microvesicular steatosis, inflammatory infiltration and severe hepatic fibrosis (accumulation of collagen). In addition, alcohol feeding increased tissue expression of TNF-alpha as demonstrated by immunohistochemical localization and Western blot. Alcohol-induced microvesicular steatosis, inflammatory infiltration, hepatic fibrosis and inflammation were absent or reduced in animals with the PVN transplants of BEP neurons. These findings are the first evidence for a role of hypothalamic BEP neurons in influencing liver functions. Additionally, the data identify the potential use of BEP cell therapy for alcohol-induced liver disease. (Supported by R37 AA08757)

0081

ROLE FOR INTESTINAL CYP2E1 IN ALCOHOL-INDUCED CIRCADIAN GENE-MEDIATED INTESTINAL PERMEABILITY

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Introduction. Alcohol-induced intestinal permeability to endotoxin plays a critical role in the pathogenesis of alcoholic liver disease (ALD). Identifying mechanisms through which alcohol promotes intestinal permeability could provide new avenues for prevention and treatment of ALD. We have recently shown that alcohol promotes intestinal permeability in Caco-2 cell monolayers through induction of expression of the circadian (24h rhythm) gene proteins Clock and Per2. Cytochrome P450 2E1 (CYP2E1) is a P450 enzyme isoform that has been shown in many studies to play a critical role in ALD. Early studies from other labs showed that CYP2E1 was also expressed in intestine and was induced with alcohol feeding. We hypothesized that alcohol-induced induction of intestinal CYP2E1 activity and the resulting oxidative stress, might be driving the circadian gene expression (Clock and Per2) that we have shown are required for gut leakiness.
Methods. To test this hypothesis we used our Caco-2 intestinal epithelial cell line *in vitro* model of intestinal permeability. We measured the effects of alcohol stimulation on CYP2E1 protein expression by western blotting and CYP2E1 activity in the microsomal fraction. We also measured Cyp2e1 protein expression in intestinal tissue from chronically alcohol fed mice. We used siRNA to knock down expression of CYP2E1 in Caco-2 cells and measured the effects on alcohol-induced intestinal permeability and CLOCK and PER2 protein expression.
Results. We found that alcohol (0.2%) treatment increased CYP2E1 protein expression by about 70% and CYP2E1 activity by about 60% in Caco-2 cells *in vitro* after only 4h of treatment. We also found that chronic alcohol feeding (8wk Nanji diet) resulted in a 70% increase in Cyp2e1 protein in BL/6 mouse colon. MRNA levels of CYP2E1 (Caco-2) or Cyp2e1 (BL/6 colon) were not significantly increased by alcohol treatment. SiRNA knockdown of CYP2E1 in Caco-2 cells prevented alcohol-induced intestinal hyperpermeability as well as preventing the alcohol-induced induction of the circadian CLOCK and PER2 proteins.
Conclusions. Our data support a novel role for intestinal CYP2E1 in alcohol-induced intestinal hyperpermeability via a mechanism involving CYP2E1-dependent induction of circadian clock genes Clock and Per2 by alcohol stimulation. Thus intestinal CYP2E1 may represent a new therapeutic target for preventing alcohol-induced gut leakiness in the pathogenesis of ALD.
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0082

ROLE OF CYP2E1 IN HEPATIC STEATOSIS AND INJURY BY BINGE ALCOHOL

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Although many scientists reported that acute binge alcohol can damage many tissues, the role of ethanol-inducible cytochrome P450 2E1 (CYP2E1) in acute alcohol-mediated inflammatory liver injury remains elusive because of the contradictory reports. We hypothesized that acute alcohol elevates CYP2E1 levels in the liver and other organs to promote oxidative stress, contributing to tissue injury/inflammation and that alcohol-induced liver steatosis and/or damage can, therefore, be prevented or decreased in *Cyp2e1*-null mice. To study the role of CYP2E1 in promoting alcohol-induced steatosis and acute inflammatory liver injury, young wild-type (WT) mice and *Cyp2e1*-null mice were treated with binge ethanol or dextrose in saline (negative control). Alcohol-exposed WT or *Cyp2e1*-null mice were euthanized at 1 and 6 h after the binge ethanol. Liver histology and key markers of liver injury, oxidative stress and inflammatory cytokines were evaluated. Our results showed that the portal vein endotoxin levels were significantly increased at 1 and 6 h after the binge ethanol exposure in WT mice. In contrast, the portal vein endotoxin levels were not significantly elevated in ethanol-exposed *Cyp2e1*-null mice. We also observed significant elevation of steatosis, necroinflammatory foci, and TUNEL-positive apoptotic cells in ethanol-exposed WT mice while *Cyp2e1*-null mice showed very few signs of alcohol-induced steatosis and liver injury. Consistent with the histological data, the levels of CYP2E1 activity and protein, carbonylated proteins, and lipid peroxidation were significantly increased in the WT mice exposed to binge ethanol compared with those of the ethanol-exposed *Cyp2e1*-null mice. Furthermore, the levels of inflammatory cytokine TNF-alpha, interferon-gamma, and plasminogen activator inhibitory protein (PAI-1) were significantly elevated in ethanol-exposed WT mice but not in the corresponding *Cyp2e1*-null mice. All these results strongly suggest that CYP2E1 plays an important role in promoting, at least partially, steatosis and inflammatory liver injury in our binge alcohol model.

0083

ROLE OF CYP2E1 IN PROMOTING INSULIN RESISTANCE AND NONALCOHOLIC STEATOHEPATITIS

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It is well-established that ethanol-inducible cytochrome P450 2E1 (CYP2E1) is involved in promoting oxidative stress with increased oxidation of cellular DNA and proteins. We have recently reported that CYP2E1 plays an important role in protein oxidation and nitration followed by ubiquitin-mediated protein degradation during toxicity caused by CYP2E1 substrates alcohol and acetaminophen, respectively. To study the role of CYP2E1 in promoting insulin resistance and nonalcoholic fatty liver diseases (NAFLD), young male wild-type (WT) mice and *Cyp2e1*-null mice were fed a low (LFD, 10% energy derived) or high fat diet (HFD, 60% energy-derived) in a 2 x 2 design for 9 weeks. Liver histology and the levels of key mediators of NAFLD in the 4 groups were evaluated in our study. Our results showed that only WT mice fed HFD achieved the non-alcoholic steatohepatitis (NASH) score of 5 with marked necroinflammation compared to the other groups. Markers of oxidative stress such as elevated CYP2E1 levels and activity, lipid peroxidation, protein carbonylation, and protein glycation were all markedly elevated in HFD-fed WT mice only. Furthermore, markers of inflammation such as osteopontin, TNF-alpha, and F4/80 were also prominently elevated in HFD-fed WT mouse group compared with the other 3 groups. In addition, the oxidative stress sensitive (death) signaling pathway phospho-JNK was also higher in WT-mice fed HFD and this increase was accompanied by increased apoptotic cells. Finally, WT mice fed HFD exhibited increased insulin resistance and impaired glucose tolerance compared to the other groups (including the HFD-fed *Cyp2e1*-null mice), probably due to increased oxidative stress and inflammation. Collectively, these data suggest a critical role of CYP2E1 in promoting insulin resistance and inflammation in the mouse model of high-fat induced NASH.

0084

ACUTE ALCOHOL INTOXICATION SUPPRESSES EXPRESSION OF GUT ANTIMICROBIAL PEPTIDES REG3β AND REG3 γ FOLLOWING BURN INJURY

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Interleukin (IL)–22, a cytokine released predominantly by Th17 cells, is indispensable in the expression of various antimicrobial peptides (AMPs), including Reg3β and Reg3γ. Current evidence suggests that Reg3β and Reg3γ are crucial in regulating mucosal immunity. While Reg3γ predominately binds and kills Gram-positive bacteria through modulation of peptidoglycan, Reg3β defends against Gram-negative bacteria, including *E. coli*. Our laboratory has previously demonstrated that acute alcohol (ethanol) exposure prior to burn injury results in intestinal T cell immune suppression as well as enhanced bacterial translocation. Clinically, adult burn patients with a measureable blood ethanol level at the time of hospital admission have an increased risk of morbidity and mortality. This study examined the effects of ethanol exposure and burn injury on intestinal tissues levels of IL-22 as well as expression of Reg3β and Reg3γ. Male mice, ~25 g, were gavaged with ethanol (2.9mg/kg) to achieve blood ethanol levels of 90–100 mg/dL prior to receiving a 12–15% total body surface area full thickness burn. Animals were sacrificed one day post injury and intestinal tissue homogenized for IL-22 measurement by ELISA or RNA extracted for analysis of Reg3β and Reg3γ mRNA expression. When combined with ethanol intoxication, burn injury results in a decrease in intestinal IL-22 (90%, $p<0.01$) as compared to burn injury alone. Moreover, acute ethanol exposure prior to burn decreases expression of Reg3β and Reg3γ (75% and 78%, respectively, $p<0.05$), as compared to sham injury. These finding suggest that acute alcohol intoxication perturbs intestinal IL-22 and subsequent expression of AMPs Reg3β and Reg3γ, following burn injury. Together this may contribute to increased bacterial translocation following combined insult.
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0085

ACUTE ALCOHOL INTOXICATION DOWN-REGULATES T CELL microRNA-155 and microRNA-182 EXPRESSION FOLLOWING BURN INJURY

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MicroRNAs (miRNAs) are a class of small non-coding RNAs (approx. 20–25 nucleotides in length) that post-transcriptionally regulate gene expression and play an important role in T cell differentiation, proliferation and apoptosis. Previous studies from our laboratory show that acute ethanol (EtOH) intoxication combined with burn injury suppresses T cell IL-2 and IFN-γ production. In this study we determined whether acute alcohol intoxication combined with burn injury alters the expression of miRNA-155, miRNA-181a, miRNA-182 and miRNA-184 in T cells. Male C57BL/6 mice were divided into four groups: Sham Vehicle; Sham EtOH; Burn Vehicle and Burn EtOH. Animals were gavaged with H_2O or EtOH (2.9 mg/Kg) to achieve a blood EtOH level of ~100 mg/dL prior to receiving a ~12.5% total body surface area sham or burn injury. One day after injury, mice were sacrificed and spleen T cells were isolated. T cells were cultured with plate bound anti-CD3 (2μg/ml) for 24h and cells were harvested. miRNA was extracted and expression of miRNA-155, miRNA-181a, miRNA-182 and miRNA-184 was determined by qRT-PCR. No significant difference was observed in miRNA-181a and miRNA-184 expression in T cells from any group. However, a significant decrease in expression of miRNA-155 was observed in T cell obtained from burn EtOH animals, as compared with shams. A tendency towards a decrease in T cell miRNA-155 expression was observed in T cells obtained from burn injury alone animals, but this did not reach statistical significance, as compared with sham animals. Furthermore, there was significant decrease in T cell miRNA-182 expression in burn EtOH group, as compared to others. To confirm a relationship between decreased miRNA-155/miRNA-182 and IFN-γ/IL-2 production, T cells from sham vehicle and burn EtOH animals were cultured with anti-CD3 for 48h, T cells were collected to determine miRNA-155 and miRNA-182 expression, and cell culture supernatants were harvested to measure IL-2 and IFN-γ by ELISA. We observed a significant decrease in T cell miRNA-155 and miRNA-182 expression, as well as in IL-2 and IFN-γ production, following alcohol and burn injury, as compared with sham animals. These findings suggest that acute alcohol intoxication combined with burn injury down-regulates expression of miRNA-155 and miRNA-182, which may play a role in suppression of IL-2 and IFN-γ production. (NIH R01AA015731 (MAC), F30AA020167 (JLR) and the Dr. Ralph and Marian C. Falk Medical Research Trust).

0086

IMPACT OF ETHANOL ADMINISTRATION ON MYCOBACTERIUM TUBERCULOSIS INFECTION IN RHESUS MACAQUES

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Purpose: Ethanol has been linked to worsened infection with *Mycobacterium tuberculosis* (Mtb) in humans and mice. It is not known if Mtb infection in nonhuman primates (NHP) is also adversely affected by ethanol.
Methods: We used an established 5 hour per day, 7 day per week regimen of intragastric ethanol administration to 6 nonhuman primate (NHP) rhesus macaques at the Tulane National Research Primate Center (TNRPC) for 11 weeks, following a 6 week period for jacket and tethering conditioning prior to gastrostomy tube placement. Four of the NHPs were then infected with Mtb CDC1551 at a dose of 250–500 cfu by aerosol inoculation. Body weights, temperature, blood alcohol levels, CXR, blood chemistries and bronchoalveolar lavages (BAL) were done pre- and post-infection. BAL fluid and blood were analyzed by flow cytometry pre-infection, 2 and 4 weeks post-infection, and at the 6 week necropsy. Also at necropsy, lung cultures and flow cytometry of lung tissues were performed, and lung tissues banked.
Results: During ethanol feedings, blood alcohol levels ranged between 55–62 mM. Ethanol significantly increased the lung burden of Mtb 6 weeks after infection compared to historic control Mtb-infected NHPs, but systemic and lung inflammatory profiles were not altered significantly. Body weights, temperatures, and blood C-reactive protein levels were likewise not different from control NHPs.
Conclusion: Despite lack of systemic signs of infection, ethanol consumption by NHPs adversely alters the containment of Mtb in the lung. We speculate that ethanol impacts control of NHP Mtb infection by altering inflammatory events in the innate and/or adaptive arms of the immune system.
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0087

ACUTE ALCOHOL INHIBITS STAT3 INDUCTION OF REG3G IN PULMONARY EPITHELIUM DURING MRSA PNEUMONIA IN MICE

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RATIONALE: The incidence of community-associated Methicillin-resistant *Staphylococcus aureus* (CA-MRSA) pneumonia in previously healthy individuals has increased in the past 5 years. Such infections are associated with bronchiectasis, compromised lung function, and high mortality rates, making it a significant public health concern. The mechanisms of pulmonary host defense against this pathogen are not characterized. However, patients diagnosed with MRSA, as opposed to MSSA are more likely to have abused alcohol in the past and these patients are more likely to die from sepsis. In the United States, USA300 is the predominant strain that causes necrotizing pneumonia leading to destruction of lung function.
METHODS: To investigate whether acute ethanol exacerbates MRSA pneumonia, mice were intraperitoneally administered of 4.0 g/kg of EtOH (20% v/v) 30 minutes before oropharygeal aspiration of $2x10^7$ CFU of USA300.
RESULTS: Increased pulmonary bacterial burden in alcohol mice at 16 and 24 hours was associated with decreased levels of interleukin (IL)-6, IP-10, and RANTES. IL-6 activates STAT3 as part of acute phase response of infection. Reg3γ, an antimicrobial c-type lectin, is induced by signal transducer and activator of transcription 3 (STAT3) signaling in the paneth cells in response to gram-positive bacteria found in the gut. In addition to being expressed in paneth cells, we show by *in situ* hybridization that Reg3 γ is also expressed lung epithelium. Moreover, *in vitro* EtOH (50 mM) inhibits IL-6 induction of STAT3-luciferase-reporter signaling and Reg3 γ expression in mouse lung epithelial (MLE12) cells. Furthermore, pulmonary administration of recombinant Reg3γ four hours after MRSA infection in alcohol mice rescues USA300 clearance.
CONCLUSION: Acute alcohol intoxication leads to decreased MRSA clearance from lung by inhibiting IL-6/STAT3 induction of antimicrobial protein, Reg3 γ, by pulmonary epithelium.
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0088

CHRONIC ALCOHOL SUPPRESSES THE TH17 RESPONSE AND DELAYS BACTERIAL CLEARANCE IN RHESUS MACAQUE WITH PULMONARY *S. PNEUMONIAE* INFECTION

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Background: Bacterial pneumonia is the most common cause of lower respiratory tract infection in immunocompromised populations, including the alcohol-abusing patient. Chronic alcohol exposure suppresses the immune system by decreasing the recruitment and activation of immune cells such as T cells. Th17 cells are a distinct T helper cell lineage essential to host defense against extracellular bacteria. The aim of this study is to investigate the effects of chronic alcohol administration on Th17 responses against *S. pneumoniae* infection in Rhesus Macaques.
Methods: Chronic binge alcohol consumption was established by feeding ethanol via a permanently indwelling intragastric catheter once a day to achieve a plasma ethanol concentration of 50 to 60 mM at 2 hours after alcohol feeding. Control macaques were infused isocaloric sucrose. After 7 months of alcohol or sucrose feeding, animals were infected with *S. Pneumoniae* in the right lower lobe of lung. PBMCs were obtained at one month prior, day 0, day 1, day 3 and day 7 post infection. Cells were cultured in the presence of heat-killed *S. Pneumoniae* or anti-CD3/CD28 for 96h. Th1 cytokines IFN-γ, Th2 cytokines IL-4, IL-5, IL-13 and Th17 cytokines IL-17 and IL-22 levels in the culture supernatants were analyzed by Luminex and ELISA. IL-17 and IL-22 producing cells were analyzed by flow cytometry. Bronchial brushings and BAL cell pellets were also harvested and gene expression analyzed by real-time RT-PCR. Bacterial counts in BAL fluid were also analyzed.
Results: Alcohol had no effect on the Th1 or Th2 responses. Alcohol had minimal effects on the Th17 responses pre-infection, or days 0, 1 and 3 post infection. However, animals receiving chronic alcohol feeding had a significant decrease in Th17 response at Day 7. Epithelial anti-microbial gene expression was also suppressed by alcohol feeding. Alcohol fed but not sucrose fed animals had *S. Pneumoniae* culture positive BAL fluids on Day 7 post infection.
Conclusions: Chronic alcohol consumption delayed *S. pneumoniae* clearance which was associated with late suppression of the circulating Th17 response.
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0089

EFFECTS OF ALCOHOL CONSUMPTION ON ANTIGEN-SPECIFIC CELLULAR IMMUNE RESPONSES TO SIV IN RHESUS MACAQUES

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Background: We have previously shown simian immunodeficiency virus (SIV) infection in macaques chronically receiving alcohol results in significantly higher plasma viral loads and more rapid progression to disease. However, the mechanisms resulting in the increased viral replication associated with alcohol use are not clear. The objective of the current study was to determine if there was an indirect correlation between virus-specific cellular immune responses and the increased viremia observed in alcohol treated animals. Our hypothesis was that the increased plasma viral load in alcohol treated macaques would correlate with an absence of, or lower antigen-specific cytokine responses in this model.
Methods: Rhesus macaques were administered ethanol or caloric matched sucrose (n=12 per group) by indwelling gastric catheter 4 days/wk for 3 months, and then intravenously infected with SIVmac251. Blood was examined for plasma viremia and virus-specific cellular immune responses to SIV Nef, Gag or Env peptide pools using a cytokine flow cytometry assay to detect virus specific IFN γ and TNF α responses.
Results: Surprisingly, animals receiving alcohol had significantly higher levels of virus-specific responses compared to the sucrose-treated group. As expected, the emergence of virus specific cytokine responses temporally correlated with the decline in mean plasma viral load after 14 days pi in both the alcohol and sucrose treated groups of SIV infected animals, suggestive of at least a partial role of virus specific cellular responses in regulating early plasma viremia. However, neither the breadth, specificity nor the magnitude of virus-specific CD8+ T cell responses correlated with the early post peak reductions in plasma viral loads. In fact, CTL responses to pools of gag, gp41, gp120, and Nef were higher in animals receiving alcohol compared to controls, suggesting that CTL directly correlated with viremia/antigen persistence, rather than alcohol use.
Conclusions: Impaired or diminished virus specific cellular immune responses do not seem to play a role in the higher viral loads observed in macaques receiving alcohol. Persistently higher CTL responses in animals receiving alcohol are likely an effect of the higher viral loads and antigen persistence rather than a cause of the increased viremia.

0090

ALCOHOL AND HIV-ANTIRETROVIRAL THERAPY INDUCED LIVER INJURY

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Antiretroviral therapies (ART) used to treat human immunodeficiency virus (HIV) infection produce direct adverse drug reactions (ADR) that are encountered predominantly in the liver. Moreover ART in combination with ethanol consumption may induce idiosyncratic reactions including hypersensitivity syndrome reactions. Highly active antiretroviral therapy (HAART) has a positive influence on the quality of life and longevity in HIV patients. However, HAART produces a spectrum of ADRs. Alcohol consumption can interact with HAART. Other co-infections that occur in HIV, such as hepatitis viruses B or C, cytomegalovirus, or herpes simplex virus, pneumonia and tuberculosis, further complicate the etiology of HAART-induced ADRs. The aspect of liver pathology including liver structure and function are crucial to patient safety.
The materials used provide a data-supported approach. They are based on systematic review and analysis of recently published world literature (MedLine search) and the experience of the authors in the specified topic.
We conclude that therapeutic and drug monitoring of ART, using laboratory identification of phenotypic susceptibilities, drug interactions with other medications, drug interactions with herbal medicines and alcohol intake might enable a safer use of this medication.

0091

CHRONIC ETHANOL (ETOH) FEEDING RESULTS IN T CELL SUBSET LOSS AND HYPO-RESPONSIVENESS IN THE SKIN AND SKIN DRAINING LYMPH NODES (SDLNS)

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Infection is a prominent cutaneous manifestation of alcoholism. While the basis for this requires further clarification, the sensitivity of skin immune cells to EtOH has been demonstrated. Murine models of alcoholism have shown that EtOH reduces skin dendritic cell (DC) numbers and compromises their migratory capacity following skin sensitization. In addition to DCs, the skin is home to multiple T cell subsets, which play pivotal roles in skin immunity. T cells are the primary source of IL17, which is essential for host defense against cutaneous bacterial infection. The extent to which T cell alterations contribute EtOH induced cutaneous immune deficiency is unknown. We used cell culture and flow cytometry to study the effects of EtOH feeding on skin T cell maintenance and function. In the epidermis, EtOH feeding caused a reduction of dendritic epidermal T cells (DETCs). The reduction in DETC numbers corresponded with decreased expression of the co-stimulatory molecules JAML, CD69 and NKG2D following short-term stimulation with PMA/ionomycin (PMA/I). In the dermis, EtOH feeding resulted in a reduction in the baseline number of CD103+ FoxP3+ T regulatory cells (Tregs) as well as both Vγ3+ and Vγ3- subsets of dermal $\gamma\delta$ T cells. As in the epidermis, the EtOH induced numeric defects corresponded with T cell hypo-responsiveness. Following short-term stimulation with either anti-CD3 or PMA/I, a reduction in IL17 production was observed in Th17 cells. An inspection of analogous T cell populations in the SDLNs revealed that EtOH induced a similar reduction in the number of CD103+ FoxP3+ Tregs. Additionally, diminished IL17 production by $\gamma\delta$ T cells was observed in SDLN suspensions prepared from EtOH fed mice. Tumor necrosis factor-α (TNF-α) is a major mediator of EtOH induced tissue damage and inhibition of TNF-α signaling has been shown to protect against numerous EtOH induced lesions. We used TNF receptor 1 (TNF-R1) knock out (KO) mice to determine if TNF-α signaling underlies the skin T cell defects occurring in EtOH fed mice. We found that TNF-R1 KO mice were not protected from EtOH induced T cell subset loss suggesting that the Thurman cascade does not impact the maintenance of skin T cells. Given the importance of T cells to cutaneous immunity, EtOH induced perturbation of their maintenance and function may help explain why alcoholics are more susceptible to skin infection than non-alcoholics. This work was supported by NIH R01 AA019438 and AA019568.

0092

MODERATE ETHANOL EXPOSURE AND REACTIVE OXYGEN SPECIES EXPOSURE IMPAIRS EPIDERMAL ANTIMICROBIAL RESPONSES

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Alcohol intoxication prior to injury augments the severity and frequency of cutaneous wound infections and delays wound closure. Since over half of trauma patients have positive blood alcohol levels, our goal was to understand how moderate ethanol exposure and the byproducts of its metabolism, such as hydrogen peroxide (H_2O_2) reactive oxygen species (ROS), modulate normal wound healing and antimicrobial responses. In this study, we first utilized an excisional wound infection model with *Staphylococcus aureus* in mice exposed to multi-day binge ethanol to assess the levels of candidate antimicrobial peptides (AMPs) by immunohistochemical (IHC) analyses. We previously demonstrated that acute ethanol exposure prior to excisional wounding in mice delayed wound healing and limited the response to infection. When compared to control mice, infected wounds from ethanol treated mice had a robust decrease in the candidate AMPs, Cathelicidin-Related Antimicrobial Protein (CRAMP) and mouse Beta-Defensin-3 (mBD3). We then investigated the direct effect of ethanol and ROS exposure on the gene expression of AMPs and AMP-dependent proteins in normal human epidermal keratinocytes (NHEKs) by quantitative PCR (qPCR). We found that the relative gene expression of *Cathelicidin* (*CAMP*) and human Beta-Defensin-2 (*hBD2)* AMPs was decreased in ethanol-exposed NHEKs compared to vehicle-treated NHEKs in response to 1,25-$(OH)_2$ Vitamin D3 ($VitD_3$) and Macrophage-Activating Lipoprotein-2 (MALP-2), factors which are known to induce epidermal AMPs. Furthermore, we determined that pretreatment with H_2O_2 decreased the relative expression of $VitD_3$+MALP-2 induced *hBD2* and the expression of the microbial pattern recognition receptors, *Cluster of Differentiation 14* (*CD14*) and *Toll-like Receptor 2* (*TLR2*) expression in NHEKs. This suggests that ROS regulates keratinocyte innate immune responses. Hence, altered AMPs or microbial pattern recognition receptors (TLR2/CD14) may increase the susceptibility to wound infection and delayed wound closure observed in our murine model and in trauma patients who have a positive blood alcohol level at the time of injury. (Supported by NIH AA012034 (EJK), AA013527 (EJK) and the Ralph and Marian C Falk Medical Research Trust)

0093

ALCOHOL IMPAIRS MARROW LKS CELL PROLIFERATION IN RESPONSE TO BACTEREMIA

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Alcohol abusers with serious bacterial infection frequently present with granulocytopenia which predicts poor outcomes. Previous studies from our group have shown that marrow lineage $(lin)^-$stem cell factor receptor $(c\text{-}kit)^+$stem cell antigen-1 $(Sca\text{-}1)^+$ (LKS) cells increase their proliferation during bacterial infection. This enhancement of LKS cell proliferation supports the granulopoietic response. To determine whether alcohol affects the increase in primitive hematopoietic precursor cell commitment to granulocyte lineage development in response to systemic bacterial infection, acute alcohol intoxication was induced in mice maintained on a Lieber-DeCarli low fat liquid alcohol diet for 5 weeks by intraperitoneal injection (i.p.) of alcohol (20% alcohol in saline at a dose of 5 g alcohol/kg). Control animals on the Lieber-DeCarli low fat liquid control diet received i.p. injection of saline. Thirty minutes after the i.p. injection, *E. coli* (1×10^6 or 5×10^7 CFUs/mouse) or saline was given to mice by penile vein injection. Intravenous BrdU (1 mg/mouse) was administered 24 hours before the termination of each experiment. The number of LKS cells in the bone marrow increased significantly 24 hours post *E. coli* infection. Bacteremia stimulated marrow LKS cell proliferation as reflected by a significant increase in BrdU incorporation into these primitive hematopoietic precursors. Alcohol treatment impaired this LKS cell proliferative response. Following the systemic *E. coli* challenge, marrow granulocyte lineage committed cells bearing granulocyte lineage marker Gr1 also showed an increase in Sca-1 expression. Alcohol administration suppressed this increase in Sca-1 expression in marrow $Gr1^+$ cells. Alcohol treatment also blocked the increase in the number circulating PMNs 48 hours after challenge with 5×10^7 *E. coli* and impaired bacterial clearance from the circulation as well as vital organ tissues following bacteremia. Our results indicate that excessive alcohol intake impairs the proliferative expansion of marrow LKS cells. This defect of LKS cell proliferation restricts the granulopoietic response at the initial stage of increase in primitive hematopoietic precursor cell commitment to granulocyte lineage development (Supported by NIH R01AA019676).

0094

EFFECTS OF ACETALDEHYDE ON HLA-DR AND IL-6R EXPRESSION IN THP-1 MONOCYTES

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The balance between alcohol and acetaldehyde oxidation rates and their resultant plasma concentrations may impact an individual's response to pathogenic or traumatic insult. Monocytes contribute significantly to the systemic inflammatory response after injury and patterns of aberrant monocyte activation characterize and sustain chronic inflammation disorders. The aim of this study was to determine the effect of acetaldehyde (AA) on the expression of CD40, CD86 and HLA-DR, receptors involved in antigen presentation, and on IL-6R, which plays a role in monocyte differentiation to dendritic cells.
Methods: THP-1 monocytes were pretreated with AA (5 or 25 μM) for 2 hours before being stimulated with LPS (20 ng/mL), in the absence or presence of AA, for 24 hours. Expression of CD40, CD86, HLA-DR and IL-6R was determined by FACS analysis.
Results: While AA had no effect on CD40 and CD86 expression it increased the percentage of IL-6R positive monocytes by ~20% at both 5μM and 25μM (74.0±4.3 vs 89.2±3.2 and 86.7±1.7, n=5, $p<0.05$), when compared to untreated control. IL-6R mean fluorescent intensity (MFI) was also increased in these cells, with a 76% increase in the presence of 5μM and a 53% increase in the presence of 25μM. AA treatment increased the number of HLA-DR positive monocytes, by 50% and 65% for 5μM and 25μM, respectively, when compared to control and MFI was also increased, by ~90% for both 5μM and 25μM treatments (47.5±8.8 vs 83.8±8.4 and 93.5±25.6, n=4, $p<0.05$). There was a decrease in the number of IL-6R positive monocytes and IL-6R MFI when cells were exposed to LPS, with an additional 15% and 35% decrease in the presence of LPS and 5 μM or 25 μM AA, respectively. IL-6R MFI was also further reduced by 35% and 50% when monocytes were coincubated with LPS and 5 μM and 25 μM AA, respectively. When monocytes were stimulated with LPS there was a 2.5 fold increase in the both the number of HLA-DR positive cells and the HLA-DR MFI. Coincubation with AA significantly inhibited the LPS-mediated increase in HLA-DR positive cells by ~35% (5 or 25 μM) and the MFI was reduced by 40% and 35% in the presence of 5 and 25 μM AA, respectively.
Conclusion: Acetaldehyde, at physiologically relevant concentrations, differentially affected both the basal and LPS-mediated levels of HLA-DR and IL-6R in THP-1 monocytes. These effects of acetaldehyde may contribute, in part, to the abnormal immune response observed in patients following alcohol intoxication or abuse.

0095

ALTERATIONS IN SERUM CYTOKINES, CHEMOKINES, INTERFERONS, GROWTH FACTORS AND C-REACTIVE PROTEIN IN ALCOHOL-DEPENDENT INDIVIDUALS COMPARED WITH SOCIAL DRINKERS

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Preclinical research has implicated immune system dysregulation in models of alcohol dependence. However, a detailed study examining inflammatory markers levels in alcohol-dependent individuals has not been performed. Group differences in a panel of serum inflammatory markers that included the pro- (interleukin-1β (IL-1β), IL-6, IL- 12 (IL-12 p40), IL-18, tumor necrosis factor-α (TNFα), soluble TNF receptor-type 1 (sTNFR1) and anti-(IL-4, IL-10) inflammatory cytokines, chemokines (macrophage inhibitory factor 1 (MIF-1), macrophage inflammatory protein 1(MIP-1), monocyte chemotactic protein 1 (MCP-1), interferons (INF-α), the acute phase C-reactive protein (CRP) and the anti-inflammatory growth factor, transforming growth factor- β (TGF- β), were assessed over two separate days, in thirty-four recently abstinent, treatment-seeking alcohol dependent (AD) individuals and 35 demographically matched social drinkers (SDs) using the enzyme-linked immunosorbent assay (ELISA). Significantly higher mean (±sd) in the pro-inflammatory markers IL-1β ($p<0.05$), MCP-1 ($p<0.05$), IL-18 ($p<0.001$) and CRP ($p<0.05$), were observed for the AD group compared to the SDs. AD patients also demonstrated significantly lower levels of the anti-inflammatory markers IL-4 ($p<0.01$), IL-10 ($p<0.01$) and TGF-β ($p<0.05$) compared with SDs. These results suggest an induction of a persistent state of chronic inflammation in alcoholics that involves a shift in the homeostatic balance of specific pro/anti-inflammatory markers. Further characterization of IL-1β, MCP-1, IL-18, IL-4, IL-10, TGF-β and CRP as predictors or surrogate markers of chronic alcohol abuse and their roles in relapse outcomes is warranted (supported by R01-AA013892; UL1-DE-19586).

0096

MICROGLIAL CHANGES PERSISTS TWENTY EIGHT DAYS FOLLOWING BINGE ETHANOL EXPOSURE IN THE HIPPOCAMPUS

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Excessive alcohol intake, characteristic of an alcohol use disorder (AUD), results in hippocampal neurodegeneration which has been linked to a variety of cognitive deficits. Neuroinflammation is thought to be one of the factors leading to neurodegeneration, and microglia activation is a key component of the neuroinflammatory response. We have shown previously that microglia react in a binge model of an AUD, including microglia proliferation 2 days after exposure. However, it is not known if this proliferation event affects the number of microglia or how long microglial activation persists. Therefore, we quantified the number of microglia and assessed whether they appeared activated 28 days following the Majchrowicz four-day binge paradigm. In this model, adult male Sprague-Dawley rats received ethanol (25% w/v) in nutritionally complete diet 3x a day for four days with an initial dose of 5g/kg with later doses based on intoxication levels. This model resulted in 9.3g/kg/day of ethanol, which produced an average blood ethanol concentration of 405mg/dL. Twenty-eight days following ethanol exposure, perfused rat brains were obtained and stained with Iba-1, a calcium binding protein that labels all microglia. Microglial cells in the subregions of the hippocampus (dentate gyrus, CA1, and CA2/CA3 fields) were quantified by stereology. Simultaneously, microglia cell morphology was qualitatively assessed. Microglia were characterized as resting, activated, or phagocytic based on ramified, bushy, or amoeboid morphology, respectively. There was a 76% increase ($p< 0.05$) in the number of microglia in the CA2/CA3 region of ethanol treated animals (25,654 ± 1743 cells, n=8) compared with controls (19495 ± 1974 cells, n=7) but no significant differences in the dentate gyrus or CA1. The change in number did not correlate to an increase in the activation of the microglia. Based on morphology, more activated microglia were observed in the CA1 region of ethanol exposed animals (12.6 ± 0.1%) compared to controls (9.2 ± .1%; $p< 0.05$) but not in the CA2/CA3 or dentate gyrus. This data provides further evidence that the change in microglia activity persists following binge ethanol exposure. Persistent microglia activation is associated with neurodegeneration and could therefore be detrimental in chronic alcohol abuse.
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0097

IN SILICO ANALYSES PREDICT AN AGE EFFECT OF MINOCYCLINE TREATMENT OUTCOMES

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Complex responses to alcohol consumption pose challenges with respect to defining targets and developing pharmacotherapeutics for alcoholism. In silico bioinformatics analyses of a whole genome, brain microarray screen completed for "Drinking in Dark" (DID) ethanol-exposed adolescent and adult FVB/NJ x C57BL/6J F1 hybrid mice identified several over-represented pathways for both age groups, generating a new hypothesis: that neuroimmune function is an important ethanol response factor in adult, but not, adolescent mice. Hence, we tested our hypothesis using the known neuroimmune modulator, minocycline. Ethanol intake was measured under a standard 4hr/day, 4 day duration, DID paradigm and included treatment with 50 mg/kg minocycline or saline 20 hrs prior to ethanol administration. Minocycline caused significant reduction in ethanol drinking in the adult male (n=9, $p < 0.05$) and female (n=11, $p < 0.001$) mice but had no effect on the adolescent male (n=7, p=ns) and female (n=9, p=ns) mice when compared to age and gender matched mice treated with saline. Minocycline treatment caused no change in the blood ethanol levels in the adolescent and adult, male and female mice (p=ns). Furthermore, ethanol elimination analysis was performed in the adult mice following minocycline administration to evaluate its effect on pharmacokinetic properties of ethanol as a possible confounding mechanism in reducing ethanol consumption. Minocycline or saline were administered i.p. to adult mice 20 hrs prior to 4g/kg i.g. ethanol. Blood samples were drawn at 90, 120, 150, and 180 min post-gavage to obtain a blood profile during the elimination phase of ethanol. Minocycline treatment did not alter the pharmacokinetics of ethanol in the adult mice as suggested by the lack of any significant difference in the slope of the elimination curve between the saline and minocycline treated male (n=4 for saline, n=6 for minocycline, p=ns) and female (n=7 for saline, n=7 for minocycline, p=ns) mice. These results are suggestive of a pharmacodynamic, rather than a pharmacokinetic, effect of minocycline in reducing ethanol consumption. Overall, our study, initiated as a result of bioinformatics analyses, suggests that neuroimmune pathways may form a good target, and anti-inflammatory drugs may form a new treatment against late, but not, early onset alcoholism. (Supported by NIAAA INIA grant U01AA13475 and the South Plains Alcohol and Addiction Research Center.)

0098

ALCOHOL AND RAC2 MEDIATED SIGNALING IN THE EXPRESSION OF INFLAMMATORY CYTOKINES IN MOUSE DERIVED MACROPHAGES

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BACKGROUND: It is well known that acute ethanol exposure increases the risk for acute lung injury and susceptibility to infection. Alveolar macrophages play a central role in host defense against infection by many pathogens but also in regulation of immune responses and inflammation. In this study we investigated the molecular role of small GTPase Rac and acute ethanol exposure on bone marrow-derived macrophages (BMDM) isolated from WT and Rac2 null mice and monitored their role in TLR4 mediated expression of cytokines and chemokines.
METHODS: We isolated BMDM from 8-10wk old C57BL/6 male mice. BMDM were cultured as described in our published results (Azim et al, Am J Physiol Lung Cell Mol Physiol. 2007). Isolated BMDM were harvested and treated with 25 mM of ethanol in ethanol saturated chambers for more than 3 hours prior to,lipopolysaccharide (100 ng LPS) stimulation. Supernatants were collected and subjected to cytokine assay by using Bio-Rad multiplex assay kit.
RESULTS: Our results suggest a key role of small GTPase Rac2 as a key regulator in the expression of cytokines and chemokines in response to endotoxin. Rac2 null mice derived macrophages showed 2.5 fold less expression of IL-8 in response to LPS and ethanol treatment than the WT cells. On the contrary Rac2 null mice derived macrophages showed 3 fold increase in the expression of IL-12p40/IL-23. TNF-α was reduced 1.5 fold under similar conditions. Interestingly IL-6 and IL-10 levels were unaffected.
CONCLUSIONS: Acute alcohol exposure and small GTPase Rac2 play an important role in the regulation of IL-8, IL-12p40, TNF-α but not IL-6 and IL—10 after TLR4 receptor ligation. Our results suggest that alcohol and small GTPase Rac2 modulate TLR4 receptor and affect the downstream transcription factors in the expressiom of cytokine and chemokines.

0099

P2X7 RECEPTORS PLAY A ROLE IN ACUTE AND CHRONIC ALCOHOL-INDUCED NEUROINFLAMMATION

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Alcohol exposure leads to immune disturbances that may contribute to neuroinflammation and brain damage. Evidence suggests that ATP-gated purinergic P2X7 receptors (P2X7Rs) are important mediators of neuroimmune responses. P2X7Rs can exert dual roles, contributing to neuroinflammation and neuroprotection. The contribution of P2X7Rs to alcohol-induced processes of neuroinflammation/neuroprotection is unknown. Building evidence suggests that alcohol differentially affects the immune response depending on the length and amount of alcohol exposure. The present study tests the hypothesis that P2X7Rs play a role in acute and chronic alcohol-induced neuroinflammation. To test this hypothesis, we determined the effects of alcohol on P2X7R expression in hypothalamus, amygdala, prefrontal cortex, hippocampus, midbrain, striatum, thalamus and cerebellum using short- and long-term alcohol exposures. Ten days of alcohol exposure of C57Bl/6 mice using a two-bottle choice drinking paradigm (10% v/v, 8–10 g/kg/day) increased P2X7R protein expression levels in the amygdala, hippocampus and midbrain. In contrast to the 2-bottle choice paradigm, alcohol consumption for 2 weeks in a single-bottle no choice model (20% v/v) that produced significantly higher levels of alcohol consumption (25–30 g/kg/day), significantly reduced P2X7R expression levels in the amygdala, prefrontal cortex and hippocampus. Moreover, alcohol consumption in the single bottle model for 3 months significantly reduced P2X7R protein expression in all tested brain regions except thalamus and cerebellum. Initial studies tested for possible involvement of P2X7Rs in alcohol-induced modulation of neuroinflammatory responses by measuring secretion of IL-1b from cultured BV2 microglia. ATP-activation of P2X7Rs enhanced acute ethanol (24 h) increase of LPS-induced IL-1β release. Collectively, the results suggest that: the effects of alcohol on P2X7R expression depend on the: 1) amount and length of alcohol exposure and 2) specific brain region. Overall, our findings suggest that P2X7Rs play an important role in alcohol-induced modulation of neuroimmune responses. Hence, pharmacological modulation of P2X7R activity and/or expression during acute and chronic ethanol exposure may provide a novel approach for reducing alcohol-induced neuroinflammation and resultant brain damage. [Support: NIAAA/NIH AA017243, 017029, 13992, 03972 and the USC School of Pharmacy]

0100

ADULT RATS SUBJECTED TO REPETITIVE BINGE-PATTERN ETHANOL EXPOSURE SHOW EVIDENCE OF NEUROINFLAMMATION INVOLVING ELEVATED AQUAPORIN-4, PLA2 AND PARP-1

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Prolonged binge ethanol treatment in adult rats causes neurodegeneration and neuroinflammation in hippocampus (HC) and entorhinal cortex (ECX), but the mechanisms are unresolved. We examined whether a repetitive binge-pattern ethanol protocol (Przybycien-Szymanska et al., PLoS ONE 2011:e18350) activated neuroinflammatory pathways in these brain regions that entail aquaporin-4 (AQP4) water channels, phospholipase A2 (PLA2) enzymes, poly (ADP-ribose) polymerase (PARP-1) and caspase-3. Male Wistar rats, ethanol-intoxicated (3 g/kg/d i.p.) for 6 d beginning at 68 d of age, were sacrificed 1 hr after the last dose (BEL, ~200 mg/dl); other rats were given the binge treatment as juveniles (age 37 d) prior to adult binging, and controls received saline treatments at both ages. Immunoblot assays revealed that the adult binge ethanol exposure significantly increased AQP4 ~50% in both brain regions, but not in the ECX of rats previously juvenile-binged. Ca^{+2}-dependent PLA2 (cPLA2 IVA) and its activated phospho-form (p-cPLA2) were elevated 2- to 4-fold in both regions after adult-binging; however, hippocampal p-cPLA2 was unchanged in adult-binged rats that were juvenile-binged. In addition, secretory PLA2 (sPLA2 IIA) in adult-binged rats was significantly increased ~2-fold in the HC, with a similar ECX elevation that did not reach statistical significance. In contrast, Ca^{+2}-independent PLA2 (iPLA2 VI) levels in HC and ECX were reduced ~50% by the adult binge, with a preceding juvenile binge tending to normalize ECX levels in adults. Interestingly, these PLA2 changes in binged adults resemble those reported in rats fed omega-3 fatty acid-deficient diets. Although neurodegenerating cells were not measured, robust elevations in PARP-1 and cleaved (89 kD) PARP in HC and ECX along with negligible caspase-3 activation after adult binging indicated a non-apoptotic neurodamage process termed "parthanatos". Requiring further study is possible cellular tolerance implied in the neutralization by juvenile binging of selected adult binge effects. Overall, binge-pattern ethanol exposure promoted a neuroinflammatory process involving PLA2-based activation in concert with elevated AQP4 and potential PARP-1-mediated parthanatos. The data shed light on possible unappreciated molecular mechanisms of neurodegeneration in binging alcoholics that could lead to therapeutic interventions. Supported by NIH AA018279, AA013527, AA018398 and the Loyola Alcohol Research Program.

0101

PHOSPHOLIPASE A2 (PLA2) ACTIVATION IN REPETITIVE BINGE ETHANOL-INDUCED OXIDATIVE STRESS AND NEURODAMAGE IN RAT ADOLESCENT BRAIN SLICES IN CULTURE

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Experiments with rat organotypic hippocampal-entorhinal cortical (HEC) slice cultures of 3–4 wks brain age have indicated neuroinflammatory pathways possibly important in neurodegeneration caused by repetitive ethanol exposure and withdrawals. Our laboratories have reported that binge ethanol-induced neurodamage in HEC cultures is downstream of augmented arachidonic acid (AA) liberation, as both AA release and neurodegeneration are blocked by a general inhibitor of phospholipase A2 (PLA2), an enzyme superfamily often considered rate-controlling for AA-derived neuroinflammation. Indeed, our accompanying abstract describes significant increases in PLA2 members in the above brain regions of adult rats after binge-pattern ethanol exposure (Tajuddin et al.). However, hydrolysis of the endocannabinoid, 2-monoarachidonylglycerol (MAG), *via* MAG lipase (MAGL) has been reported crucial in providing AA for prostaglandins during brain neuroimmune insults (Nomura et al., Science 334:809, 2011). We used relatively specific inhibitors to ascertain the PLA2 families involved in binge ethanol-dependent oxidative stress and neurodamage in HEC slice cultures, and whether MAGL also plays a role. The results implicate secretory PLA2 (sPLA2) and Ca^{+2}-independent PLA2 (iPLA2)—but surprisingly, not Ca^{+2}-dependent cPLA2 (cPLA2)—in oxidative stress (elevated protein nitrotyrosine and 4-hydroxynonenal) and/or neurodegeneration (increased propidium iodide staining) provoked in adolescent-age HEC slices by binge-pattern ethanol (100 mM with 4 withdrawals over 6 days). The increased sPLA2 is consistent with *in vivo* findings in adult rats after binge-pattern ethanol, but the other PLA2s differ (increased cPLA2 and reduced iPLA2 in Tajuddin et al.), which could be due to markedly dissimilar ethanol-induced signaling mechanisms in developing versus adult brain. Interestingly, the specific MAGL inhibitor, JZL184, failed to reduce neurodegeneration, arguing that binge ethanol-induced AA mobilization does not involve MAG hydrolysis in this *in vitro* adolescent model. These data point to neuroinflammatory PLA2 signaling components in ethanol's brain damage mechanism that, based on evidence with diuretics, we suggest are triggered by ethanol-induced brain edema and aquaporin-4 upregulation (Neurotox. Res. 21:70–78, 2012 and Tajuddin et al. abstract). Supported by NIH AA018279 and AA011543, and the Loyola Alcohol Research Program.

0102

LONG-TERM ALCOHOL CONSUMPTION INDUCES DNA DAMAGE AND NEURONAL CELL DEATH IN MOUSE BRAIN

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Chronic alcohol abuse results in a variety of pathological effects including damage to the brain. However, cellular and molecular mechanisms of alcohol-induced brain pathology are presently unclear. Alcohol metabolism generates potentially genotoxic reactive oxygen species (ROS) and acetaldehyde which can play roles in alcohol-induced neurotoxicity. Using histological (immunohistochemistry and stereological counting) and biochemical (LC/MS/MS and qPCR) assays, we show that chronic 3-week- exposure of mice to 5% ethanol (Lieber-deCarli diet) results in increased ROS- and acetaldehyde-produced DNA damage, reduced DNA repair and neuronal cell death (TUNEL staining) in parietal cortex and hippocampus. We also found that neurons in brains of mice chronically exposed to ethanol display protein PARylation, a marker of poly (ADP-ribose) polymerase-1 (PARP-1) activation, firmly implicated in DNA damage-induced cell death. Reduced DNA repair leading to genomic instability and extensive DNA damage are considered as unified genetic mechanism leading to variety of neurodegenerative disorders. We suggest that chronic alcohol-induced DNA repair dysfunction results from one-carbon metabolism (OCM) impairment, as evidenced by corresponding markers - a sustained hyperhomocysteinemia and global DNA hypomethylation. OCM is vital for both DNA methylation and synthesis of DNA precursors, and its dysfunction impacts genomic stability. We conclude that alcohol is genotoxic for neurons, and this genotoxicity may cause chronic alcohol-induced damage to the brain. This provides new insights into the mechanisms of chronic alcohol-induced brain damage.
This work is supported by grant from the Foundation for Alcohol Research and Alcoholism (IK) and the South Plains Alcohol and Addiction Research Center.

0103

INDICATION OF ER STRESS IN PURKINJE NEURONS OF ACUTE CEREBELLAR SLICES FROM ETHANOL FED ADULT F344 RATS

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Chronic ethanol consumption alters the morphology of the extensive Purkinje neuron (PN) smooth endoplasmic reticulum (SER), a component of the endoplasmic reticulum (ER). This laboratory has demonstrated decreases in the sarco/endoplasmic reticulum Ca^{2+} ATPase pump (SERCA2b) which may induce the ER stress response. The purpose of the present study was to determine whether hallmarks of the ER stress response, such as ATF6 cleavage and caspase-12 activation, were enhanced in cerebellar slices from chronically-fed ethanol rats. SER stress was induced in the slices by blocking the SERCA 2b pump with thapsigargin. Forty, eight mo old rats were fed the AIN-93 M ethanol or control diet (20/ group) for a period of 10 (14/group), 20 (10/ group), or 40 (16/ group) weeks. Rats were anesthetized and 300 μm acute cerebellar slices prepared by standard means. The first group of slices served as controls. The second group of slices were depolarized with KCl for 20 minutes and the KCl was then washed out. The third group of slices were simultaneously depolarized with KCl and exposed to 1μM thapsigargin for 20 minutes. KCl was then washed out of the slices and thapsigargin replaced. Following three hr in oxygenated ACSF, slices were removed, fixed, sectioned at 80 um, and double labeled with anti-ATF6 and anti-calbindin or an antibody against cleaved caspase-12 and anti-calbindin. Sections, labelled with fluorescent secondary antibodies, were photographed on a Zeiss Axioimager fluorescent microscope. Comparison of the images labeled with ATF6 and calbindin or activated caspase-12 and calbindin allowed for determination of the percentage of ATF6 and activated caspase-12 PN in a given field within each slice. ANOVA analysis of three pairs of 40 wk rats showed that the percentage of PN expressing the whole or cleaved form of ATF6 was not altered in ethanol-fed or control rats. The number of PN showing caspase-12 activation, however,was enhanced in thapsigargin-treated cerebellar slices from the ethanol-fed group (P=.01) but not in the pair-fed group (P=.95). Upon completion of analysis in the 40 week group, a finding of increased ethanol-induced caspase-12 activation would suggest that ethanol increases the susceptibility of the PN to ER stress. This would contribute to ethanol-related cerebellar dysfunction. Analysis of the 10 and 20 wk durations will determine the onset of this response. (Supported by NIAAA grant AA017195)

0104

A PUTATIVE ROLE OF CHOLINERGIC BASAL FOREBRAIN IN ALCOHOL AND NICOTINE CO-ABUSE

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Background: Nicotine and alcohol co-abuse is highly prevalent in society especially among college students. Clinical and pre-clinical studies also suggest that nicotine increases alcohol self-administration. Recently, cholinergic basal forebrain (BF) has been implicated in alcohol use disorders and nicotine addiction. Moreover, alcohol and nicotine independently activate the nucleus accumbens (NAc), a region critically involved in mediating drug reward. We hypothesize that nicotine via BF further enhance alcohol-induced activation of reward pathway suggesting a novel mechanism of their co-abuse.
Methods: Under aseptic conditions and using standard surgical procedure, male Sprague-Dawley rats (300–400g) were stereotaxically implanted with microinjector guide cannula in the brain targeting the BF region. After 5–7 days of surgery, rats were divided into two groups; control and experimental. At the dark onset, the experimental group received intra-BF microinjections of nicotine (500nl; 35ng; N=4), whereas, the control group was administered artificial cerebrospinal fluid (N=3). Immediately after nicotine, both the group was intragastrically administered alcohol (3g/Kg). After 2 hours, the rats were euthanized, brain removed and processed for c-Fos immunohistochemistry in the NAc.
Results: Our initial results suggest that BF administration of nicotine along with systemic alcohol showed significant ($p<0.05$) increase in the number of cells expressing c-Fos immunoreactivity in the NAc as compared to the alcohol treated controls.
Conclusions: Our preliminary results suggest that a) BF administration of nicotine coupled with systemic alcohol enhances the activation of anatomical substrate of reward pathway. b) BF may be an important neuroanatomical substrate for nicotine and alcohol co-abuse.

0105

INCREASE IN DOUBLECORTIN AND NEURO-D INDICATES AN INCREASE IN PROGENITOR CELLS AND NEUROGENESIS AFTER BINGE ETHANOL EXPOSURE IN ADOLESCENT RATS

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Alcohol use disorders like alcohol abuse are prevalent in adolescents and result in hippocampal neurodegeneration. Neural stem cells are instrumental to hippocampal structure and function and are affected by ethanol exposure. Recently, we discovered a reactive burst in neurogenesis at 7 days of abstinence in adolescent rats following binge ethanol exposure using the exogenous marker BromodeoxyUridine (BrdU). Therefore, we first confirmed increased neurogenesis with an endogenous marker of adult neurogenesis, Doublecortin (DCX). Then, we investigated NeuroD, a marker of type 2b and type 3 (neuroblasts) proliferating neural progenitor cells, in the subgranular zone (SGZ) of the hippocampal dentate gyrus in a time course following ethanol exposure (7, 14, 30 days following exposure). Adolescent male Sprague-Dawley rats (PND 35) were administered 25% (w/v) ethanol or isocaloric control diet via gavage every 8 hours for 4 consecutive days according to the Majchrowicz model. Animals received an average of 12.1 ± 0.2 g/kg/day of ethanol, had an average blood ethanol concentration of 347.5 ± 12.5 mg/dl, and underwent withdrawal with an average withdrawal behavior score of 1.2 ± 0.3 (tail tremor) and peak withdrawal score (highest score achieved) of 2.7 ± 0.2 (general or head tremor). Animals were perfused; brains were removed, fixed, sectioned in a 1:12 series, and processed for DCX and NeuroD immunohistochemistry. DCX-immunoreactivity (DCX+IR) was quantified using densitometry (pixles/mm^2) and t-test revealed a 60% increase over controls ($p<0.05$) at 14 days post ethanol, which confirmed the increase in neurogenesis previously observed with BrdU. NeuroD-positive (NeuroD+) cells were increased by 70% over controls ($p<0.01$) along the SGZ of the dentate gyrus at 14 days of abstinence. However, there was no difference between ethanol and control groups at 7 or 30 days. Further, at 14 days post ethanol there was a correlation between the number of NeuroD+ cells and mean but not peak withdrawal score ($p<0.01$), which suggests a relationship between ethanol withdrawal and reactive neurogenesis. These data are consistent with our hypothesis that the progenitor cells proliferate around day 7 then survive and mature, resulting in increased differentiated progenitors (NeuroD+ and DCX+IR cells) by day 14. Funded by NIAAA R01AA016959.

0106

CHARACTERIZATION OF PROGENITOR CELL PHENOTYPES INVOLVED IN ENHANCED HIPPOCAMPAL NEUROGENSIS DURING ABSTINENCE FOLLOWING BINGE ALCOHOL EXPOSURE

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In humans, excessive alcohol intake characteristic of alcohol use disorders is associated with neurodegeneration, but evidence suggests that this degeneration may recover during abstinence. In select regions of the brain, such as the hippocampus, neural stem cells are instrumental to proper structure and function and have been implicated in the recovery process. In adult rats, binge alcohol exposure produces neurodegeneration in the dentate gyrus of the hippocampus but this initial cell loss is followed by a compensatory increase in neurogenesis during abstinence. Recent work in our laboratory has revealed that the increase in neurogenesis observed one week following the last alcohol exposure could be attributed to in an increase in neural progenitor cells being recruited into the cell cycle, as evidenced by an increase in Sox2+ cells, without alterations in cell cycle dynamics. However, whether alcohol differentially affects certain phenotypes of progenitor cells is not known. To further examine the phenotypes involved, adult male Sprague-Dawley rats (298.8 g; 70 days old) were intragastrically gavaged with either ethanol diet or an isocaloric dextrose containing diet following the Majchrowicz binge protocol for four days (mean dose: 9.7 ± 0.3 g/kg/day, mean BAC: 310.8 ± 17.9 mg/dl). Following one week of abstinence, rats were transcardially perfused then brains were extracted, fixed, and sectioned using a vibrating microtome. Tissue was then simultaneously stained for markers of Ki67, GFAP, Sox2, and NeuroD using a newly developed quadruple fluorescent labeling technique that allows for the differentiation and quantification of actively dividing type 1, type 2a, type 2b and type 3 progenitor cells. Because we have previously reported an increase in Sox2+ cells, we first quantified dual Sox2+/NeuroD+ type 2b progenitor cells. Results revealed no significant difference in type 2b cells between ethanol and control diet exposed rats one week following binge ethanol exposure (2% of Sox2 versus 2.75% of Sox2, respectively). Analysis of other progenitor phenotypes is ongoing. Future research will then investigate a potential role for these actively dividing progenitors in recovery following binge alcohol exposure. (This work is supported by NIAAA R01AA016959 and NIDA T32DA007304)

0107

MECHANISMS CONTRIBUTING TO CEREBROVASCULAR DYSFUNCTION DURING ALCOHOL CONSUMPTION

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Chronic heavy consumption of alcohol is a major contributing factor to the pathogenesis of hemorrhagic and ischemic stroke. The increase in the incidence of ischemic stroke during alcohol consumption may be related to an alteration in vascular function of large and small cerebral arteries/arterioles to limit cerebral blood flow. The purpose of this presentation is to discuss regional responses of large and small cerebral vessels during alcohol consumption, possible mechanisms that contribute to altered responses of cerebral vessels during chronic exposure to alcohol, and implications of alterations in vascular function to brain injury following cerebral ischemia/reperfusion. We measured *in vivo* reactivity of pial arterioles and the basilar artery to eNOS-, nNOS- and K+ channel-dependent and -independent agonists in rats pair fed a nonalcohol diet or an alcohol-containing diet (6.4% w/v). We also examined a potential role for an increase in oxidative stress in regional-induced impairment of vascular function by chronic consumption of alcohol. Lastly, we measured brain infarct volume following occlusion of the middle cerebral artery in nonalcohol- and alcohol-fed rats, and the potential role for an increase in oxidative stress in brain injury. We found that chronic alcohol consumption impaired eNOS-dependent responses of large and small cerebral blood vessels, nNOS-dependent responses of pial arterioles, and selective K+ channel-dependent responses of pial arterioles and the basilar artery. We also found that an increase in oxidative stress could account for impaired responses of large and small cerebral blood vessels during chronic consumption of alcohol. Lastly, we found an increase in infarct volume in animals fed the alcohol diet and this increase in infarct volume could be reduced by inhibition of oxidative stress. Thus, we suggest that chronic heavy alcohol consumption impairs NOS- and K+ channel-dependent responses of large and small cerebral arteries/arterioles via a mechanism that appears to be related to an increase in oxidative stress. In addition, brain injury following cerebral ischemia/reperfusion was increased by alcohol consumption and this was also related to an increase in oxidative stress. We suggest that chronic alcohol consumption may disrupt neurovascular coupling, and thus to contribute to an increase in brain damage following ischemic stroke.
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0108

INCREASE OF AQUAPORIN-4 EXPRESSION AFFECTS BRAIN EDEMA UNDER ETHANOL CONSUMPTION WITH HYPONATREMIA

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Traumatic brain injury (TBI) with ethanol is more severe than without. We previously reported that prior ethanol (EtOH) injection decreased animal's survival rate by augmentation of brain edema after TBI (Katada et al, 2009. J Neurotrauma). And we reported that aquaporin-4 (AQP4), an water channel, can be related to augmentation of brain edema after TBI under EtOH consumption. On the other hand, AQP4 expression is increased by hyponatremia. AQP4 expression is regulated by ion channels, for example, Na-K ATPase, Na(+)-K(+)-2Cl(-) cotransporter and transient receptor potential vanilloid 4. Therefore, we hypothesized that sodium ion may have effect on the up-regulation of brain AQP4 after TBI under EtOH consumption. To elucidate whether AQP4 augments brain edema or not, we used AQP4 inhibitor (acetazolamide, AZA) in the rat TBI model under EtOH consumption. And to elucidate the relation between AQP4 expression and EtOH and hyponatremia, we used rat primary astrocyte under ethanol and hyposodium medium. EtOH (3 g/kg b.w.) was administered i.p. 1 hr before TBI in Wistar/ST rats (approximately 300 g b.w.). In AQP4 inhibition group, AZA (10 mg/kg) was administered i.p. 12 hr after TBI. We performed TBI model by weight-drop device. Brain edema was estimated by MRI (7.0 tesla). AQP4 expression was evaluated by western blotting and immunohistochemistory in brain. Blood electrolytes concentration was measured by Spotchem D concept (ARKRAY, Japan). Primary rat astrocyte cultures was obtained from 2–4 days old newborn Wistar/ST rat pup cerebral cortices. Cells were cultured in normal MEM (NaCl: 680 mg/dL) supplemented with 10% calf serum and hyposodium MEM medium (NaCl: 410 mg/dL). EtOH (0–50 mM) was added to each mediums. AQP4 expression in cells was estimated by western blotting temporally. Survival rate in ethanol group was approximately 50% 24 hr after TBI. AZA treatment recovered survival rate to 100% after TBI. AZA significantly decreased AQP4 expression around TBI lesion at 24 hr after TBI. Sodium ion concentration was decreased significantly in ethanol group at 24 hr after TBI. AZA recovered it 24 hr after TBI. AQP4 expression in astrocytes was changed in hyposodium MEM. These findings suggest that prior EtOH administration increases AQP4 expression by with hyponatremia to augment brain edema after TBI. AQP4 inhibition treatment may be effective on brain edema in TBI patients under EtOH consumption.

6. FETAL ALCOHOL SYMDROME/DEVELOPMENT

0109

QUANTITATIVE HIGH THROUGHPUT DIGITAL MRNA & ITRAQ-LABEL BASED PROTEOMIC UTEROPLACENTAL ANALYSES FOR MATERNAL ALCOHOL CONSUMPTION DURING PREGNANCY

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Introduction: Quantitative high throughput systems are valuable for FASD mechanistic insights, diagnosis & therapeutic intervention. We utilized multiplexed digital system to quantitate alcohol-induced uterine angiogenesis-related mRNA abundance & label-based iTRAQ for the proteome.
Methods: 4 biological replicates (mRNA, proteomic) & 3 technical replicates (mRNA) of uterine arterial endothelial cells from 3rd trimester ewes were FAC sorted, validated, cultured, treated without or with alcohol (300 mg/dl) for 3 h on 3 days in a compensating system for 2 weeks. 2 sequence probes for 85 angiogenesis-related & 5 housekeeping genes (for normalizing) were constructed. One probe was covalently linked to an oligonucleotide-containing biotin & the other to a colored molecular tag & the extracted RNA was analyzed using Nanostring nCounter system. For proteomics, lysates were TCA precipitated, solubilized, trypsin digested, labeled with isobaric ITRAQ tags, SCX fractionated, analyzed using MS Bioworks nano LC MS/MS, MASCOT searched & quantitated.
Results: Of the 85 angiogenesis genes, 20 were downregulated (↓) & 1 receptor upregulated (↑); ↓angiopoietin-L3(P=0.01), ↓ANPEP(P=0.003), ↓collagen (COL)18A1(P=0.046), ↓COL4A3 (P=0.02), ↓HAND2(P=0.034), ↓hepatocyte growth factor(GF)(P=0.042), ↓HPRT1(P=0.02), ↓ID1(P=0.009), ↓integrina5(P=0.041), ↓leptin(P=0.003), ↓NOTCH4(P<0.001), ↓platelet derived GF A(P=0.006), ↓platelet factor 4(P=0.004), ↓placental GF(P=0.022), ↓plasminogen (P=0.003), ↓plexin domain c1(P=0.049), ↓ribosomal L13A(P=0.019), ↓ribosomal largeP1 (P=0.015), ↓TGFa(P=0.04), ↑TGFβR1(P=0.017) & ↓TIMP3(P=0.031). Proteomics had 0% false discovery rates with 14 ↑ & 17 ↓ including those related to cell structure (eg. ↓tubulin β, P=0.002; ↓vimentin, P<0.001), transcription & translation (↓elongation factor 1α, P<0.001; ↑40S ribosomal protein-S19, P=0.002), histones (↑H4, P<0.001; ↑H2B-1k, P=0.036), Ca+2/nitric oxide(NO) (↓HSP90β, P=0.014; ↑calmodulin, P<0.001) & redox balance(↓thioredoxin, P=0.017).
Conclusions: 1. These data establish detrimental alcohol effects on uteroplacental angiogenesis suggesting an important role for this compartment in FASD pathogenesis. 2.Alcohol targets at multiple levels (epigenetic, transcriptional & translational) modulating redox balance, Ca+2/NO/ angiogenesis, growth and blood-related factors. 3.Large scale assays have promising utility to pursue biomarkers, mechanisms and therapeutic strategies for FASD. NIH AA19446,HL49210,HL83144,HD38843.

0110

PRENATAL ALCOHOL EXPOSURE: FETAL PROGRAMMING OF NEUROIMMUNE AND NEUROENDOCRINE FUNCTION RESULTS IN A PRO-INFLAMMATORY BIAS IN ADULTHOOD

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Prenatal alcohol exposure (PAE) affects development, regulation and function of many physiological systems, resulting in a wide array of deficits, many of which persist into adulthood. Both hypothalamic-pituitary-adrenal (HPA) and neuroimmune deficits are common following PAE. Due to the extensive bidirectional feedback between HPA and immune systems, we hypothesize that fetal programming of these systems by PAE results in a primed, vulnerable, pro-inflammatory-biased organism that is predisposed to increased responsiveness to immune challenge in adulthood.
Pregnant dams were assigned to:1) PAE – *ad libitum* access to a liquid ethanol diet (36% EtOH-derived calories); 2) Pair-fed (PF) - liquid control diet with maltose-dextrin isocalorically substituted for ethanol in the amount consumed by a PAE partner; or 3) Control (C) - *ad libitum* access to control diet. At the onset of puberty, female offspring were exposed to Chronic Mild Stress (CMS) or remained undisturbed (non-CMS). CMS consists of exposure to a series of stressors, at unpredictable times, for ten days and is designed to simulate mild psychological stress, as may be experienced during the human period of adolescence. To test functional immune status in adulthood, offspring received an immune challenge, in the form of Complete Freund's adjuvant (CFA), which induces arthritis (adjuvant-induced arthritis, AA). Initial results indicate that prenatal treatment has effects on the incidence, severity and recovery from inflammatory challenge. In the non-CMS condition, PAE and PF animals display the highest incidence of AA, with 78% and 75%, respectively, developing clinical signs of inflammation compared to 50% in C animals. Exposure to CMS in adolescence increases the incidence and severity of AA in all groups, with 100% of both PAE and PF animals developing inflammation. Finally, recovery was severely impaired in the PAE non-CMS group, with only 50% showing recovery, as compared to 88% in PF and 100% in C animals. Preliminary analyses indicate that PAE animals do not mount an appropriate corticosterone response to AA, suggesting alterations in neuroendocrine systems that mediate the inflammatory response. The findings presented above have important implications for the development of therapeutic interventions in the treatment of immune and neuroendocrine alterations seen in children with FASD. Supported by: NIH/NIAAA R37 AA007789 to JW, NIH/NIMH MH081797 (Project 2) to JW, GGM, MSK and NSERC CGS-D to TB.

0111

EFFECT OF ALCOHOL EXPOSURE IN *UTERO* ON VITAMIN A METABOLISM IN ADULT RATS

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Intrauterine alcohol exposure is one of many factors known to predispose offspring to adult disease by deregulating developmental and/or metabolic pathways heavily interconnected to one another. Alcohol exposure in utero has been shown to perturb vitamin A metabolism in the developing tissues, although the exact mechanisms of this interference have not been clarified yet. Vitamin A is an essential nutrient that regulates many crucial biological functions during adult life and embryogenesis. Both excess and deficiency of vitamin A in the developing tissues lead to congenital defects or lethality. In addition, many adult pathological conditions have been associated with alterations of the metabolism of this nutrient. Therefore, to better understand the mechanisms whereby prenatal alcohol exposure compromises health later in life, this study investigates the effects of prenatal alcohol exposure on adult retinoid metabolism. Plasma, liver, lung and prostate tissues were collected from 60–75 days-old males and females Sprague Dawley rats born from dams: 1) fed with liquid diet containing 6.7% alcohol between GD 7 and 21 (AF); 2) pair-fed with isocaloric liquid diet during the same gestational window (PF); or 3) fed ad libitum with rat chow throughout pregnancy (AD). Plasma and tissues retinol and retinyl ester levels were analyzed by reverse-phase HPLC. Lung retinyl ester levels were significantly reduced in both males and females from AF dams compared to those from PF mothers. Additionally, hepatic retinyl ester levels were reduced and serum retinol levels were increased only in males from AF dams compared those born from PF mothers. Finally, ventral prostate retinyl ester levels were significantly reduced in males from AF dams compared those from PF mothers.
This study is the first to report that prenatal alcohol exposure in rats affects retinoid metabolism in adult life, in a tissue and sex dependent manner. Giving the crucial role of vitamin A in maintaining the health of the body throughout life, these data warrant further studies to investigate the molecular mechanism through which alcohol exposure during embryonic development compromises vitamin A metabolism of adult organs such as liver, lung and prostate, likely predisposing to detrimental consequnces on health. (Supported by NIH grant R37 AA08757).

0112

VARENICLINE MODULATES GABAERGIC SYNAPTIC TRANSMISSION AND MITIGATES ETHANOL-INDUCED DEFICITS IN GABAERGIC SIGNALING IN BASAL FOREBRAIN NEURONS

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Children who suffer ethanol exposure *in utero* are at risk for Fetal Alcohol Spectrum Disorders which can include devastating brain injury and cognitive impairments that persist into adulthood. No pharmacological interventions effectively prevent or reverse these neurobehavioral deficits; although, there has been much interest in the promise of neurotrophic agents, neuroactive peptides, dietary antioxidant or choline supplements, and NMDA receptor antagonists. Varenicline, an agonist at nicotinic receptors and FDA approved for smoking cessation, reduces ethanol drinking behavior and improves ethanol-induced learning deficits in mice. We tested whether varenicline might have potential for reversing the effects of perinatal ethanol exposure. Ethanol exposure in rat pups on postnatal days (PD) 4-9, in a human 3rd trimester equivalent model, induces a 'GABA deficit'. Maturation of $GABA_A$ receptor ($GABA_AR$)-mediated miniature postsynaptic currents (mPSCs) show reduced amplitude and frequency, but increased decay time constants in septal cultured neurons and medial septum / diagonal band (MS/DB) neurons in brain slices after ethanol intoxication (DuBois et al., 2004, 2006; Wang et al., SfN Abst 570.16, 2007). Using whole-cell patch-clamp recordings in brain slices, we measured the effects of acute bath applied varenicline (10 mM) on $GABA_AR$ mPSCs. Indicative of increased GABA release, varenicline significantly enhanced mPSC frequency in MS/DB slices (K-S test, $P < 0.01$). $GABA_AR$ mPSC amplitude and decay kinetics were not consistently altered. In a separate set of experiments, rat pups were exposed (PD 4-9) to varenicline (1 mg/kg/day), ethanol (5.25 g/kg/day), or varenicline plus ethanol by intragastric intubation. $GABA_AR$ mPSCs were recorded from brain slices (PD 11-33). Pups exposed to binge-like ethanol showed reduced $GABA_AR$ mPSC amplitude and frequency (K-S test, $P < 0.01$) with variable effects on decay kinetics while pups co-treated with ethanol plus varenicline showed improved mPSC amplitudes and frequency when compared to ethanol alone (K-S test, $P < 0.01$). These data indicate that varenicline acting through nAChRs located on GABAergic presynaptic sites within the MS/DB can regulate GABA synaptic transmission and might influence 'GABA deficits'. Together these findings suggest varenicline may be capable of improving ethanol-induced deficits in GABAergic function and potentially cognitive and memory function. Supported in part by AA012386.

0113

ASTROCYTES PRE-TREATED WITH ETHANOL INDUCE AN INCREASE IN HIPPOCAMPAL SYNAPSES

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The developing fetus exposed to ethanol presents with numerous deficits, including a range of cognitive disabilities. Problems with learning and memory in children with Fetal Alcohol Spectrum Disorder suggest the involvement of the hippocampus and effects on synapse formation and function. Recent work has shown that the factors released by astrocytes are important in the development of synapses and interruption of their typical functions may influence the development of disease. How astrocytes modulate the ethanol effect on synaptogenesis has not been sufficiently investigated. We have previously reported that primary rat hippocampal neurons (E21) grown in culture for 14 days and co-cultured for 24-hours with primary astrocytes pre-treated with ethanol (50 mM) show an increase in synaptic structure formation compared to neurons co-cultured with control astrocytes. Immunocytochemical staining and 3-dimensional object analysis of confocal images show that pre-treatment of astrocytes with 50 mM ethanol induces a 2.9 fold increase in pre-synaptic synaptophysin puncta, a 2.2 fold increase in post-synaptic PSD-95 puncta, and a dramatic 4.5 fold increase in their overlap. To corroborate that the observed increase in structure is reflected in an increase in functionality, we measured spontaneous, miniature excitatory post-synaptic currents in neurons after astrocyte co-culture using whole cell patch clamp techniques. Preliminary analysis suggests that the frequency of events in neurons co-cultured with ethanol-treated astrocytes is higher relative to neurons co-cultured with control astrocytes, suggesting more functional synapses. However, a second, distinct population of neurons in the same treatment group was observed to have a frequency lower than those neurons co-cultured with control astrocytes. No difference in the mean amplitude or the mean of the maximum amplitude between the two treatment groups was observed, suggesting no change in the number of post-synaptic receptors. Interestingly, the median time to decay for events in neurons co-cultured with ethanol-treated astrocytes was 1.8 times slower than that of the controls, suggesting a potential difference in AMPAR subunit composition. Additional studies will be performed to confirm these findings. (Supported by F31AA019868, AA008154).

0114

ROLE OF 3RD TRIMESTER EQUIVALENT CHRONIC ETHANOL EXPOSURE AND GLUTAMINE SUPPLEMENTATION ON UTERINE AND FETAL BRAIN HEMODYNAMICS: OVINE MODEL

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Glutamine (GLN) plays roles in modulating redox potential, glutathione synthesis, cell size and volume, glucose regulation, transamination, angiogenesis, etc. We reported that acute ethanol exposure reduces availability of GLN and GLN related amino acids in the maternal and fetal compartment. We hypothesized that 3rd trimester equivalent chronic ethanol exposure affects the uterine and fetal brain hemodynamics and L-GLN supplementation alters the effects of ethanol. Pregnant sheep were assigned to 4 groups: saline control, ethanol, ethanol + GLN, saline + GLN. Ethanol or saline infusions were given IV over 1 hour from gestation day (GD) 99 to 121, 3 consecutive days per week to mimic a weekend binge drinking pattern.The 1stfour doses of ethanol were 1.75, 2, 2.25 and 2.25 g/kg respectively and thereafter were 2.5 g/kg. 100 mg/kg of GLNdose was administered IV as a 4.5% w/v aqueous bolus three times a day. On GD 116, catheters were place in the maternal and fetal vasculature and a Doppler flow probe was placed around the maternal uterine artery. On GD 121, the first isotopically labeled non-radioactive microspheres were injected into the fetal vena cava and simultaneously blood was withdrawn from fetal artery using a precision syringe pump with a known withdrawal speed. At the end of 60 minutes, all fetal tissues were collected and weighed. Microspheres were retrieved and quantified to calculate the blood flow. Uterine artery flow at the beginning, baseline of the acute infusions was 38% lower (though not significantly) compared to the saline control group (p= 0.605). At the end of the acute infusions, uterine arterial (32% increase, p< 0.02) and fetal cerebellar blood flows (58% increase, p= 0.347) were higher (significantly and not significantly respectively) in the ethanol group compared to the saline control group. Ethanol + GLN supplementation group showed a protective trend compared to the ethanol group but data was not statistically significant (44% increase, p= 0.647, N=2). We conclude that 3rd trimester equivalent chronic ethanol exposure alters uterine and fetal brain blood flow specific to the ethanol vulnerable cerebellum. These findings support the conclusion that prenatal ethanol exposure alters uterine vascular function that may play a role in neurodevelopmental defects and GLN is a potential protective therapeutic agent against the teratogenic effect of ethanol. Supported by NIAAA RO1 AA010940 (TAC) & K08AA018166-01 (SW).

0115

GESTATIONAL ALCOHOL EXPOSURE DYSREGULATES FETAL IRON HOMEOSTASIS UNDER MATERNAL IRON SUFFICIENCY AND DEFICIENCY

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Prenatal alcohol exposure (PAE) impairs brain development, leading to lifelong deficits in IQ and executive function found in fetal alcohol spectrum disorders (FASD). Intriguingly, gestational iron deficiency (ID) mimics FASD's neurodevelopmental disabilities. We previously showed that maternal iron status influences FASD outcomes and dietary prevention of gestational maternal ID diminishes alcohol's developmental toxicity. In adults, alcohol dysregulates iron homeostasis; the molecular and developmental consequences of iron dysregulation to fetal and maternal development are poorly understood. Using a 2nd trimester rat gestational PAE model, we studied the impact of PAE upon fetal iron homeostasis. Specifically, we measured the iron homeostatic biomarkers of ferritin (FTN), transferrin (TF), and transferrin receptor (TFRc) in fetal brain and liver under the conditions of maternal iron sufficiency (IS) and ID. Preliminary data indicate that PAE inhibits the fetus from correctly interpreting maternal iron status, thus leading to interruptions in the proper homeostatic adaptations. PAE appears to disconnect the signals that communicate iron status between the fetal brain and liver. Under both IS and ID, PAE increases fetal liver FTN expression at the expense of the FTN expressed by the brain. Moreover, data indicate that PAE further dysregulates the fetal brain's ability to compensate for ID, as evidenced by reductions in brain TF and TFRc expression. In contrast, a dysregulation of TF and TFRc expression is not observed in the IS alcohol-exposed fetus. With respect to the fetal liver, PAE does not induce considerable changes in TF and TFRc expression regardless of maternal iron status. As a whole, our data suggest that PAE during disrupts the ability of fetal brain to correctly adapt to maternal iron status, and these adaptive mechanisms are more dysregulated under maternal ID. This is a first step to build a detailed portrait of alcohol's effect upon iron homeostasis during gestation. Understanding the impact of maternal iron status during PAE will inform whether clinical intervention with maternal iron supplements will be efficacious in improving developmental outcomes in FASD. Supported by AA17281.

0116

GENE X ALCOHOL EXPOSURE: WHAT DOES THIS INTERACTION TELL US ABOUT PHENOTYPIC VARIATION IN FETAL ALCOHOL SPECTRUM DISORDERS?

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It is critical that we better understand why there is substantial phenotypic variability following prenatal alcohol exposure. It is likely that genetic and environmental risk factors affect the degree to which prenatal alcohol exposure results in the characteristic features of fetal alcohol spectrum disorders. Genetic screens using the zebrafish model have been particularly useful in advancing our understanding of vertebrate development. Depending upon the mutated gene, zebrafish exposed to alcohol during early embryonic development have variable craniofacial defects of the jaw, palate and skull base. Using this model, several genes within the Platelet-Derived Growth Factor (PDGF), Fibroblast Growth Factor (FGF), and Bone Morphogenetic Protein (BMP) pathways appear to have gene x alcohol exposure interactions – suggesting that these genes may play a role in the variable effects of prenatal alcohol exposure. To further explore these genes, we utilized genotypic data from a genomewide SNP array in a sample of 240 individuals with variable alcohol exposure. All individuals completed a uniform neurobehavioral evaluation and most also had a 3D facial image. Brain (MRI) imaging was available for 70 subjects. Initial analyses were performed to evaluate 11 candidate genes in the PDGF, FGF, and BMP pathways. Analyses were limited to the Caucasian subset (n=94) due to racial differences in facial measurements. Based on the results of analyses in the zebrafish, 5 anthropometric measurements, corrected for age and gender, were initially analyzed: inner canthal width, outer canthal width, lower facial height, lower facial depth, and midfacial depth. The analytic model included the main effects of SNP genotype and prenatal alcohol exposure (Yes or No) as well as the interaction of SNP with prenatal alcohol exposure (the key variable of interest).Promising evidence of association was found with 6 SNPs in *PDGFRB (*genotype x exposure $p < 3 \times 10^{-3}$) with the phenotypes of mid and lower facial depths. One SNP in *PDGFRA* provided evidence of association with several anthropometric measures ($p < 1.7 \times 10^{-3}$). Ongoing analyses are examining these candidate genes for their association with specific neurobehavioral and brain imaging phenotypes.
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0117

FETAL ALCOHOL-RELATED GROWTH RESTRICTION FROM BIRTH THROUGH YOUNG ADULTHOOD AND MODERATING EFFECTS OF MATERNAL PRE-PREGNANCY WEIGHT

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Fetal alcohol exposure leads to growth restriction *in utero* and during infancy, but studies have yielded differing results regarding effects on growth later in life. Animal studies suggest that maternal nutrition during pregnancy may impact fetal alcohol-related outcomes, but the degree to which maternal nutritional status modifies fetal alcohol effects on development in humans remains largely unstudied. This study examined the effects of prenatal exposure on longitudinal growth from birth through young adulthood and the degree to which maternal pre-pregnancy weight and body mass index (BMI) may moderate these effects. 480 mothers were recruited at their first prenatal clinic visit to over-represent moderate-to-heavy use of alcohol and/or cocaine during pregnancy, including a 5% random sample of low-level drinkers and abstainers. They were interviewed at every prenatal visit about their alcohol consumption using a timeline follow-back approach and about their smoking and drug use. Their children were examined for weight, height, and head circumference at birth, 6.5 and 13 mo and 7.5, 14, and 19 yr. In multiple regression models with repeated measures (adjusted for confounders), prenatal alcohol exposure was associated with longitudinal reductions in weight, height, and weight-for-height/BMI that were largely determined at birth. At low-to-moderate levels of exposure, these effects were more severe in infancy than in later childhood. By contrast, among children born to women with alcohol abuse and/or dependence who had consumed 4 or more standard drinks/occasion, severity of alcohol-related growth restriction remained relatively constant. In addition, effects on weight and height were markedly stronger among children born to mothers with lower pre-pregnancy weight and BMI. These findings indicate that fetal alcohol exposure was associated with reductions in weight, height, and weight-for-height/BMI that persisted through young adulthood. Maternal pre-pregnancy weight modified the effects of prenatal alcohol exposure on growth, with stronger effects seen in children born to smaller mothers. This interaction between alcohol consumption and maternal weight may be due to attainment of higher blood alcohol concentrations in smaller mothers for a given amount of alcohol intake or to increased vulnerability in infants born to women with poorer nutrition. Grants: NIAAA K23AA020516, RO1AA06966, RO1AA09524; NIDA R21DA021034; Joseph Young, Sr., Fund, State of MI.

0118

POSTNATAL BRAIN DYSMORPHOLOGY INDUCED BY PRENATAL ALCOHOL EXPOSURE: A MRI STUDY IN MOUSE

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Varying brain retardation is one of the most critical features of Fetal Alcohol Spectrum Disorders (FASD). MRI studies have shown regional patterns of dysmorphology including microcephaly, and altered cortical thickness, corpus callosum, and cerebellar vermis structures. However, how do alcohol dose and timing affect variable brain dysfunction is not clear. Our recent studies have shown the dose- and exposure-length dependent alcohol effects on the craniofacial as well as skull bone volume developments. This study investigated how comparable the brain and craniofacial developments were impacted under the alcohol influence in the same set of mice. C57BL/6J dams were randomly assigned into three alcohol exposure (ALC) groups subjecting to 4.2% v/v (E7—E11 or E7—E16) or 3.6% v/v (E7—E16) respectively. The pair-fed (PF) and CHOW groups were included to serve as non-alcohol and overall controls. On postnatal days (P) 21, mouse heads were imaged using a 9.4T preclinical MRI system with 3D gradient echo (GRE) sequence to acquire volumetric images with voxel size as low as 40 microns. Regions of interests including the whole brain, olfactory bulbs, cortex, and cerebellum were segmented and the volumes were calculated. Data was examined by ANOVA followed with paired comparison between treatment groups to test the effect of prenatal alcohol exposure.Calculating from amount of food intake, we found liquid diet group consume similar level of calories but less amount of micronutrient (<50% across the elements, e.g. iron, zinc, vitamin B1). The 4.2% ALC treated group (E7—E16) showed consistently smaller mean volumes for brain regions measured than the other two groups, indicating that prenatal alcohol exposure hampered fetal brain development. Comparing PF with CHOW pups, only cerebellum volume was observed to be significantly different. These results suggest that alcohol and nutrition both could contribute to brain volume reduction. Alcohol under restricted micronutrient has broader impact in more brain regions. Furthermore, the effect of alcohol on brain volume reduction is dose dependent. These results are comparable with craniofacial and skull bone volume analyses performed on the same subjects. These results demonstrated that alcohol exposure led to comparable effect on brain volume reduction and degree of facial dysmorphology, and demonstrated an important information how facial dysmorphology might be a mirror of the brain in FASD. Supported by NIH UO1 AA17123.

0119

EFFECTS OF DURATION AND DOSE OF PRENATAL ALCOHOL EXPOSURE VIA MATERNAL LIQUID DIET ON FACIAL DYSMORPHOLOGY IN C57BL/6J MICE

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Fetal alcohol syndrome (FAS) is diagnosed using criteria of growth retardation, nervous system damage, and a distinct pattern of facial dysmorphology. Fetal alcohol spectrum disorders (FASD) show a wide spectrum of pathognomonic facial features that are thought to be attributed to differences in alcohol dose, or the developmental period of exposure. This study explored alcohol induced facial abnormalities attributed to varied alcohol dose and or distinct developmental periods, Using a mouse model of liquid diet alcohol exposure we examined alcohol doses of 4.0% v/v and 3.1% v/v with exposure stages from embryonic day 7 (E7) to E11 and E7-E16. Female C56BL/6J mice were divided into three groups. Chow groups were given ad libitum chow and water throughout the experimental period. The alcohol groups (Alc) were given a liquid diet of either 3.1%v/v or 4.0%v/v alcohol for 1 week prior to mating. During pregnancy the Alc groups were alcohol diet on embryonic days 7 (E7)-E11 or E7-E16. The Pair-fed (PF) dams were given equal volumes of an isocaloric diet parrelled to Alc groups. All embryos were analyzed at E17 using 15 facial measurements (derived analogs of human anthropometry), along with measures of crown-rump, weight, and head circumference. Statistical analysis was performed using both 2 and 3-way analysis of variance (ANOVA) models, testing individual treatment effects within groups and effect of stage, dose, and txt (alc vs pf). At 4.8% alcohol dose exposure stages demonstrated altered whisker pad, all facial depth measurements, and lower facial height at E7-E16 with only upper facial depth, and minimal frontal height differences within E7-E11. At 3.1% dose, differences were minimal between with dysmorpholgy of columella and philtrum at longer exposure not seen at E7-E11. Variations effected by alcohol dose were pronounced with width, height and depth measurements at 4.0% not seen at 3.1%. There were distinct difference in columella and philtrum at 3.6% not seen at the 4.0% dose comparing longer stage exposure. The dose and duration of alcohol exposure are important factors contributing to the severity of facial dysmophology and growth retardation. High dose alcohol demonstrated more dysmorphic features then lower dose, with distinct morphological changes between doses. The shorter stage (E7-E11) exposure showed less dysmorphology in both alcohol doses. NIAAA UO1 AA17123 & P50AA07611-FAS (FCZ, CG).

0120

EFFECT OF FETAL ALCOHOL EXPOSURE ON CRANIOFACIAL BONE DEVELOPMENT IN C57BL/6J MOUSE MODELS: A DOSE AND TIMING STUDY

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Introduction: Craniofacial bone dysmorphology is an important but under explored diagnostic feature of Fetal Alcohol Spectrum Disorders (FASD). This study aims to examine effects of dose and timing of fetal alcohol exposure on a set of craniofacial bones in a mouse model, while co-varying for the head size variation.
Methods: C57BL/6J dams were randomly assigned into three different alcohol treatment groups representing two doses (high vs. low) and two timings (long vs. short) at post-pregnancy: a 10-day exposure from embryonic day 7 (E7) to E16 on either 4.2% v/v (high dose long exposure, HDLE) or 3.6% v/v (low dose long exposure, LDLE) respectively, and a 5-day exposure during E7-E11 with 4.2% v/v (high dose short exposure, HDSE). A CHOW group, fed with ad libitum mouse chow and water throughout the experiment, served as the controls. The Micro-CT scan yielded volumetric data for each mouse sample with 40x40x40 um^3 voxel spacing. Pups born to all treated dams were scanned at postnatal 7 day (P7) and at P21 for longitudinal studies of craniofacial bone development. Using the Amira software,17 landmarks on the craniofacial bone surfaces were defined to estimate a head size, and the frontal, parietal, occipital and mandible bones were segmented. The volumes of the four bones were analyzed using general linear model with SPSS 19 to examine effect of alcohol disposure on craniofacial bone development while controlling for the head size. Multiple comparison was corrected by the Sidak method.
Results: At P7, HDSE showed less volume in all four bones than any other group ($p<0.001$). At P21, compared with CHOW, HDSE showed reduced volume in all four bones ($p<0.027$), HDLE in parietal bone only ($p=0.006$), and LDLE in frontal, parietal and occipital bones ($p<0.03$). LDLE showed less frontal bone development than HDLE ($p=0.048$), and HDSE showed less mandible development than HDLE ($p=0.005$).
Conclusion: These results demonstrated that prenatal alcohol exposure had a dose-and timing-dependent impact on reducing craniofacial bone development after birth. And, the short exposure had an early and sustained effect on all the bones throughout the tested age range, while the long exposure affected only selected bones at a later stage. Further studies on general craniofacial measures will help delineate effects of quantity and frequency of fetal alcohol exposure to enable diagnosis of FASD. Supported by NIH UO1 AA17123.

0121

HEAD CIRCUMFERENCE AS PREDICTED BY FACIAL MEASURES IN MOUSE MODEL OF FASD

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Intrauterine exposure to ethanol produces a myriad of anomalies, many tied to the developing brain. Both dose and duration of exposure are suggested to have cumulative effects on brain growth, validating the assumption that measures of brain volume might provide a proxy for ethanol damage. However, brain volume is difficult to obtain directly, so a commonly used indirect measure of brain volume has been the occipital frontal circumference (OFC) in humans (Malina and Bouchard). In this study, we investigated the relationship of craniofacial measurements and exposure histories against skull OFC in C57BL/6J (Jackson Laboratory) mice. Three alcohol treatment groups were used, which differed in dose of alcohol administered (3.6% or 4.8% v/v) and/or the duration of treatment during gestation days (E7-E17 or E11-E17). All pups were surrogated at birth with normal dams and received microCT at postnatal day (P) 21. Individual measurement comparisons were made between treatment groups and a control sample of chow fed and with a group of pair-fed (isocalorically linked liquid diet). Eleven linear craniofacial measurements were derived from micro-CT images, and a measure of head circumference was constructed using the MxView software (Philips) (defined as the outer perimeter of skull enclosure at the level of nasion, in the Frankfort plane). A multiple linear regression was used to evaluate the facial measurements that best predicted circumference. Variables chosen for and strength of the model predicating OFC differed by group. The best model was found for the low dose, long exposure group (R^2 = .91) using inner canthal, minimal frontal and bigonial widths; the remaining models were much less reliable: pair fed (R^2 =.61) using bigonial and palpebral fissure widths and nasal length; high concentration, short exposure (R^2 = .57) using bigonial and bitragal widths and lower facial depth; high concentration, long exposure (R^2 = .57) using depth of the mandible and lower face and bitragal width. The chow model was the least reliable (R^2 = .55) using inner orbital and bitragal widths and lower facial depth. Except for the low dose, long exposure group, multiple regression models did not define reliable predictions of OFC. A limited exploratory study (N = 6) of fMRI calculated brain volumes also showed a low correlation to OFC (R^2 = .013) suggesting that other measures may be better suited to assessing brain volume in mice. Supported by U01 AA017123 (FCZ).

0122

CRANIOFACIAL DYSMORPHOLOGY AS A FUNCTION OF DOSE AND DEVELOPMENTAL TIME OF ALCOHOL EXPOSURE IN THE C57BL/6J MOUSE MODEL

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The cause of the high variability in facial dysmorphology in the fetal alcohol spectrum disorders (FASD) remains elusive. The purpose of current study is to determine how dose and timing of alcohol exposure might affect the variant cranial-facial dysmorphology via liquid diet consumption in the C57BL/6J mouse model. Mouse dams were randomly assigned into three different alcohol treatment groups: a exposure from embryonic day 7 (E7) to E16 on either 4.2% v/v (high dose long exposure, HDLE) or 3.6% v/v (low dose long exposure, LDLE) respectively, and a exposure during E7-E11 with 4.2% v/v (high dose short exposure, HDSE). A Pair-Fed (PF) group free of alcohol but isocalorically matched with alcohol group (ALC), and a CHOW group fed with ad libitum mouse chow and water, served as the controls. On postnatal days (P)7 and 21, craniofacial bones were imaged using 3D microCT, and 13 craniofacial measurements defined as mouse equivalents of a subset of anthropometric measures used in human study were performed. Data was examined by ANAOVA and Logistic Regression to discern features that predict alcohol exposure. Longitudinal changes were tracked within each group.HDLE caused persistent craniofacial dysmorphology for ALC vs. PF. In contrast, the HDSE displayed minimal impact, and LDLE was associated with only transient effects. PF to Chow comparisons resulted in measurable differences as well, indicating a nutrition effect (liquid diet groups were measured to consume less micro-nutrition than CHOW group); but these differences decreased as animals reached older age P21. Greater disparity was found for ALC vs. CHOW than ALC vs. PF thus indicating an enhanced teratogenicity at the combination of malnutrition and alcohol exposure. Relative growth from P7 to P21 are greater for ALC and PF animals than CHOW animals. Discriminate analysis (using logistic regression) showed that measurements that differentiate exposed animals from non-exposed animals change with animal age, exposure dose and exposure length. The effect of alcohol exposure and nutritional disparity is synergistic. Nutrition limitation alone is a causal factor for cranial facial dysmorphology at early age, but can be outgrow by proper postnatal nurturing. The alcohol induced dysmorphology changed with age, in part due to increased relative growth of exposed individuals. This information could be important to assist in the understanding of clinical variants of FASD. Supported by NIH AA016698.

0123

SYNERGISTIC GENE-ALCOHOL INTERACTIONS CAUSED VIA PI3K INHIBITION GENERATE VARIABLE CRANIOFACIAL DEFECTS IN ZEBRAFISH

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Gene-environment interactions can cause variation in human birth defects. Our goal is to characterize these interactions. We chose Fetal Alcohol Spectrum Disorders (FASD) as a model for gene-environment interactions because FASD have highly variable craniofacial defects and are modulated by largely unknown genetic factors. In a genetic screen for ethanol susceptibility loci, we found that *platelet-derived growth factor receptor a* (*pdgfra*) interacted synergistically with ethanol in zebrafish. Untreated zebrafish *pdgfra* mutants have cleft palate due to defective neural crest cell migration while *pdgfra* heterozygotes develop normally. Ethanol-exposed *pdgfra* mutants have profound craniofacial defects and ethanol treatment revealed latent haploinsufficiency in 70% of *pdgfra* heterozygotes. Ethanol treatment induced neural crest apoptosis in *pdgfra* mutants and heterozygotes, a defect not present in untreated mutants or ethanol-treated wild types. The PI3K pathway mediates both the migratory and protective functions of Pdgfra, while the protective function of Pdgfra is mediated via mTOR, downstream of PI3K. This mechanism predicts that other PI3K-dependent signaling pathways would interact synergistically with ethanol. Indeed, *fibroblast growth factor 8a* interacts with ethanol to generate a different set of craniofacial defects. Collectively, our data show that combined genetic and environmental attenuation of the PI3K pathway causes synergistic gene-ethanol interactions, a mechanism that may explain some of the variability of FASD. This work was supported by a grant from the ABMRF, NIH/NIDCR R01DE020884 and NIH/NIDCR R00DE018088 to J.K. Eberhart and NIH/NIAAA F31AA020731 to N. McCarthy.

0124

EFFECTS OF MODERATE DRINKING DURING PREGNANCY ON PLACENTAL PROTEIN EXPRESSION

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Introduction. Most children adversely affected by maternal drinking during pregnancy cannot be identified early in life using current diagnostic criteria for Fetal Alcohol Spectrum Disorder (FASD). We are investigating whether alterations in placental gene and protein expression at term may provide a reliable and sensitive diagnostic indicator of fetal alcohol exposure as well as a prognostic indicator of risk for functional brain damage leading to adverse neurobehavioral and cognitive outcomes in affected offspring. We previously reported that moderate drinking during pregnancy differentially affects placental genes, including those coding for proteins associated with nervous, vascular and immune system development. In the current study, we used a combination of proteomic analyses and western blotting to confirm the identification of proteins altered by moderate drinking during pregnancy.
Methods. Pregnant Long-Evans rats were assigned to one of two experimental groups. One group consumed a 5% ethanol solution (in 0.066% saccharin water) four hours each day throughout gestation, resulting in a mean maternal peak serum ethanol concentration of 84 mg/dL. A control group consumed a matched volume of saccharin water. At term (Gestational Day 20) placentas were harvested, saline-perfused to remove blood from the tissue, and processed for analysis of protein expression.
Results. Two-dimensional polyacrylamide gel analysis of placental tissue detected 1181 protein spots, twenty of which were significantly altered by maternal drinking during pregnancy. Fourteen of the altered protein spots have been identified via mass spectroscopic analysis. Some of the identified proteins play critical roles in placental and neural development, angiogenesis or apoptosis. Recently, western blotting has confirmed the ethanol-induced alterations for two of the identified proteins, namely, Annexin IV and Cerebral Cavernous Malformation Protein 3.
Conclusions. These results indicate that placental proteins associated with vascular remodeling are altered by moderate drinking during pregnancy and could serve as biomarker candidates for fetal ethanol exposure and fetal ethanol effects. Further, these results provide insights on novel mechanisms of how ethanol may directly or indirectly mediate teratogenic effects through alterations in placental function. Supported by AA17068, AA015420, AA014127, IREB and INSERM.

0125

IMPACT OF MATERNAL DRINKING DURING PREGNANCY ON GENE EXPRESSION AND MICROVASCULAR DEVELOPMENT IN FETAL CEREBRAL CORTEX

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We have reported that moderate drinking during pregnancy alters placental expression of genes associated with nervous and vascular system development. Gonzalez and colleagues have shown that daily injections of 3 g/kg ethanol in mouse dams (maternal serum ethanol concentration of ~200 mg/dL) causes striking distortions in the density and radial orientation of the cerebral cortical microvascular network in PD2-old offspring. The present study addressed two questions: 1) Does moderate maternal drinking during pregnancy alter the expression of fetal cortical genes associated with neural and vascular development in a manner similar to the changes previously observed in placenta, and 2) does more moderate ethanol exposure affect fetal cortical microvascular development? Long-Evans rat dams voluntarily consumed either a 0% or 5% ethanol solution in 0.066% saccharin water for four hours each day throughout gestation. The mean daily ethanol consumption of 2.72 g/kg, which produces a peak maternal SEC of 84 mg/dL, did not affect maternal weight gain, litter size or birth weight. On GD20, rat placental:fetal units were removed by Caesarian section and both placenta and cerebral cortex were processed for mRNA expression array analysis. In addition, fetal frontal cortices were evaluated for vascular density in the cortical plate (CP), intermediate zone (IZ), and ventricular zone (VZ) layers. Fetal alcohol exposure (FAE) significantly altered the expression of 686 genes in fetal cortex and 529 genes in placenta. Gene ontology analyses revealed a significant enrichment in genes associated with neural and vascular development in both tissue types from ethanol-exposed offspring. Ethanol exposure decreased vascular density in all three layers of cerebral cortex. The reduction was statistically significant in the ventricular zone. No changes in the radial orientation of the microvascular were observed. These results indicate that moderate levels of fetal ethanol exposure affect both the expression of genes associated with vascular development as well as the microvasculature in the developing cortex. Our data suggest that further investigation of the connection between cerebral microvascular development and neural development is warranted to uncover mechanisms of fetal alcohol-induced damage. Supported by AA017068 and INSERM.

0126

MRI DERIVED VOLUMETRIC BRAIN MEASUREMENTS IN THE OVINE

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Prenatal alcohol abuse causes important structural and functional brain defects and is the leading cause of preventable retardation in the United States. Fetal alcohol spectrum disorder (FASD) is a broad term used to describe individuals exposed prenatally to alcohol and encompasses a broad range of birth defects including facial abnormalities and learning, motor, and behavioral deficits. Despite promoting alcohol abstinence during pregnancy, the incidence of FASD has failed to decline and individuals lacking cardinal facial abnormalities and historical exposure are increasingly difficult to identify. Three-dimensional magnetic resonance imaging (MRI) is readily available, provides superior brain contrast, and in previous human studies of FASD has shown significant volume reductions in various brain structures. We hypothesize that postnatal MRI derived volumetric brain measurements can predict prenatal alcohol exposure. Pregnant ewes received 2.5 g/kg alcohol (N = 5) IV three consecutive days per week from gestation day 4–41 (mimicking a binge drinking pattern in the first trimester of pregnancy) while remaining ewes were controls (N = 5). Lambs were sacrificed at 5 months of age, their brains were perfused with fixative, and MRI's were performed immediately post mortem.T1-weighted images were used to calculate cerebellar volume (Inveon Research Workplace software, Siemens). Mean cerebellar volume in controls (10,655.02 ± 943.51mm^3) did not significantly differ from the alcohol group (10,519.18 ± 181.87 mm^3) (p = .891). These MRI findings are consistent with a our previous work utilizing stereological methods on the fetal cerebellum and the same first trimester alcohol exposure. The total estimated cerebellar Purkinje cell number and Purkinje cell density decreased significantly in the alcohol group compared to the control group but no significant differences existed between cerebellar volumes. Cerebellar volume is therefore a poor predictor of first trimester alcohol exposure at this alcohol dose and pattern in sheep, but MRI derived volumetric measures of other brain structures may be beneficial and further studies are warranted. Supported by Texas A&M CVM Post Doctoral Grant (SB) and NIAAA Grant AA0171290 (TAC). All or part of this work was done in conjunction with the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD), which is funded by grants from the National Institute on Alcohol and Alcohol Abuse (NIAAA).

0127

WITHDRAWN

0128

PLACENTAL FATTY ACID ETHYL ESTERS ARE INCREASED IN ALCOHOL-EXPOSED PREMATURE NEWBONS

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Meconium fatty acid ethyl esters (FAEEs) have been described as one biomarker of *in utero* alcohol exposure in term newborns. Because alcohol use significantly increases the risk of premature delivery, we continue to evaluate the identification and the consequences of *in utero* alcohol exposure on the premature newborn. We *hypothesized* that elevations of placental FAEEs would assist in the identification of the alcohol-exposed premature newborn. After informed consent, alcohol use during pregnancy was determined in mothers who had delivered a premature newborn <1500 grams via an extensive maternal questionnaire. Alcohol exposure was defined as maternal admittance to drinking alcohol during the pregnancy. Placental tissues from alcohol-exposed (n=12) and non-exposed (n=39) pregnancies were evaluated for FAEEs via Gas Chromatography/Mass spectroscopy. Data were not normally disturbed and were natural log transformed for analyses via SPSS. Maternal alcohol use during pregnancy significantly increased total placental FAEEs compared to non-exposed pregnancies (p=0.041). Furthermore, the combination of Oleic + Linoleic + Linolenic and Arachidonic Acids (OLL + AA) was significantly elevated in alcohol-exposed placentas compared to non-exposed (p=0.029). These results suggest that placental tissue FAEEs are elevated with alcohol exposure in the premature newborn. Inclusion of the placenta in investigations for the development of biomarkers including FAEEs may assist in accurately identifying the alcohol-exposed newborn.

0129

VALIDITY AND FEASIBILITY OF NEONATAL SCREENING FOR PRENATAL ALCOHOL EXPOSURE BY MEASURING PHOSPHATIDYLETHANOL IN DRIED BLOOD SPOTS OF A NEWBORN

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Accurate identification of prenatal alcohol exposure (PAE) presents a unique challenge because of the unreliability of maternal reporting and low sensitivity of traditional alcohol biomarkers. Phosphatidylethanol (PEth) is a novel and promising ethanol biomarker, but its validity in newborn children is not established. We evaluated feasibility of collecting an additional dry blood spot (DBS) card during routine newborn screening and the background prevalence of PAE as assessed by a positive PEth test in a de-identified sample of newborn children (Phase I). Electronic orders to collect DBS cards from newborns who continue to bleed after the routine newborn screening were initiated for all infants delivered at the University of New Mexico (UNM) Hospital. The number of collected cards (with or without blood) was compared against the daily admission logs. During the 6 weeks of Phase I, 240 infants were admitted, 230 (95.8%) cards were collected, and 201 (87.4%) of them had ≥1 full DBS - an amount sufficient for PEth analysis. PEth analysis indicated that 6.5% of the cards were 'positive' (PEth >20ng/mL), indicative of potential PAE in late pregnancy. In Phase II, the validity of PEth in DBS was evaluated in 28 infants born to a well-characterized cohort of pregnant women enrolled in the UNM Biomarkers in Pregnancy Study. None of the 17 controls (children born to alcohol abstainers, as evident from self-report and other biomarkers) were positive for PEth in DBS suggesting 100% specificity. Among 11 patients classified into the alcohol-exposed group based on the alcohol use in early pregnancy, 4 were positive for PEth. None of these patients admitted alcohol use during the 2 weeks prior to delivery (the detection window for PEth) on the TLFB interview and 3 were negative on all other maternal biomarkers. A newborn with the highest PEth concentration (406 ng/mL) was also positive for 3 maternal biomarkers (PEth, GGT, urine EtG/EtS). These results indicate that a majority of infants have enough blood after the routine heel prick to fill an additional card for PAE screening. The acceptability of such screening by parents and corresponding ethical issues remain to be investigated. Our preliminary data on PEth validity suggest that this biomarker is highly specific and can identify infants with PAE who would have been missed by other biomarkers and maternal report. Supported by 1R03AA020170, National Children's Study, 1P20AA017608.

0130

METABOLIC BIOMARKERS OF PRENATAL ALCOHOL EXPOSURE IN HUMAN EMBRYONIC STEM CELL-DERIVED NEURAL LINEAGES

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Background: Fetal alcohol spectrum disorders (FASD) are a leading cause of neurodevelopmental disability. The mechanisms underlying FASD are incompletely understood, and biomarkers to identify those at risk are lacking. Here, we detail the metabolomic analysis of embryoid bodies and neural lineages derived from human embryonic stem (hES) cell, and we identify the neural secretome produced in response to ethanol exposure.
Methods: WA01 and WA09 hES cells were differentiated into embryoid bodies, neural progenitors or neurons. Cells along this progression were cultured for four days with 0%, 0.1% or 0.3% ethanol. Supernatants from the last 24hr of culture were subjected to C18 chromatography followed by ESI-QTOF-MS. Features were annotated using public databases and the identities of four putative biomarkers were confirmed with purified standards and comparative MS/MS.
Results: Ethanol treatment induced statistically significant changes to metabolite abundance in human embryoid bodies (180 features), neural progenitors (76 features) and neurons (42 features). There were no shared significant features between different cell types. Fifteen features showed a dose-response to ethanol. Four chemical identities were confirmed; L-thyroxine, 5'-methylthioadenosine, and the tryptophan metabolites L-kynurenine, and indoleacetaldehyde. One feature with a putative annotation of succinyladenosine was significantly increased in both ethanol treatments. Additional features were selective to ethanol treatment but were not annotated in public databases.
Conclusions: Ethanol exposure induces statistically significant changes to the metabolome profile of human embryoid bodies, neural progenitors and neurons. Several of these metabolites are normally present in human serum, suggesting their usefulness as potential serum FASD biomarkers. These findings suggest the biochemical pathways that are affected by ethanol in the developing nervous system and delineate mechanisms of alcohol injury during human development. [Supported by NIH Award #AA16958]

0131

FATTY ACID ETHYL ESTERS SHOW SIGNIFICANT CORRELATION WITH IN UTERO ALCOHOL EXPOSURE

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Identification of the newborn infants exposed to alcohol *in utero* is essential to establishing early intervention strategies. Previous studies have shown that fatty acid ethyl esters (FAEEs), non-oxidative metabolites of alcohol, in meconium are potential biomarkers of fetal alcohol exposure in term newborns. However, the identification of specific FAEEs and threshold concentrations of FAEEs which correlate with exposure remains under investigation. The aim of this study was to evaluate FAEEs in the meconium of infants and identify a concentration and pattern of FAEEs to serve as accurate biomarkers of *in utero* ETOH exposure.
Pregnant women were recruited from the University of New Mexico substance abuse clinic during one of the first prenatal care visits and categorized into: a) *alcohol-exposed* (≥1 binge episode or ≥3 drinks/wk on average since the last menstrual period [LMP]); and b) *controls* (alcohol abstainers since LMP).
FAEEs were measured in the meconium of 38 infants born to cohort participants (12 exposed and 26 controls). Meconium was extracted and analyzed using gas chromatography/mass spectroscopy. The data (ng of FAEEs/g of meconium) was not normally distributed and was therefore log-transformed and analyzed via the Mann-Whitney U test. Cut off analysis was performed using Chi-Square.
FAEEs were detectable in all meconium samples. Concentrations of Stearic FAEE were elevated in alcohol-exposed infants compared to non-exposed infants (p=0.058). The set threshold of significance for the amount of FAEEs (specifically Linoleic and Linolenic) was set as greater than 10,000 ng/g of meconium. The observed difference in quantity of Linoleic and Linolenic FAEEs (ng/g of meconium sample) in control vs exposed infants could potentially trend towards significance with a larger sample number [11.5% of control infants vs. 41.6% of alcohol-exposed infants (p=0.08)].
Based on these results, infants exposed to alcohol in utero (based on maternal report) trended towards higher concentrations of Stearic in their meconium compared to control infants and they had four-fold elevated levels of Linoleic+ Linolenic ethyl esters compared to non-exposed newborns. While other investigators have shown that one FAEE (i.e. Linoleic ethyl ester) is found in higher concentrations in alcohol-exposed newborns, we have shown that a combination of FAEEs at certain threshold values holds further promise for more accurate identification of the alcohol-exposed newborns.

0132

DNA METHYLATION IN INFANT BLOOD IS SENSITIVE TO PRENATAL ALCOHOL EXPOSURE AND RELATED TO CHILD BEHAVIORAL OUTCOMES

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Fetal Alcohol Spectrum Disorder (FASD) persists as a major public health concern. Confidence in diagnosis for ''non-FAS'' FASD is limited by the absence of facial features and by variable neurobehavioral effects. Our goal is to identify an ''epigenetic'' profile as a pattern of DNA methylation in infant blood that is a valid biomarker of prenatal alcohol exposure (PAE) and a sensitive predictor of neurobehavioral outcomes that together may aid in early detection and diagnosis of FASD.
Methods. Subjects from a large prospective pregnant African American cohort with assessments of maternal alcohol use beginning at the first antenatal visit were selected based on our validated metric of prenatal ''at-risk alcohol exposure'' (Chiodo et al., 2009) and available subsequent neurobehavioral assessment. With maternal consent, infant heel-stick ''blood spots'' were obtained from the Michigan Neonatal BioBank archive for 5 at-risk PAE infants and 7 non-exposed infant controls. DNA was extracted, subjected to bisulfite conversion, hybridized to an Infinium HumanMethylation27 BeadChip®, fluorescent stained, scanned, and whole-genome CpG methylation status for >27,000 sites determined. Differentially methylated sites were filtered with a cut-point at $p<0.01$.
Results. At-risk PAE was associated with a set of significantly hypermethylated DNA sites in dried infant blood. Among the 50 most differentially methylated sites, all 5 PAE infants had 9 to 15 to hypermethylated sites whereas 5 of 7 non-exposed infants had zero. The other two non-exposed controls had only 2 or 3 (χ^2=12.0, p=.007). No sites were significantly hypo-methylated after PAE. The degrees of DNA hypermethylation in many of these same sites were correlated significantly with memory, behavior and fine motor problems (but few with birth weight or IQ) in these children at 4 years of age. DNA hypermethylation was also related to other measures of risk drinking (e.g., average amount of alcohol drunk per drinking day across pregnancy & the TACER-3 screen).
Conclusions. Differential patterns of DNA methylation (or ''epigenetic marks'') in blood may effectively detect infants exposed to at-risk maternal drinking and predict life-long FASD. Other predictors, factors, genes or outcomes, as well as potential 'mechanisms of pathology' that may be indicated by which genes are altered, all remain to be determined in future analyses.

0133

FASD SCREENING PROFILES IN MINNESOTA: AN APPLICATION OF THE 4-DIGIT DIAGNOSTIC CODE

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The 4-Digit Diagnostic Code is a rigorous FASD diagnostic protocol based on measurements of growth, face, brain damage, and prenatal alcohol exposure (Astley, 2004). To date only one study in Washington is known to describe the characteristics of persons screened for FASD based on the 4-Digit Diagnostic Code criteria (Astley, 2010). This paper provides comparative data to begin to explore the validity and discuss the consistency of the 4-Digit Diagnostic Code criteria by examining 863 cases from Minnesota.

Five Minnesota clinics were involved in the data collection efforts related to the FASD screening. Two clinics were in Minneapolis, two in northern Minnesota and one was in the southeast region of the state. The data are based on chart reviews of patients who were screened for FASD in 2001 to 2003. Prior to this study two of the five clinics were involved in the diagnosis of FASD. The other three clinics received training from staff at the University of Minnesota and the University of Washington. The sample included 863 persons who had been referred to one of five Minnesota FASD diagnostic clinics.

Most of the 863 cases (795; 92.4%) were 18 years or younger and confirmed to be born in the United States (662; 76.7%). The cases were predominately white (44.0%) and non-Hispanic (98.5%). Of those cases where the mothers' age at birth was known (55.4%), almost half of the participants were born to mothers who were 25 years or younger at the time of the birth. 164 (19.0%) of the cases were diagnosed with Fetal Alcohol Syndrome or Partial Fetal Alcohol Syndrome [FAS/PFAS], 295 (34.3%) with static encephalopathy [SE], and 174 (20.2%) with neurodevelopmental disorder [ND]. Of the remaining cases, 30 (3.5%) did not receive a FASD related diagnosis and 197 (22.8%) did not fall within the four digit code diagnostic area; and 135 had the unknown history of alcohol exposure [AE]. Examination of comorbidity by diagnostic status revealed significant differences in the distribution of ADHD, conduct disorder/ODD, learning disorders, mental retardation, and anxiety disorder by FASD diagnosis. In general FAS/PFAS and Static Encephalopathy/Alcohol Exposed diagnoses had the greater prevalence of these four additional diagnoses.

This report documents the characteristics of person screened for FASD using the 4-Digit Diagnostic Code. Future comparative studies across states (e.g., Minnesota and Washington) should be pursued to further validate the diagnostic tool.

0134

ADVANCED GESTATIONAL AGE INCREASES SERUM CARBOHYDRATE DEFICIENT TRANSFERRIN LEVELS IN ABSTINENT PREGNANT WOMEN

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Carbohydrate-deficient transferrin, now expressed as a percent of disialotransferrin from total transferrin (%dCDT), is a well-established and highly specific biomarker for sustained heavy consumption of alcohol. However, in pregnant women the specificity of this biomarker might be affected by advanced gestational age, even after accounting for increased transferrin concentrations in pregnancy. The goal of this study was to assess the variability in %dCDT during pregnancy among patients recruited into the University of New Mexico (UNM) Biomarkers in Pregnancy Study. Patients were recruited during one of the first prenatal care visits (first blood draw) and followed-up to term (follow-up collection). The sample size was restricted to 31 patients who abstained from alcohol use during pregnancy, as evident from their self-report and laboratory results for a panel of five other validated alcohol biomarkers (GGT, EtG, ETS, PEth, and PEth in dried blood spots of a newborn). The sample included a large proportion of ethnic minorities (74.2% Latina, 6.5% Native American. 3.2% Black) and socially-disadvantaged (51.6% < high school education, 100% Medicaid-insured) pregnant women. The mean maternal age at recruitment was 24.7±3.9 years. Serum samples were collected at each visit and sent to the Medical University of South Carolina for analysis by an internationally-validated HPLC and spectrophotometric detection method. Mean %dCDT concentrations at both visits were compared for each patient using a paired t-test. At recruitment (mean gestational age 22.1 ± 7.5 weeks), the mean %CDT concentration was 1.47 ± 0.30%, while at term the mean increased to 1.65 ± 0.29% (p=0.002). Using a conventional cut-off concentration %dCDT > 1.7%, 23.3% and 40% of the sample would be classified as 'positive' for this biomarker at recruitment and at term, respectively. However, none of the control patients had %dCDT concentrations above 2.0%. These results suggest that a conventional cut-off of 1.7% might be too low for pregnant women and would generate false positive results. Thus, we propose %dCDT > 2.0% be used as a cut-off concentration indicative of alcohol exposure in pregnant women. The sensitivity of %dCDT at this cut-off for heavy drinking during pregnancy needs to be further assessed. Supported by the NIAAA 1P20AA017608 and ABMRF grants.

7. DETERMINANTS OF ALCOHOL CONSUMPTION IN HUMANS

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0135

POLYSUBSTANCE USERS ARE UNIQUELY DIFFERENT FROM ALCOHOL DEPENDENT INDIVIDUALS IN MAGNETIC RESONANCE-BASED BRAIN METABOLITE CONCENTRATIONS

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Our previous magnetic resonance studies have shown region-specific abnormalities of brain metabolite levels in the anterior cingulate cortex (ACC) of alcohol dependent individuals (ALC) that largely normalized within one month of abstinence from alcohol. However, the majority of patients seeking treatment today abuse stimulants and other drugs together with alcohol. The specific goal of this analysis was to identify group differences in region-specific brain metabolite levels between polysubstance users (PSU) and ALC and their relationships to lifetime substance use.

28 treatment seeking PSU (alcohol + cocaine and/or methamphetamines primarily) and 40 ALC were imaged at 4 Tesla after approx. 1 month of abstinence from alcohol and substance use. Magnetic resonance spectroscopy (MRS) was performed in the ACC, the dorsolateral prefrontal cortex (DLPFC) and the posterior occipital cortex (POC). Concentrations of metabolites N-acetylaspartate (NAA, neuronal viability marker), creatine (Cr, energy metabolism marker), choline (Cho, cell synthesis/turnover marker), myo-inositol (mI, astrocytic marker), glutamate, glutamate + glutamine and gamma aminobutyric acid (Glu, Glx, GABA, neurotransmitters) were compared statistically to data from 16 light drinking controls (LD). Metabolite measures were correlated with participants' anxiety (STAI), depression severity (BDI), and cocaine consumption.

Main group differences in several metabolite concentrations (NAA, mI, Cr, Cho) were observed in the DLPFC, where PSU had abnormalities in contrast to ALC and LD. PSU and ALC did not differ significantly on alcohol consumption. ALC did not differ from LD at this stage of recovery. Metabolite levels in ACC and POC were largely normal in the groups. In PSU, DLPFC Cr and mI concentrations were positively and GABA negatively correlated with monthly average cocaine consumption over lifetime and 1 year before treatment. Glx concentration was negatively related to BDI. Furthermore, higher mI concentration in DLPFC was positively related to age in PSU, but not in ALC.

These findings suggest that polysubstance use is primarily associated with neuronal and glial abnormalities specific to the DLPFC and related to cocaine consumption. The DLPFC is critical for the development and maintenance of addictive disorders, and these metabolite abnormalities persist at one month of abstinence. PSU are uniquely different from ALC on these region-specific frontal brain metabolite levels.

0136

FRACTIONATING DELAY DISCOUNTING IN ALCOHOL USE DISORDERS: AN FMRI STUDY

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Delayed reward discounting (DRD) is proposed to be a fundamental behavioral process of drug dependence. Neuroimaging studies have investigated DRD in a variety of substance abuse samples, including nicotine, stimulant, and alcohol; however, additional research is needed to further characterize the neural correlates of DRD in substance abuse. The purpose of this study was to use functional MRI (fMRI) to investigate the neural correlates of DRD in alcohol use disorders (AUDs). A sample of 25 heavy-drinking males [M (SD) age = 22.6 (2.6) years; 52% of whom met DSM-IV criteria for an AUD] completed an event-related fMRI paradigm that comprised choices between smaller and larger amounts of money ($10 – $100), available immediately or after a delay (1 day – 1 year). In separate analyses, DRD choices were classified as either impulsive (choice of immediate reward) vs. restrained (choice of delayed reward) or hard (choices made near the individual's DRD curve) vs. easy (choices made far from the DRD curve). AUD+ participants consumed significantly more drinks/wk ($p < .01$), had significantly higher AUDIT scores ($p < .05$), and were significantly more impulsive ($p < .05$), compared to AUD- participants. Temporal discounting rate (k) was also positively correlated with AUDIT scores ($r = .41$, $p < .05$). Across all participants, significant positive correlations between k and BOLD activation were found in medial PFC, posterior cingulate, posterior parietal cortex, and insula (rs .40-.58, ps <.05), and a positive correlation was found between AUDIT scores and activation in left insula ($r = .41$, $p < .05$). Categorical comparisons between AUD groups showed that AUD+ participants had significantly greater BOLD responses in dorsolateral prefrontal cortex (DLPFC), middle temporal gyrus, and posterior insula during impulsive choices. When making restrained choices, AUD+ participants showed significantly greater neural activity in DLPFC, precuneus, and striatum. Finally, AUD+ participants showed elevated response during hard choices in medial prefrontal, dorsolateral prefrontal and inferior frontal cortices, among other regions. No group differences were observed for easy choices. Taken together, these results suggest that individuals with AUDs may exhibit some degree of neural inefficiency and require greater resources to support more cognitively demanding DRD choices.

0137

PSYCHOLOGICAL AND NEUROPHYSIOLOGICAL CORRELATES OF BINGE DRINKING IN YOUNG ADULTS

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Binge drinking is a recurring problem within the college population that has not been investigated as thoroughly as chronic alcoholism. Previous literature has reported differences in electrophysiological response to multiple types of stimuli in individuals who abuse alcohol compared to their non-drinking peers. Specifically, researchers have observed differences between groups in their neural responses to alcohol related images (Porjesz, 1998). Research from our lab sought to address whether these differences that have been observed in past studies assessing chronic alcoholics would also exist for college-aged binge drinkers. In addition, our study added image types that not only assessed response to alcohol images compared to neutral images, but also included a variety of other affective images. We investigated electrophysiological responses to positive, neutral, negative and alcohol related images between college aged binge drinkers and nondrinkers. Results suggest significant differences between groups for initial attention as measured through the P2 component for the positive images (p=.02), negative images (p=.0002) and alcohol related images (p=.0005) with no significant difference for the neutral images (p=.099). However, no significant differences were found for the later occurring late positive potential component (LPP) between groups in response to any image type. These differences lead to the conclusion that there is a difference in how binge drinkers initially process not only alcohol related images but also emotional images and that this difference disappears in later processing. One question that arose is whether there may be attentional differences between those that drink and those that do not. These differences in early attention to alcohol and emotional stimuli may have significant implications, associated with various variables such as anxiety and depression, which will be discussed further.

0138

RESTING STATE SYNCHRONY RELATED TO SET SHIFTING IN LONG-TERM ABSTINENT ALCOHOL DEPENDENCE

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BACKGROUND: Alcohol dependence is a disorder with an impulsive and compulsive ''drive'' towards alcohol consumption and an inability to inhibit alcohol consumption. Neuroimaging studies suggest that these behavioral components correspond to an increased input in decision making of limbic regions mediating appetitive drive and a reduced input of frontal regions mediating inhibitory control. Little is known, however, about whether these characteristics persist or change after long periods of abstinence.
METHODS: Resting state functional magnetic resonance imaging data were collected to examine resting-state synchrony differences between 23 long-term abstinent alcoholics (LTAA; 8 females, age: M=48.46, SD=7.10), and 23 non-substance abusing controls (NSAC; 8 females, age: M=47.99, SD=6.70). Using seed-based measures, we examined resting-state synchrony with the nucleus accumbens (NAcc) and the subgenual anterior cingulate cortex (ACC).
RESULTS: Compared to NSAC, LTAA showed (a) decreased synchrony of limbic reward regions (e.g., caudate and thalamus) with both the ACC seed and the NAcc seed and (b) increased synchrony of executive control regions (e.g., DLPFC) with both the NAcc seed and the subgenual ACC seed.
DISCUSSION: The results support the notion of ongoing compensatory resting state changes in long-term abstinent alcoholics in which decision making networks show reduced synchrony with appetitive drive regions and increased synchrony with inhibitory control regions. These resting state findings may facilitate the behavioral control required to maintain abstinence.

0139

NEURAL RESPONSES TO ACUTE IV ALCOHOL IN HEALTHY MODERATE DRINKERS

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Alcohol abuse has been linked to the subjective experiences it produces. People who experience stimulant-like effects enjoy alcohol more and are at greater risk of alcohol abuse. Conversely, people who experience strong sedative effects are less likely to abuse alcohol and develop addiction. It is not clear whether individual differences in these effects of alcohol reflect differences in alcohol's effects in the brain. This study examined the real-time acute effects of alcohol upon BOLD response with relation to subjective alcohol effects.
Healthy moderate drinkers participated underwent two fMRI scans with a double-blind IV infusion of alcohol (80mg%) or placebo in randomised order. BOLD data and real-time subjective drug effects were acquired during the scans. Imaging data were analysed using voxelwise non-linear regression and a difference of exponentials signal model. Data were corrected for multiple comparisons at $p<0.05$.
Overall, alcohol increased ratings of feel drug, drug liking and drug wanting, and activated the dorsal medial and anterior nuclei of the thalamus, medial frontal and temporal cortices and the insula. Alcohol differentially activated the dorsolateral prefrontal cortex and parahippocampus among individuals who reported stimulant effects and those who did not; subjects who reported feeling stimulated exhibited net signal decreases while subject who did not report feeling stimulated exhibited net signal increases. Sedative alcohol effects were positively associated with activation in the prefrontal cortex and negatively with activation in the cingulate cortex.
These findings show that dynamic alcohol-induced regional changes in BOLD signal can be detected using a waveform model-based analysis strategy without performance-induced activation. They show that alcohol directly activates regions of striato-thalamic-prefrontal cortical circuits that have been implicated in drug addiction. Alcohol effects upon BOLD signal varied as a function of subjective alcohol experiences, in particular the stimulant and sedative effects of alcohol, which have been linked to alcohol consumption and the development of alcoholism. These data provide a basis for future investigations of the direct effects of alcohol upon the brain which can help us to elucidate sources of individual difference in susceptibility to alcohol use disorders. This research is supported by NIAAA R21 DA20716 and [in part] by the Intramural Research Program of the NIH, NIDA.

0140

LARGER ACCUMBENS VOLUME IS ASSOCIATED WITH INCREASED DRINKING BEHAVIOR AMONG ADOLESCENTS

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Adolescent drinking results in both short and long-term consequences, including decreased academic performance, negative impacts on health, risky decision-making, and death. Adolescence is also a period of significant neural development. During this period of development, bottom-up (pleasure-seeking/emotion-motivated) processes have a significant influence on behavior through the differential development of bottom-up limbic systems (like the nucleus accumbens), as compared to the top-down executive control systems. The purpose of the current study was to determine whether a relationship exists between neural development in adolescence and drinking behavior. For this study, 220 adolescents participated in magnetic resonance imaging (MRI) and completed behavioral measures designed to assess drinking behavior. Larger accumbens volume was associated with increased frequency and quantity of alcohol consumption. Accumbens Ratio, defined as the ratio of accumbens volume to cerebral cortex volume, was also positively correlated with several drinking variables, including frequency and quantity of alcohol consumption and degree of hazardous drinking. To investigate the preferential development of subcortical regions like the accumbens to frontal regions, the ratio of accumbens volume to medial frontal gyrus (MFG) was computed. The ratio of accumbens volume to MFG volume was positively correlated with frequency of alcohol consumption, level of alcohol dependence, and level of hazardous drinking. These findings support a theory of bottom-up motivation versus top-down control with respect to drinking behavior in adolescents.

0141

RELATIONSHIPS BETWEEN RESTING CEREBRAL BLOOD FLOW AND ALCOHOLISM RISK

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Background: Impulsive behavior is a risk factor for alcoholism and thought to be elevated in those with a family history of alcoholism (FHA). The current study investigates relationships between resting regional cerebral blood flow (rCBF) in frontal cortical areas linked to behavioral inhibition and traits associated with alcoholism risk (family history, impulsivity, sociopathic behavior).
Methods: The rCBF of heavier drinking subjects (5.4±3.5 drinks/drinking day, mean±sd) with (19m, 11f; age 23.9±2.9) and without (22m, 6f; age 24.6±3.0) FHA was measured using pulsed arterial spin labeling (PASL) in a 3T Siemens Trio-Tim scanner. Imaging data were analyzed using SPM8 (height threshold $p \leq 0.001$, uncorrected). Prior to imaging, subjects completed the Eysenck I7 inventory to assess impulsivity, an inventory of anti-social behaviors, and the Family History Assessment Module of the SSAGA interview to assess FHA.
Results: Impulsivity was negatively correlated with rCBF within the right lateral pre-motor region (BA6), while number of sociopathic behaviors negatively correlated with rCBF more rostrally in the right frontal cortex (BA8). rCBF was also lower in those with FHA in two distinct right frontal regions: in the dorsolateral prefrontal cortex (BA10) and in a more caudal lateral cluster (BA9). A subset of the sample (n = 32) also underwent functional magnetic resonance imaging (fMRI) while performing a stop signal task– a behavioral measure of inhibition. The blood oxygenation level dependent (BOLD) fMRI response to successful inhibition trials (compared to successful go trials) was elevated in right frontal regions where rCBF was related to FHA, impulsivity, and sociopathy.
Conclusions: rCBF in right frontal regions important to behavioral inhibition is inversely related to trait impulsivity, sociopathy and FHA. Supported by NIAAA P60 AA007611 and R-21 AA018020.

0142

FMRI REVEALS DIFFERENTIAL LIMBIC RESPONSE TO ALCOHOL CUE DISTRACTORS ACROSS STAGES OF ALCOHOL DEPENDENCE

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Background: Prior research on emotional distraction during cognitive processing has revealed that healthy adults engage a ventral brain system including the amygdala in response to task-irrelevant affective distractors. In this study, brain activations to alcohol distractors embedded in an attention-demanding cognitive task were isolated, with a focus on evaluating limbic reactivity, across stages of alcohol dependence.
Methods: FMRI data were collected from alcohol dependent individuals (n=44) across illness phase (currently drinking, recently abstinent, long-term abstinent) and healthy controls (n=20) while performing a visual-oddball alcohol-cue task. Frequent standard stimuli (probability=.8), infrequent target stimuli (probability=.1) and task-irrelevant alcohol (probability=.05) and non-alcohol (probability=.05) beverage distractors were presented during scan acquisition.
Results: Repeated measures ANOVA yielded a Group*Distractor Type interaction effect in the amygdala, driven by significant group differences in response to alcohol distractors (p=.001). Tukey-corrected post-hoc tests of this omnibus alcohol distractor effect is explained by the healthy control group showing more amygdala response than long-term abstinent (p=.001) and recently abstinent (p=.02) groups, as well as the currently drinking group showing more amygdala response than the long-term abstinent group (p=.007). There was no main effect of Group for brain activation to non-alcohol distractors (p>.05) within the amygdala.
Conclusion: FMRI response to incidental alcohol cue exposure differentiated phase of alcohol dependence, with long-term and recently abstinent groups showing decreased engagement of the amygdala. Results suggest that recovery from alcoholism may be associated with functional brain changes in regions related to saliency detection of stimuli with affective significance.
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0143

PHENOTYPIC VARIATION AND RISK FOR ALCOHOL PROBLEMS IN YOUNG ADULTS

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Introduction and Methods: The genotypic and phenotypic underpinnings of alcohol use disorders are being identified and refined. Various phenotypes likely interact to enhance or reduce the development of alcohol use disorders. We have investigated the relationship of three phenotypes—sweet-liking phenotype (SL), high novelty seeking (NS)(70^{th} percentile or higher), subjective response to ethanol at first use (SRE-A)—and their interaction with regards to alcohol-related problems in young adults. The phenotypes tap into different domains of interest: SL to hedonic processing, NS to a component of externalizing behavior, SRE-A to innate tolerance to ethanol. We hypothesized that the phenotypes would show independence from one another and that a greater number of risk phenotypes within an individual would increase risk for alcohol problems as assessed by any positive response to the alcohol use disorders section of the SCID. 124 young adults, 18–26 years old, 49% male, from UNC-Chapel Hill were recruited using e-mail techniques with a goal to balance gender and AUDIT scores < or ≥ 8. Classification tree analysis, random forest plots and Odds Ratios were used to analyze phenotype effects.
Results: 36 subjects had alcohol problems. Classification tree analysis showed that both SL and SRE-A ≥4.125 were important for predicting alcohol problems. Random forest plots identified SL, SRE-A and high NS as important factors for predicting alcohol problems. We then looked at Odds Ratios for alcohol problems comparing individuals with the positive phenotypes of SL, high NS, and high SRE-A (n=7) to individuals without SL, low NS, and low SRE-A (n=34) and the OR was 179.1. Examination of other phenotypic combinations revealed that the presence of all three positive phenotypes increased the OR for alcohol problems compared to other combinations (OR range from 4.49 to 56.98).
Comment: We have previously shown that a combination of SL and high NS work together to greatly increase the likelihood of alcohol problems in young adults, OR 27.5 (Lange et al, Alcohol 45:431, 2010). The present data suggest that adding another phenotype, SRE-A, further increases the probability of having an alcohol problem. We would propose that identifying a variety of phenotypic and genotypic risk markers associated with the development of alcohol problems will enhance understanding of processes leading to alcohol problems and aid in predicting risk.

0144

LATE ADOLESCENTS WITH AN EVENING CHRONOTYPE EXHIBIT BOTH INCREASED ALCOHOL DEPENDENCE AND ALTERED REWARD-RELATED BRAIN FUNCTION

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Evening chronotypes not only differ from morning-types in their sleep and circadian timing, but also in their degree of behavioral and psychological dysregulation. Evening-types are particularly prone to problematic outcomes involving reward function, including higher levels of affective disturbance, sensation seeking, and substance involvement, as well as other risk-taking behaviors. The present analyses explored the neural mechanisms underlying these chronotype differences by comparing reward-related brain function in late adolescent morning- and evening-types.
Chronotype was determined via the Composite Scale of Morningness. Using a monetary reward fMRI paradigm, we compared the neural response to reward in 13 morning-types and 21 evening-types (all 20 y/o males). Region of interest (ROI) analyses focused on the medial prefrontal cortex (mPFC) and ventral striatum, both of which are implicated in reward function. Two-sample t-tests compared the chronotype groups in these ROIs during reward anticipation vs. baseline and win outcome vs. baseline, using a threshold of $p<0.05$ and a minimum extent of 10 contiguous voxels. All analyses adjusted for time of scan. Chronotype groups were also compared on psychiatric diagnoses, various substance-related measures, and sleep quality (using the Pittsburgh Sleep Quality Index (PSQI)).
Consistent with prior studies, evening-types showed a tendency towards more mood, alcohol, and substance use disorders, greater alcohol and drug involvement, and greater sleep disturbance, although these differences were only statistically significant on the Alcohol Dependence Scale and PSQI. Furthermore, evening-types showed reduced mPFC reactivity and enhanced striatal reactivity relative to morning-types during both the anticipation and receipt of rewards.
This preliminary data indicates that oft-noted increases in reward-related problems among evening-types are accompanied by altered neural responses to reward that are consistent with reduced regulatory control and elevated reward reactivity. Future studies should examine potential explanatory mechanisms for reward dysfunction among evening-types, such as social jet lag.

0145

EXECUTIVE COGNITIVE FUNCTION, SUBSTANCE USE DISORDERS, AND THE SUPERIOR LONGITUDINAL FASCICULUS

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Purpose: The superior longitudinal fasciculus (SLF) is a major white matter (WM) tract constituting part of the fronto-parietal network. Several prior studies have indicated that fronto-parietal WM shows diminished organization among individuals with substance use disorders (SUD). Furthermore, reduced fronto-parietal WM organization has been observed to be associated with diminished executive cognitive function (ECF). This study examined relationships among childhood ECF, SUD, and adulthood SLF organization.
Methods: Subjects were recruited and initially assessed in late childhood (age 10–12 years) for a longitudinal study on SUD etiology. At the initial assessment, childhood ECF was determined by a composite score from 6 neuropsychological tests, including Stroop, Vigilance, Porteus Maze, Motor Restraint, Forbidden Toys and WISC-R Block Design tasks. In a young adulthood follow-up (n=94; mean age 25.4; 66% males; 34% African American, 66% white), current SUD was diagnosed by DSM-IV criteria and diffusion tensor imaging (DTI) was conducted. Tract-Based Spatial Statistics (TBSS) was used to compare subjects with SUD (n=21) and without SUD (n=73) on DTI fractional anisotrophy (FA).
Results: Poorer childhood ECF predicted young adulthood SUD (Wald = 7.6; p<.01). TBSS showed that subjects with current SUD, compared to subjects without current SUD, exhibited reduced fractional anisotropy (FA) in a left superior parietal SLF cluster (lspSLF: F=9.4, p<.001). Poorer childhood ECF predicted lower lpsSLF FA (F=5.7, p=.02). In a stepwise multivariate regression model controlling for gender and ethnic group, current SUD predicted lpsSLF (t=3.7, <.001), and current age, past SUD and ECF did not account for significant variance.
Discussion: These findings suggest that ECF predicts SUD and SUD is associated with diminished SLF organization. Longitudinal studies with serial DTI assessments are needed to optimally model these relationships. Supported by P50DA05605, R21AA017312, and PA-HEAL SPH00010.

0146

WHITE MATTER FIBER COMPROMISE CONTRIBUTES TO ATTENTIONAL AND EMOTIONAL PROCESSING IMPAIRMENT IN ALCOHOLISM, HIV INFECTION, AND THEIR COMORBIDITY

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Alcoholism (ALC) and HIV-1 infection (HIV) each affects the integrity of brain white matter fibers. Here, we examined whether attentional and emotional processing is associated with microstructural integrity of fiber systems supporting these functions. Accordingly, 19 ALC, 17 HIV, 16 comorbid (ALC+HIV), and 15 healthy control (CTL) participants underwent diffusion tensor imaging (DTI) and completed an emotional Stroop Match-to-Sample task, requiring subjects to match the color of a cue to that of an emotional word (HAPPY/ANGRY); non-matched cue-word color pairs tapped selective attention. Half of the trials contained a picture of an emotional face (happy/angry) that matched the Stroop word's content; face/word trials tapped emotional interference. Relative to CTL, DTI-based fiber tracking revealed lower fiber integrity, indexed as low fractional anisotropy (FA), in the inferior longitudinal fasciculus (ILF) (connecting frontal and posterior attentional regions) in HIV (p<0.007) and ALC+HIV (p<0.05) and in the uncinate fasciculus (UF) (connecting frontal to limbic emotional regions) in the 3 patient groups (p's<0.013). Despite similar color-match performance by all groups, the patient groups were mildly impaired in color-nonmatch performance (HIV p<0.02; ALC+HIV p<0.05, ALC p<0.06). Stroop-match effects correlated with FA in several fiber tracts, including the cingulum in ALC (*rho*=-.47) and superior longitudinal fasciculus (SLF) in ALC+HIV (*rho*=-.57); longer Stroop-nonmatch response times correlated with lower FA in the UF of HIV (*rho*=-.49) and SLF of ALC+HIV (*rho*=-.61). For emotional face priming of the Stroop word content, CTL exhibited response delays for angry but not happy face trials, whereas ALC, HIV, and ALC+HIV showed similar response delays in happy and angry face trials. Here, lower cingulate fiber FA predicted greater response delays in emotional face trials in ALC (*rho*=-.70) and ALC+HIV (*rho*=-.53), but not in HIV or CTL. These results indicate that individual variability in fiber integrity in ALC, HIV, and their comorbidity contributes to attentional and emotional processes and is reflected in enhanced attentional interference while processing emotional information. These results highlight the functional relevance of selective association brain fiber tracts and their integrity in alcoholism and HIV infection to enable emotion processing and selective attention. Support: AA012388, AA017168, AA017347, AA018022

0147

ALCOHOL INDUCED DISINHIBITON: BEHAVIORAL AND NEURAL CORRELATES

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Successful response inhibition is associated with brain activity of the inferior frontal gyrus, premotor and supplementary motor areas, as well as subcortical brain structures such as the subthalamic nuclei and the basal ganglia. Although it is known that alcohol reduces behavioral response inhibition the underlying neural mechanisms are widely unknown. Thus, the goal of our study is to investigate the effects of a moderate dose of alcohol (0.06%) on the neural activation of the fronto-subcortical response inhibition network during a stop-signal task.
In our ongoing study, 29 physically and mentally healthy young adults (11 females; mean age: 18.6 ± 0.9 years) performed the stop-signal task during a rapid event-related fMRI experiment. Alcohol was administered in a single-blind, placebo-controlled, cross-over design. On two separate days, participants received either a continuous alcohol (breath alcohol concentration: 0.06%) or a placebo infusion using an auto-clamp procedure. The stop signal reaction time (SSRT) was estimated by subtracting the mean stop signal delay (SSD) from the median Go RT.
fMRI data were preprocessed and analyzed with SPM8. At the individual level, we modeled stop success, stop error and go error trials as separate events for the alcohol and the placebo session using a single general linear model. On the group level, we ran a 2×2 factorial model with the factors stopping (stop success vs. error) and drug (alcohol vs. placebo). We additionally included the individual alcohol induced response disinhibition ($SSRT_{alcohol} - SSRT_{placebo}$) as a covariate.
Analysis revealed that alcohol significantly increased the SSRT (placebo: 205 ± 30 ms, alcohol: 218 ± 43 ms), while the median Go RT was not affected (placebo: 393 ± 54 ms, alcohol: 399 ± 59 ms).
Stop trials compared to go trials elicited a substantial bilateral activation of the response inhibition network including the IFG, the anterior cingulate cortex, the supplementary motor cortex, the striatum and the thalamus. Alcohol decreased activation in the IFG, caudate, thalamus and insula. In addition, we found that alcohol-induced neural deactivation in the IFG and putamen was most pronounced in subjects with marked alcohol-induced response disinhibition at the behavioral level (alcohol-induced SSRT increase).
We conclude that alcohol induced behavioral disinhibition is mediated by a neural deactivation in the fronto-subcortical response inhibition network.

0148

BRAIN WHITE MATTER ABNORMALITIES IN SUBJECTS AT HIGH RISK FOR ALCOHOL DEPENDENCE: A DIFFUSION TENSOR IMAGING STUDY

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Alcohol dependence (AD) is an etiologically complex disorder with significant genetic transmission. Several endophenotypes have been investigated in individuals at high-risk for AD, which implicate a possible neurodevelopmental delay in the pathogenesis of AD and may manifest as externalizing symptoms (ES). Diffusion Tensor Imaging (DTI) is a modality which allows us to study the microstructure of the white matter tracts. Previous DTI studies in AD have found altered white matter microstructure, which correlate positively with the neurobehavioral measures. Are there white matter abnormalities in individuals at high-risk for AD and could they indicate another enodphenotype?
Our study aimed at examining for differences in white matter tracts in specific regions of the brain using the DTI parameters- fractional anisotropy (FA) and Mean Diffusivity (MD) and to examine the correlation between the ES profile & white matter abnormalities in subjects at high and low risk for AD.
The study included 15 right handed males aged between 10 and 25 years with high family loading of AD compared to 19 age, sex and handedness matched subjects having no such family history. Written informed consent was obtained from all participants and from parents of minors. DTI scan was then performed on the subjects fulfilling the study criteria with 3Tesla MRI machine. The data was analyzed using appropriate statistical tools.
The HR subjects had a significant higher ES than LR subjects; significantly increased MD in the corpus callosum (genu and splenium), the right and left superior longitudinal fasciculi, right and left inferior longitudinal fasciculi, left uncinate fasciculus and right anterior thalamic radiation; significantly increased AD in the corpus callosum: genu &splenium, the right and left superior longitudinal fasciculi, the left inferior longitudinal fasciculus and the right anterior thalamic radiation.
The finding of higher externalizing symptom scores in HR subjects is consistent with previous studies. The differences in the white matter microstructure in specific regions, even before onset of alcohol use in the HR group, suggest that white matter abnormalities in the brain could be a potential trait marker for AD and could indicate a risk for developing AD.

0149

P300 ABNORMALITIES, BRAIN VOLUME DEFICITS AND EXTERNALIZING SYMPTOMS IN SUBJECTS AT HIGH-RISK FOR ALCOHOL DEPENDENCE

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A reduction in the amplitude of the P300 component of the Evoked Response Potential (ERP) is considered a potential risk endophenotype for Alcohol Dependence (AD). This deficit is suggested to occur due to a developmental lag in frontal P300 generators. This study was aimed to explore the relationship between P300 abnormalities, grey matter (GM) volume deficits [bilateral superior frontal & anterior cingulate gyri, and amygdale being the apriori regions of interest (ROI)] and measures of behavioral undercontrol in subjects at high-risk (HR) and low-risk (LR) for AD. A subsidiary aim was to examine the developmental trajectory of these measures.
Right-handed, HR (n=16) and LR (n=18) subjects, matched for age, gender and education were assessed for psychopathology [including externalizing symptoms (ES)] and family-history of alcoholism, using the Semi-Structured Assessment for the Genetics of Alcoholism II and the Family Interview for Genetic Studies. HR subjects were alcohol-naïve offspring of early-onset alcohol-dependent fathers from multiplex families. Visual ERPs were recorded during 250 trials with simple target/nontarget visual task. Structural MRI was done with 1.5 T scanner. The optimized voxel based morphometry protocol was implemented within Matlab 6.1 through Statistical Parametric Mapping 2. Comparative & correlative analyses examining ROIs (extracted using Wake Forest University pickatlas masks) were performed using SPSS. HR subjects had significantly lower P300 amplitudes over frontal electrodes. They also had significantly reduced GM volumes in the left superior frontal gyrus (SFG) and total amygdalar volume. The lower P300 amplitudes mapped on to the areas which displayed reduction in volume (SFG and amygdala). Differences in both measures were greater at younger age, tending to converge with increasing age. Also, HR subjects had significantly higher mean ES Scores which were associated with reduction in P300 amplitude and GM volumes.
HR subjects had P300 abnormalities which were mapped onto GM volume reductions in the prefrontal cortex. This is possibly the result of a maturational lag in development of frontal P300 generators as evidenced by the reduction in differences with increasing age. These findings suggest that delayed neurodevelopment leading to CNS disinhibition may be etiologically linked to the excess of externalizing behaviors in this population, which is thought to be a predisposition to developing early-onset AD.

0150

ASSOCIATION OF SMOKING WITH MU-OPIOID RECEPTOR AVAILABILITY IN ALCOHOL-DEPENDENT SUBJECTS

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Persons with a history of alcohol dependence are more likely to use tobacco and to meet criteria for nicotine dependence when compared to social drinkers or nondrinkers. The high levels of co-morbidity of nicotine and alcohol use and dependence are thought to be related to complex interactions between nicotinic, opioid and dopamine receptors, which are co-localized in several brain regions including the nucleus accumbens and amygdala. The current study examined whether individual differences in regional mu-opioid receptor (MOR) binding were associated with tobacco use, nicotine dependence, and levels of nicotine craving in alcohol dependent subjects (n=25). Alcohol dependent subjects completed an inpatient protocol, which included medically supervised alcohol withdrawal, monitored alcohol abstinence, nicotine maintenance using transdermal nicotine patches (21 mg), and Positron Emission Tomography (PET) imaging using the MOR-selective ligand [^{11}C]-carfentanil. There was an inverse relationship between nicotine use and nicotine dependence and binding potential (BP_{ND}) in alcohol dependent subjects. Subjects who regularly smoked a higher number of cigarettes per day had significantly lower BP_{ND} in mesolimbic regions including the amygdala (p=0.0001), globus pallidus (p=0.0019), thalamus (p=0.0078) and insula (p=0.016). Likewise, higher scores for the Fagerström Nicotine Dependence Test were associated with significantly lower BP_{ND} across mesolimbic regions with largest differences in the amygdala (p=0.0001). Lower BP_{ND} in amygdala was highly associated with higher nicotine craving (p=0.0001). These data suggest that intensity of cigarette smoking and severity of nicotine dependence decreased BP_{ND} across multiple brain regions in alcohol dependent subjects. These data are compelling given the high co-morbidity of alcohol and nicotine use and dependence.
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0151

DOPAMINERGIC CODING FOR ALCOHOL-RELATED NEGATIVE PREDICTION ERRORS IN ALCOHOLICS BUT NOT SOCIAL DRINKERS

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Background: Striatal dopamine (DA) codes for discrepancies between reward expectation and reward delivery (''prediction errors'', PE). PE may play a significant role in the development and maintenance of hazardous drinking. Previously, we showed that striatal DA decreased when IV alcohol (EtOH) delivery was predicted by cues, but not delivered (negative prediction error, NPE). Here, we hypothesized that non-treatment-seeking alcoholics (NTS) have a differential DA response to NPE compared to social drinkers (SD). Study goals were to (1) determine if decreases in striatal DA during EtOH-NPE are greater in NTS compared to SD; and (2) in NTS, determine if the DA response to NPE is specific to EtOH. IV caffeine (CAF) infusion served as the control drug.
Methods: [^{11}C]raclopride (RAC) PET scanning was used to assess changes in striatal DA during an NPE condition relative to a resting baseline. Four groups of otherwise healthy adults were studied: EtOH-SD (n = 8, 40.5 ± 5.24 y.o.), EtOH-NTS (n = 8, 38.1 ± 7.59), CAF-SD (n = 9, 37.1 ± 10.1), and CAF-NTS (n = 8, 37.1 ± 19.0). Groups were gender-balanced and were not significantly different in age. Depending on group assignment, subjects received either an EtOH or CAF infusion the morning of study, followed by two afternoon RAC scans (first= baseline, second= NPE). Subjects were informed that they would receive EtOH (or CAF) during the second RAC scan; however, drug was not delivered (NPE). IV infusion pumps and a confederate were used to simulate the equipment and procedures the subject had experienced during the a.m. IV infusion. Parametric binding potential (BP) images were generated from the dynamic RAC data and analyzed with SPM5.
Results: Voxel-wise analyses (paired t-test, $p < 0.01$, uncorrected) support our hypotheses that (1) NTS have a larger decrease in DA during EtOH NPE than SD, and (2) the decreases in DA during NPE in NTS subjects is specific to EtOH. Unexpectedly, SD did not exhibit a decrease in DA during EtOH NPE. Instead, there was an increase in DA during this condition in SD.
Conclusions: Decreases in striatal DA neurotransmission during NPE are specific to both the type of reward stimulus and alcohol consumption status. Supported by 5R21AA016901-02 (KKY) and the Indiana Alcohol Research Center (P60 AA007611).

0152

CHARACTERIZING THE EVOLVING ALCOHOL EXPECTANCY MEMORY NETWORKS IN CHILDREN AND EARLY ADOLESCENTS

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Cross sectional work has demonstrated that children have alcohol expectancies even prior to their first drinking experience. Children's expectancies are initially relatively negative, but gradually change and become more positive. These age-dependent changes have been assumed to reflect changes in expectancies that single individuals go through as they mature. Due to the cross-sectional nature of these past studies, however, this assumption has not been verified. To test this assumption, we tracked the alcohol expectancy memory networks of two pre-adolescent cohorts over 2.5 years. One cohort of pre-adolescent children began the study around 9 years of age. The other cohort, comprised of the first cohort's older same-sex siblings, began the study around 11 years of age. We explored alcohol-related memory networks using two methods; a free associate approach, and multidimensional scaling. Free associates were generated in response to the sentence ''How do people feel when they drink alcohol?'' Multidimensional scaling data were derived from the MMBEQ, a self-report measure of alcohol expectancies designed for use in children. One hundred sibling pairs completed 5 assessment batteries (twice a year for two and a half years). In this manner, the current study reports free associates data assessed bi-yearly, for the age range of 9–13. At the average age of 9, children reported ''bad'' 19 times and ''happy'' 9 times. Over time, frequency of reporting ''bad'' consistently decreased while frequency of reporting ''happy'' consistently increased. At the average age of 12 children reported ''bad'' 5 times and ''happy'' 21 times. MDS analysis using individual differences scaling (INDSCAL) demonstrated little change in network structure for the younger cohort, but systematically more emphasis on (weighting of) positive and arousing alcohol expectancies between ages 11 and 13. These results using longitudinal methods are consistent with previous cross-sectional studies and further support the idea that as an individual progresses into adolescence, the anticipated payoff of alcohol consumption becomes more salient in their memory networks, while the anticipated adverse effects become less salient.

0153

EXECUTIVE FUNCTIONS AND FUTURE ORIENTATION INTERACT WITH ALCOHOL ASSOCIATIONS AND USE IN GRADE 8 STUDENTS

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Recent evidence suggests that executive function (EF) capacities moderate the relationship of substance use associations and substance use. This study examined the moderation of memory associations with alcohol use by various measures of executive function and future orientation in grade 8 students (aged 13–14 year olds). 105 grade eight students participating in a larger study on adolescent substance use prevention were tested for working memory capacity (SOPT - serial order pointing task), response inhibition (GNG – Go/No Go task), and task shifting (Donkey version of the Iowa gambling task). In addition, future orientation was measured by a three factors: planning, time perspective, and anticipating consequences. As part of the larger study, simple word and situation associates (WA) were obtained along with open-ended outcome expectancies. WA responses were self-coded as either alcohol or not alcohol and outcome expectancies (OE) were self-coded in a composite score of liking versus not liking potential effects of alcohol use. The overall analysis revealed that WA and OE scores independently predict alcohol use, [b=.37, p<.001, b=.72, p<.001, respectively], last time drunk, [b=.33, p<.01, b=.79, p<.001, respectively], and intent to use alcohol, [b=.54, p<.001, b=.96, p<.001, respectively]. Moderation analyses for G/NG and OEL revealed interactions for last time drunk [b=.01, p<.01] and intent to use alcohol [b=.01, p<.02]. Individuals who report higher levels of being drunk or intentions to use alcohol also score high on outcome expectancy tasks and score low on the GO/NO-GO. No moderation effects were found for the WA measures or the SOPT and Donkey tasks. These findings suggest that the ability to inhibit responses moderates the impact of alcohol use expectancies on the early use of alcohol. Higher future orientation had effects on alcohol use and intent predicted lower use and intent. In addition, the planning subscale moderated the effects of WA on alcohol use and intent with higher levels of planning inhibiting the effects of stronger word associations. These findings suggest a complex pattern of moderation by executive function and future orientation, but suggest that tailoring prevention programs to take these moderation patterns into account may further enhance the goal of inhibiting early use of alcohol by adolescents.

0154

CLASSIFYING INDIVIDUAL DIFFERENCES IN ADOLESCENTS' ALCOHOL EXPECTANCIES USING EVENT-RELATED POTENTIALS

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Using explicit measures, expectations about alcohol have been shown to change over late childhood/early adolescence from mostly negative to more positive, possibly in relation to increases in the complexity of expectancy semantic networks. In this study we used the P300 component of event-related potentials (ERPs) to probe individual differences in expectancy associational space. ERPs offer advantages for this purpose because they index brain responses that are unfiltered through deliberative processes (that is, they are implicit), and reflect very rapid processing in memory associational pathways. In addition, they can detect processing differences to specific words, thereby revealing possible ''hubs'' in the expectancy semantic network (e.g., 'happy' and 'jolly' share similar meaning but 'happy' may be a more automatic response in adolescents). To this end, we examined self-report and ERP measures of expectancy in 78 adolescents (9–14 years; mean = 11.1; 46% female), who were recruited from a larger ongoing longitudinal study of alcohol expectancies in adolescent sibling pairs. Explicit alcohol expectancy ratings of 28 words were collected using the Memory Model Based Expectancy Questionnaire (MMBEQ); implicit reactions were indexed by P300s elicited by the same words. Participants viewed alcohol expectancy words as the terminal words in sentences while ERPs were recorded. The P300 component was extracted through principal components analysis. Results indicate that individual's reactions to some words (e.g., good) were associated with levels of endorsement in explicit measures, reflecting stronger associations and more automatic processing of these stimuli (smaller P300 because they were subjectively expected), whereas other words (e.g., sick, jolly, dumb) were unrelated to levels of endorsement on explicit measures, indicating weaker, less automatic processing. In addition, responses to some words (e.g., cocky & stupid) indicated more automatic processing in males (i.e., smaller P300s) compared to females. These findings suggest that individual differences are reflected in adolescents' ERPs, and that ERP approaches to implicit measurement of expectancies may have utility in determining which expectancies in children/early adolescents are more developed or automatized. Furthermore, these methods allow us to look at the unfolding of alcohol expectancies as individuals develop different associations (both implicitly and explicitly) through adolescence.

0155

ALCOHOL EXPECTANCIES IN ADOLESCENCE PREDICT THE COURSE OF ALCOHOL USE DISORDER

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Positive expectations about alcohol's effects have been shown to reinforce continued alcohol use and may mediate specific risks in the development of alcohol use disorders (AUD). However, little is known about how changes in alcohol expectations relate to the course of AUD. The current study used prospective data from the Minnesota Twin and Family Study to investigate the relationship between positive alcohol expectancies and the longitudinal course of AUD symptoms. Participants (N=1241) underwent multiple clinical interviews for AUD during adolescence (age 17) and young adulthood (ages 20, 24, and 29). Positive expectancy ratings were also obtained at ages 17 and 24 using a questionnaire that assessed feelings and attitudes associated with alcohol use. Participants were divided into groups based on the onset of AUD (i.e., adolescent and young adult) and course of AUD (i.e., persistent versus desistent). Those who never met criteria for AUD served as a control group. Repeated measures ANOVA was used to examine the relationship between changes in alcohol expectancies over time and the course of AUD . Those who ever met criteria for an AUD reported higher positive expectancies at age 17 and 24, $F(1,740)=13.126$, $p<0.001$, relative to controls. Among those who met criteria for AUD, significant elevations in positive expectancies were observed for those with an adolescent onset, $F(1,214) = 5.747$, $p=0.017$, and persistent course, $F(1,214) = 4.600$, $p=0.033$, of AUD. Relative to controls, those with a persistent course of AUD also showed significantly greater increases in positive expectancies over time, $F(1,639) = 10.50$, $p=0.001$. Also, men with AUD exhibited significantly greater increases in positive expectancies relative to AUD females, $F(1,214)=49.882$, $p<0.001$. In conclusion, positive alcohol expectancy is associated with developmental course of AUD including an adolescent onset and persistent course, with increases in expectancies associated with persistent alcohol problems in adulthood.

0156

EXAMINING THE INFLUENCE OF PERSONALITY AND NONDRINKING MOTIVES ON ALCOHOL USE IN ADOLESCENTS

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Nondrinking motives have been shown to relate to lower levels of alcohol use and to be differentially associated with alcohol-related cognitions. However, the influence of personality characteristics on nondrinking motives has not been examined. Trait impulsivity–alcohol use relations are well established. Recent research has refined the measurement of impulsivity to specific facets. Two of these facets include positive urgency (the tendency to act rashly when experiencing high positive affect) and negative urgency (tendency to act rashly when distressed). This study sought to test associations between positive and negative urgency and alcohol use, and investigate a meditational role for nondrinking motives. Structural equation modeling (SEM) was used to test latent factors of Positive and Negative Urgency and Nondrinking Motives on a latent factor of Alcohol Use. Both urgency traits were measured on a scale of 1 to 4, with 4 being low tendency to rash action. Nondrinking motives were measured on a scale of 0 to 4, with 4 being higher nondrinking motives. Data from a cross-sectional high school survey were analyzed using participants who reported lifetime drinking (N=466). The SEM model tested indirect paths for the mediation of nondrinking motives and included direct paths from both urgency factors to alcohol use. Overall model fit indices were substantial (CFI=.98; TLI=.98; RMSEA=.05 [CI: .04, .06]; SRMR=.03). Nondrinking motives were negatively associated with alcohol use (β = -.24; p <.001) and positive urgency was positively related to nondrinking motives (β =.16; p <.05). Positive urgency was directly related to alcohol use (β = -.18, p <.01) and the indirect path through nondrinking motives was also significant (β = -.03, p <.05), indicative of partial mediation. In contrast to expectations, negative urgency was not associated with nondrinking motives or alcohol use. However, traits of positive urgency were influential on nondrinking motives and results indicated that nondrinking motives mediated positive urgency–alcohol use relations. These results indicate that individuals with fewer tendencies to rash action when experiencing high positive affect endorsed more nondrinking motives and reported lower current alcohol use. These results suggest that nondrinking motives may be influenced by trait urgency and offer further insight on mechanisms by which personality traits influence alcohol use during adolescence.
(Supported by the ABMRF)

0157

DRINKING REFUSAL SELF-EFFICACY AS A MEDIATOR BETWEEN PARENTAL MONITORING AND ALCOHOL-RELATED NEGATIVE CONSEQUENCES IN EMERGING ADULTS

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Previous studies suggest that high drinking refusal self-efficacy in adolescents and young adults is predictive of fewer negative alcohol-related consequences (Watson, 2008). Additionally, research has found an association between high parental monitoring and decreased alcohol use among adolescents, resulting in fewer alcohol-related consequences (Beck et al., 2007; Abar et al., 2009; Barnes & Farrell, 1992). However, few studies have explored the role of drinking refusal self-efficacy as a mediator for parental monitoring and alcohol related-consequences in young adults. The current study evaluated drinking refusal self-efficacy as a possible mediator of the relation between parental monitoring and alcohol-related negative consequences in a sample of high school seniors (n=289). Participants (58.8% female, age range: 17–18) completed the current measures as part of a larger assessment battery. It was hypothesized that participants who experienced higher levels of parental monitoring would report lower rates of alcohol-related negative consequences, and that this relationship would be partially explained by drinking refusal self-efficacy. Specifically, participants with higher levels of drinking refusal self-efficacy were expected to report lower rates of alcohol-related negative consequences. Statistical analyses were conducted in accordance with MacKinnon and colleagues' (2002; 2007) recommendations for testing mediation. Parental monitoring was found to significantly predict drinking refusal self-efficacy, β=-.19, F(1, 198)=7.63, p<.01. Additionally, there was a significant effect of drinking refusal self-efficacy on alcohol-related negative consequences after adjusting for parental monitoring, β=.48, F(2, 194)=33.27, p<.001. To test for the significance of the mediation, product of the coefficients tests were conducted, revealing a significant mediated effect of drinking refusal self-efficacy on alcohol-related consequences, z=-2.60, p<.05. Specifically, results indicated that drinking refusal self-efficacy mediated the relation between parental monitoring and negative alcohol-related consequences, with drinking refusal self-efficacy indicative of fewer alcohol-related negative consequences. These results suggest that improving parental monitoring is important for increasing refusal self-efficacy, which leads to fewer alcohol-related consequences. This research was supported by NIAAA #U01 AA018276 awarded to Drs. Larimer & Berglund.

0158

COGNITIVE ABILITY AND SHIFTS IN ALCOHOL EXPECTANCY AMONG EARLY ADOLESCENTS

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The initiation of alcohol use among children is preceded by changes in expectations for the effects of the substance, where positive expectancies increase and negative expectancies become less salient. Because the development of expectancies is a process in which alcohol-related information is internalized, cognitive ability may be related to the rate at which ideas about alcohol are learned and updated. A recent study showed that, among children in 3rd-5th grade, cognitive ability mediated the relationship between grade and expectancy, where heightened cognitive ability was related to greater expectancies among older children. This finding suggests that cognitive ability may predict expectancy development at a critical age, but this possibility has not yet been examined longitudinally. In the present study, we hypothesized that individuals with greater cognitive ability would have faster acquisition of positive expectancies and a faster decrease in negative expectancies than those with poorer cognitive ability. Data was collected as part of an ongoing 5-year longitudinal study which has followed younger and older sibling pairs (younger sibling average age at entry into study: ~9; older sibling average age at entry into study: ~11). The present data spans only 2 years, and serves as a preliminary examination of this phenomenon. The Kaufman Brief Intelligence Test was used to measure cognitive ability and alcohol expectancy was assessed using the Memory Model-based Expectancy Questionnaire. Repeated measures ANOVAs were used to examine whether cognitive ability predicted changes in expectancy in younger and older siblings over the course of 2 years. Results revealed that, among older siblings (but not younger siblings), cognitive ability significantly predicted change in expectancies for the positive social, negative arousal, and sedation impairment effects of alcohol, and that those with higher cognitive ability increased positive expectancies and decreased negative expectancies at a faster rate. These findings suggest that, within a critical developmental period, intelligence predicts the rate of expectancy shifts as positive and social effects of alcohol become more relevant and the negative and impairing effects become less salient.

0159

TOWARD A DUAL-PROCESS MODEL OF ALCOHOL COGNITION DEVELOPMENT: DISTINCT CROSS-SECTIONAL AGE DIFFERENCES ON EXPLICIT VERSUS IMPLICIT MEASURES

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Our study examined cross-sectional age group differences among participants ranging from pre-adolescents to young adults on self-reported alcohol expectancies and implicit alcohol cognitions. Dual process models, and prior evidence from our lab, suggest that positive associations around alcohol may be formed relatively early in life and remain stable across time, and that these positive associations among youth are best captured via implicit measures. Self-reported expectancies, on the other hand, are highly negative among young children, begin to moderate in early adolescence, and then become most positive for those who transition into drinking behavior. In the present study, thirty-four 3rd/4th graders, 43 7th/8th graders, and 100 university students (57 drinkers and 43 non-drinkers) completed an alcohol expectancy measure and two alcohol Implicit Association Tests (IATs). On the explicit subscale measuring likelihood of positive drinking outcomes, the four respondent subgroups differed significantly (F (3, 177) = 49.8, p < .001), with young adult drinkers rating positive outcomes as significantly more likely than other respondents (M=2.6), and elementary school children rating these outcomes the least likely (M=1.4; p's < .05); middle-school and non-drinking college students did not differ from one another on this scale. However, both elementary and middle-school students gave negative *evaluation* ratings to positive drinking outcomes such as ''feeling good''; college students evaluated these same outcomes positively. On the IAT, significant positive implicit alcohol associations were observed across all subgroups, but were stronger among college students compared to younger participants, regardless of drinking status (F (3, 180) = 11.4, p < .001). Our results partially support a dual process account of alcohol cognition development, but also highlight the relative complexity of age/behavior subgroup differences in explicit expectancies, and indicate change as well as stability in implicit associations. Implications for future work on dual processes in the development of alcohol cognition and drinking behavior are discussed.

0160

USING LINEAR GROWTH MODELS TO EXAMINE CHANGES IN ALCOHOL EXPECTANCIES IN RELATION TO THE ONSET OF PUBERTY

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Alcohol expectancies are the anticipated cognitive, affective or behavioral consequences of drinking stored in memory and activated by relevant drinking contexts. Measured via explicit verbal instruments, expectancies have been shown to predict later drinking and even to mediate the influence of well-known antecedents to drinking (e.g. personality, family history). It is important, therefore, to examine the factors that contribute to how expectancies are shaped as children enter into adolescence, when many individuals first begin drinking. Prior cross-sectional research has found that overall alcohol expectancies rise with the entry into adolescence from childhood; however, this finding has not been examined longitudinally. For the current longitudinal study, we examined the effect that the onset of puberty had on expectancies over time in a sample of 202 participants (50.5% female) who were between the ages of 8 and 13 at the first assessment point. Participants were assessed for expectancies using the Alcohol Expectancy Questionnaire – Adolescent Form (AEQ-A) at 5 time points, with 6 months between each time point. Consistent with previous literature, expectancies increased as children grew older. Compared with males, females showed a slower, less dramatic increase in expectancies with age. Using linear growth models, we found that puberty was a significant predictor of changes in AEQ scores over time for males but not for females. That is, in males, changes in expectancies appeared to be a function of the entry into puberty rather than age itself. Expectancies of male participants who already had gone through puberty tended to stay relatively stable over time, while those who had not gone through puberty showed a steady increase. It may be, therefore, that the steady increases in expectancies seen in early adolescents, using some expectancy instruments and cross-sectional designs, are actually due to increasing numbers of young males experiencing puberty as they grow older. These findings also suggest a critical period during which puberty-related changes in social, biological, and cognitive factors could lead to an increase in expectancies for alcohol.

0161

GENDER DIFFERENCES IN ALCOHOL AND MARIJUANA USE ASSOCIATIONS AND USE IN GRADES 7-12

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Much recent research on substance use in young people has focused on the role of cognitive processes. Two prominent methods of measuring substance use cognitions include indirect cued associations and explicit outcome use expectancies. Both types of cognitive measures predict substance use across diverse populations. The present study assessed gender differences in alcohol use cognitions in a Canadian population of middle and high school youth. In addition, we also assessed moderation by gender in the prediction of alcohol use by substance use cognitions. A cross-sectional sample of 1653 students from grades 7 to 12 received a survey beginning with indirect measures of associations with alcohol, an alcohol outcome expectancy questionnaire (Leigh & Stacy, 1993), questions about the quantity and frequency of alcohol and other drug use, and demographics. The indirect measures included ambiguous word associations (first response to ambiguous alcohol associates such as ''draft'') and behavior outcome associates (first behavioral response to possible alcohol use outcomes such as ''having fun'' or ''feeling relaxed''). Positive alcohol expectancies and indirectly assessed alcohol associations increased over grade; whereas negative expectancies decreased. Males generated more alcohol-related responses to ambiguous words than females. They also endorsed more positive fun and sexual enhancement expectancies and more negative social expectancies. Females endorsed more positive social facilitation and tension reduction expectancies and more negative emotional, cognitive and physical expectancies. Both indirect associations and direct expectancies independently predicted drinking across this age range after controlling for demographic predictors. For males, fun and negative cognitive expectancies were stronger predictors of use than for females. For females, ambiguous word associates as well as positive sexual enhancement and negative emotional expectancies were stronger. These findings confirm that indirect measures of alcohol associations and explicit alcohol use outcome expectancies measure different aspects of the cognitive representations of alcohol that predict and may mediate alcohol use in adolescents. Gender-based moderation of the pattern of cognitive representations and their relationship to use may be critical to the development of effective gendered approaches to prevention.

0162

FACTOR STRUCTURE OF THE BRIEF COMPREHENSIVE EFFECTS OF ALCOHOL SCALE IN ADOLESCENTS

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Adolescent alcohol use is an important public health concern. In light of the high prevalence rates of alcohol use among adolescents and the negative outcomes associated with this behavior, it is important that studies that examine factors associated with adolescent drinking behaviors utilize measures that are well-validated for use with this population. Both alcohol outcome expectancies (i.e., the beliefs about the likelihood of experiencing certain outcomes as a result of alcohol consumption) and expectancy valuations (i.e., the degree to which a drinking outcome is perceived as being desirable) have been linked to adolescent alcohol use. The primary purpose of the current study was to examine the factor structure and convergent validity of the Brief Comprehensive Effects of Alcohol scale (B-CEOA; Ham, Stewart, Norton, & Hope, 2005), a measure of alcohol outcome expectancies and expectancy valuations in a sample of adolescents. Self-report data were collected from 594 high school students (53% girls; M_{age}=15.70, *SD*=1.20, range=13–18 years; 76% White/Caucasian). Results yielded support for a factor structure among high school adolescents that differs in meaningful ways from the structure that has been identified in young adult college student samples. Adolescents' beliefs about the outcomes of alcohol appeared to fall into positive and negative domains consisting of observable social outcomes (e.g., ''I would act sociable'', ''I would be loud, boisterous, or noisy''), but not items assessing internal state outcomes (e.g., ''I would feel moody''). A multigroup analysis comparing factor loadings across three levels of experience with alcohol (i.e., never used, *n*=132; non-recent users, *n*=150; and recent users, *n*=228) indicated that the factor structure did not vary based on level of drinking experience. In addition, the current findings provided support for the convergent validity of the measure. Positive alcohol outcome expectancies as well as positive and negative expectancy valuations were associated with increased levels of hazardous drinking and past 30-day alcohol use frequency. Overall, findings suggest that the B-CEOA can be useful in assessing high school students' beliefs about alcohol. Further, a greater understanding of alcohol outcome expectancies and expectancy valuations among high school students could aid in designing effective, developmentally-informed alcohol prevention efforts.

0163

THE USE OF THE BRIEF COMPREHENSIVE EFFECTS OF ALCOHOL (B-CEOA) IN A SAMPLE OF RECENTLY IMMIGRATED HISPANIC ADOLESCENTS

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National surveys indicate that Hispanic early adolescents have the highest rates of alcohol use and escalation to general maladaptive patterns of use is greater among Hispanics compared to Whites. Given the putative role of alcohol expectancies (AEs) in relation to alcohol use outcomes, the validation of alcohol expectancy measures among Hispanic adolescents is an important goal for identifying and modifying alcohol expectancies among those adolescents at higher risk for maladaptive alcohol use and alcohol-related outcomes. AEs are cognitive representations about the effects of alcohol which evolve within a social and cultural context and are proximally associated with alcohol use. An extant literature has documented that alcohol expectancies (AEs) are strong predictors of alcohol use and related outcomes. Accordingly, several instruments have been validated for measuring AEs among children, youth, and adults. The Brief Comprehensive Effects of Alcohol (B-CEOA; Ham et al., 2005) assesses anticipated positive and negative effects associated with drinking. The B-CEOA also evaluates valuations which represent the individual's evaluation of how desirable or undesirable a given effect is. Few investigations have directed their attention toward the validation of scales measuring AEs among Hispanics. In the current study a confirmatory factor analysis was implemented to assess the factor structure of the B-CEOA among Hispanic adolescents. The sample consisted of 242(51% boys; 48% girls; mean age= 15.73,*SD*=0.86). Hispanic recent-immigrant adolescents from Miami (*N*=141) and Los Angeles (*N*=101). Adolescents in Miami had lived in the US for less than 2 years and were primarily from Cuba (61%);and those in Los Angeles had lived in the US about 4 years and were primarily from Mexico(70%).Results suggested a 4-factor model (positive expectancies, negative expectancies, positive valuations, and negative valuations).The model provided an adequate fit to the data: CFI = .95, RMSEA = .05 (90% CI =.04 to .06),SRMR = .05.Factor loadings ranged between .46 and .88, all *p*s < .001. Measurement Invariance tests across cities indicated that the 4-factor structure was equivalent between Miami and Los Angeles,$\Delta\chi^2(65) = 74.28$, $p = .20$. Similar findings of measurement equivalence were supported across male and female adolescents,$\Delta\chi^2(48) = 45.76$, $p = .56$.The findings support the use of the B-CEOA for identifying AEs and valuations among recently immigrated Hispanic adolescents.

0164

IMPULSIVITY AND SENSATION SEEKING AS MEDIATORS OF THE RELATION BETWEEN ADHD AND ENGAGEMENT IN AND FREQUENCY OF ALCOHOL USE

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Children diagnosed with ADHD are at increased risk of problem alcohol use as adolescents compared to adolescents without ADHD (Molina et al., 2007; Molina & Pelham, 2003). Impulsivity and sensation seeking, traits common among those with ADHD, are thought to influence alcohol use in adolescence (Dick et al., 2010; Smith et al., 2007), but their relative contribution to different aspects of drinking among those with childhood ADHD is under-researched. This study examined adolescent impulsivity and sensation seeking, separately and simultaneously, as potential mediators of the relation between childhood ADHD and alcohol use. A two-part modeling technique tested these relations for engagement in (i.e. use versus nonuse) and for frequency of drinking, binge drinking, and drunkenness. Two hundred forty-two adolescents, 142 with childhood ADHD and prospectively followed into adolescence and 100 without ADHD, were included in the study. Impulsivity and sensation seeking were mother-reported, and the alcohol use outcomes (i.e. engagement in and six month frequency of drinking, binge drinking, and drunkenness) were adolescent-reported. Adolescents with childhood ADHD reported higher levels of impulsivity and sensation seeking during adolescence. In turn, a higher level of sensation seeking was associated with greater engagement in drinking, binge drinking, and drunkenness, before and after controlling for impulsivity. Higher sensation seeking was also associated with more frequent drinking, but not with more frequent binge drinking or drunkenness. Interestingly, impulsivity was not associated with the engagement nor the frequency of the alcohol use outcomes when sensation seeking was controlled, though it was related to some of the alcohol use outcomes when sensation seeking was not controlled for. These correlational findings suggest that adolescents with ADHD histories may be at greater risk for engagement in alcohol use, including heavy drinking, due to higher levels of sensation seeking. Given the distinctiveness of this risk trait from impulsivity, and the tendency for impulsivity to be targeted in explanations of ADHD-related risky behavior, additional research on this trait in the ADHD population relative to alcohol and other drug use is warranted.

0165

IMPULSIVITY AS A MEDIATOR AND MODERATOR BETWEEN DIFFICULITY IDENTIFYING AND DESCRIVING EMOTIONS AND ALCOHOL USE AND RELATED PROBLEMS

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Purpose: This study examined the nature of the relationship between alexithymia and impulsivity, and how they influence alcohol use and alcohol-related problems. Alexithymia (i.e., difficulty identifying and describing emotions, and externally oriented thinking) and impulsivity are constructs associated with affect-regulation difficulties, and are often considered risk factors for alcohol use and related problems. Although research on alexithymia and impulsivity suggests lack of reflective cognitive processes lead individuals to drink more and experience more alcohol related problems, no study to date has investigated the relationships between these variables. It was hypothesized that positive and negative urgency function as either mediator or moderator between alexithymia and increased alcohol use and related problems. Positive urgency (PU) reflects one's tendency to react rashly to positive emotions; negative urgency (NU) is one's tendency to react rashly to negative affect.
Methods: Data from 431 undergraduate participants between the ages of 18 and 25 was used for the study. The sample contained 32% male and 68% female. Psychometrically sound measures such as the TAS-20, UPPS-P, DDQ-M, and YAACQ were used.
Results: As hypothesized, NU mediated the relationship between alexithymia and alcohol-related problems. PU mediated the relationship between alexithymia and alcohol consumption. PU also moderated the relationship between alexithymia and alcohol-related problems. At high levels of alexithymia, there was a significant association between PU and related problems. However, at mean or low levels of alexithymia, there were no significant associations between PU and related problems.
Conclusion: These results indicate distinct relationships between alexithymia and negative and positive urgency in predicting alcohol consumption and related problems. Overall, this study showed that individuals with difficulties in identifying and describing emotions are more likely to act impulsively under negative or positive affect, and thus engage in more drinking or suffer from more negative consequences after drinking. The findings of this research contribute to the body of the literature on alexithymia, self-regulation, and etiology of alcohol misuse and related consequences. Furthermore, the findings of current study provide support for the importance of emotion identification and expression skills training in substance abuse treatment.

0166

IMPULSIVITY AND RISK TAKING IN INDIVIDUALS WITH ALCOHOL DEPENDENCE VERSUS INDIVIDUALS WITH CO-OCCURRING ALCOHOL DEPENDENCE AND BIPOLAR DISORDER

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Objective: Behavioral disinhibition has been proposed as a key neurobehavioral risk factor for alcohol dependence (AD) and bipolar disorders (BD). Research has demonstrated that individuals with co-occurring BD and AD have elevated impulsivity and risk taking relative to those with BD alone. However, no studies that we are aware of have evaluated behavioral disinhibition in individuals with co-occurring BD and AD versus those with AD alone. A recent study found that individuals with co-occurring BD and AD had higher levels of risk taking (on the Balloon Analogue Risk Task; BART) than those with BD alone, but individuals with BD alone did not differ from healthy controls. Thus, it is unclear whether BD confers additional risk for elevated behavioral disinhibition above and beyond the effect of AD on individuals with co-occurring BD and AD. The present study evaluated impulsivity and risk taking in individuals with co-occurring BD and AD versus individuals with AD alone.
Method: Sixteen individuals with co-occurring AD and BD (AD+BD) and 18 with AD alone completed the BART and the Barratt Impulsiveness Scale-11 (BIS) as part of the baseline visit of an ongoing trial of lamotrigine. All participants reported consuming alcohol within 30 days of baseline. AD+BD and AD alone groups were compared on BIS and BART using t-tests and linear regressions controlling for age, scores on the Alcohol Dependence Scale (ADS), and days since last drink.
Results: AD+BD scored significantly higher than AD alone on the total score (82.9 vs. 66.2, p=0.001), as well as all three subscales, of the BIS. These differences remained significant (e.g., total score p=0.001) when age (p=0.33), scores on the ADS (p = 0.03), and days since last drink (p=0.38) were statistically controlled. AD+BD scored non-significantly higher than AD alone on BART (e.g., explosions: AD+BD=10.1, AD=8.3, p=0.14), however, these differences became significant (p=0.04) once age (p=0.83), ADS (p=0.25), and days since last drink (p<0.001) were statistically controlled. The same pattern was observed for adjusted average number of pumps on the BART.
Conclusion: The present study demonstrated that individuals with co-occurring AD and BD have higher levels of impulsivity and risk taking than individuals with AD alone. These results support the hypothesis that BD confers additional risk for elevated behavioral disinhibition above and beyond the effect of AD on individuals with co-occurring BD and AD.

0167

THE EFFECT OF MISMEASUREING IMPULSIVITY ON ESTIMATES OF ALCOHOL USE

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Self-report measures of impulsivity have consistently been associated with alcohol use and alcohol use problems. Studies that examine these associations often take mean scores of self-report impulsivity scales in their analysis, but mean scores are known to compound variance due to measurement error with true score variance. The current study aimed to investigate the impact of accounting for error variance in estimates of the association between dimensions of impulsivity and alcohol use variables. 504 undergraduate students at a large northwestern university were administered self-report measures of alcohol use behaviors and the UPPS impulsive behavior scale, which measures impulsivity as four distinct tendencies to rash action, premeditation, negative urgency, sensation seeking and perseverance. Controlling for the effects of age, gender and ethnicity, we then regressed self-report measures of quantity/frequency of alcohol use, binge drinking, and negative consequences on mean scores from the UPPS. We compared the standardized regression coefficients to a parallel model where the UPPS variables were modeled as latent variables. Results indicate that estimates of the association change significantly and unpredictably when measurement error was partially accounted for. For example, the estimate of the association between premeditation and alcohol use increased in magnitude when measurement error was accounted for, while the estimate of the association between sensation seeking and alcohol use decreased when measurement error was accounted for. These results suggest that estimates obtained using mean scores of impulsivity subscales can be biased, potentially increasing the risk of either Type I error or Type II error for any estimate. In conclusion, we suggest that future studies using impulsivity instruments to study associations with alcohol use or alcohol use problems should examine the measurement model of the instrument to assess for potential error before using mean scores in their analyses.

0168

THE INTERACTION BETWEEN SENSATION SEEKING AND NEGATIVE AFFECT LABILITY ON ALCOHOL INVOLVEMENT

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INTRODUCTION: Sensation seeking has been associated with lower levels of negative affect (Zuckerman & Neeb, 1972) and higher levels of affect lability (Carton, Jouvent, Bungener, & Widlocher, 1992). Moreover, both sensation seeking and affect lability were associated with increased alcohol involvement (Cyders et al., 2007; Simons & Carey, 2006). However, no studies ever examined whether *negative affect lability* would interact with sensation seeking. We hypothesized that negative affect lability would enhance the effects of sensation seeking on alcohol involvement.
METHOD: Using a large sample of college undergraduate students (n = 734), the current study tested whether negative affect lability moderated the effects of sensation seeking on levels of (1) hazardous alcohol use and (2) alcohol related problems. The sample was 74.6% female and 72.7% Caucasian, and had a mean age of 22.22 (SD = 6.31). Anxiety and depression lability (ADL), along with anger lability (AL), were measured using subscales of the Affective Lability Scale (Oliver & Simons, 2004). Sensation seeking was measured using an UPPS Impulsive Behavior subscale (Whiteside & Lynam, 2001). Alcohol problems and hazardous alcohol use were measured using the AUDIT (Babor, Higgins-Biddle, Saunders, & Monteiro, 2006). The hypothesis was tested using multiple regression and interactions were probed using simple slope analyses as indicated by Cohen, Cohen, Aiken, and West (2003).
RESULTS: Negative affect lability moderated the effect of sensation seeking on hazardous alcohol use and alcohol related problems. Sensation seeking predicted greater levels of hazardous alcohol use among participants with low levels of ADL (b = .50, p < .05), but this effect weakened at high levels (b = -.06, p = .66) of ADL. Similarly, the effect of sensation seeking on alcohol related problems was strongest for participants with low levels of ADL (b = .38, p < .05), but weaker for participants with high levels (b = -.10, p = .44) of ADL. A similar sensation seeking-alcohol related problems association was present among participants with differing levels of AL.
DISCUSSION: These findings are inconsistent with our hypothesis, and suggest that concurrent negative affect lability actually diminishes the effects of sensation seeking on hazardous alcohol use and alcohol related problems. These findings highlight the importance of considering negative affect lability among sensation seekers with problematic alcohol use.

0169

LOW SELF-CONTROL PREDICTS INCREASED ALCOHOL-RELATED PROBLEMS IN AN ADULT COMMUNITY SAMPLE

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Self-control (SC) is an established predictor of alcohol consumption and problem drinking. Recent research has demonstrated the utility of SC in predicting alcohol consumption and alcohol-related problems in college students. Very little is known, however, on how SC is associated with changes in drinking in older samples with an established drinking history. The present study aimed to extend this research by examining multiple measures related to SC as predictors of changes in drinking over a 1 year period in a community sample (N=560; 280 female; M age = 35.5; SD = 5.3 years). Participants were recruited via a mailed survey and heavy episodic drinkers (5 or more drinks in one sitting for men, 4 for women, or drinking to intoxication) were oversampled. At Time 1 (T1) participants completed measures of drinking and self-report (e.g., Brief Self-Control Scale, Dysexecutive Questionnaire (DEX)) and neuropsychological (e.g., Trail Making Test (TMT), Wisconsin Card Sorting Test) measures to assess different aspects of SC. Participants returned 1 year later (T2) and completed measures related to alcohol consumption and problematic drinking. Given the oversampling recruitment strategy, analyses were conducted using sampling weights. Sequential regressions were conducted to examine the prospective associations between SC at T1 and drinking variables at T2. For each model, a T1 drinking variable was entered at step 1 and a T1 SC variable was entered at step 2. T1 drinking variables significantly predicted T2 drinking. Controlling for T1 Alcohol Dependence Scale scores (ADS), all self-reported SC variables significantly predicted T2 ADS scores such that lower SC at T1 predicted higher ADS scores at T2. Controlling for T1 alcohol consumption, DEX scores significantly predicted T2 alcohol consumption in women. Poorer performance on TMT B significantly predicted T2 alcohol consumption for both men and women. No significant results were revealed for other neuropsychological measures. These results expand previous findings on the role of SC in problem drinking to an older community sample with an established drinking history. The discrepant findings between the self-reported and neuropsychological measures related to SC is consistent with prior research demonstrating heterogeneity in the SC concept. Further research is needed to determine the exact role of SC as it relates to changes in drinking over time and ultimately how it might impact treatment and intervention.

0170

MULTIDIMENSIONALITY IN IMPULSIVITY AND ALCOHOL USE: CLEARING UP THE CONFUSION WITH META-ANALYSIS

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The current paper seeks to clarify the relationship between unidimensional aspects of self-report impulsivity and underlying dimensions of alcohol use through a thorough meta-analysis. Final data set included 129 studies and 533 comparisons between impulsivity and drinking aspects. We hypothesized that the overall effect size between impulsivity and alcohol use would be significant, small and heterogeneous. Correlation values were weighted by sample size and were converted using a Fisher's transformation. We examined the homogeneity of the effect sizes, using the Q test. We also examined important confounding variables (sex, age, sample status) by conducting weighted multiple regression analyses. A fail-safe N analysis was conducted for each relationship.
There was a significant effect size between overall impulsivity and alcohol consumption (r=.18). Alcohol use had variable relationships with the specific impulsivity constructs: lack of perseverance (r=.33), positive urgency (r=.32), negative urgency (r=.23), sensation seeking (r=.18), and lack of deliberation (r=.02). Specific alcohol use outcomes provided more detailed evidence about hetereogenous findings: Drinking quantity was most highly related to sensation seeking (r=.24) and lack of perseverance (r=.20), drinking frequency was most highly related to sensation seeking (r=.24) and positive urgency (r=.23). Drinking onset was best predicted by sensation seeking (r=-.21) and lack of perseverance (r=-.36). The largest effect sizes for alcohol abuse, alcohol dependence, addiction, and problematic alcohol use were found for negative urgency (r=.28 –r=.39) and lack of deliberation (r=.17 – r=.98). Samples that were younger and more proportionally male showed a higher effect size between impulsivity and alcohol use.
Current findings demonstrate that when personality dispositions to rash action are studied separately, and when underlying aspects of alcohol use are studied separately, what initially appeared to be a small general effect size was disaggregated into several robust relationships between impulsivity-related traits and aspects of alcohol use. Thus, researchers should specify their target traits and drinking behaviors in order to study prediction accurately. Furthermore, clinical practice should consider interventions that target negative urgency, sensation seeking, and lack of deliberation, which appear to play an influential role in the process that leads to problematic and maladaptive alcohol use.

0171

THE COMPATIBILITY EFFECT: SELF AND PARTNER IMPULSIVITY INTERACT TO PREDICT CHANGES IN ALCOHOL PROBLEMS OVER TIME IN A COMMUNITY SAMPLE OF COUPLES

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Research demonstrates that impulsivity is often associated with problematic alcohol use. Therefore, it seems likely that two highly impulsive people in an intimate relationship would only exacerbate each other's problematic behavior over time. Emerging research suggests, however, that couples composed of two highly impulsive partners experience better relationship functioning than couples composed of partners who are "mismatched" on impulsivity. To the extent that marital functioning predicts decreases in problematic alcohol use, it might be the case that two highly impulsive partners would experience fewer, rather than more, alcohol problems over time. The current study examined the effect of matching on impulsivity on changes in alcohol problems over one year in a community sample of married and cohabiting couples. Couples (oversampled for heavy episodic drinking) were recruited via a mailed survey. Participating couples (n = 280; 560 participants) completed the Go/Stop Task (a behavioral measure of impulsivity) and an assessment of alcohol problems at Time 1. One year later (Time 2) they completed the assessment of alcohol problems again. Given the oversampling recruitment strategy, analyses were conducted using sampling weights. Data were analyzed using the Actor Partner Interdependence Model (APIM) in Mplus. Terms were entered sequentially into the equations. Time 1 alcohol problems were entered first, followed by the Actor Impulsivity and Partner Impulsivity main effects, and finally the Actor Impulsivity X Partner Impulsivity interaction. Time 1 alcohol problems were positively associated with Time 2 alcohol problems. Controlling for Time 1 alcohol problems, neither Actor Impulsivity nor Partner Impulsivity predicted Time 2 alcohol problems. However, the Actor Impulsivity X Partner Impulsivity interaction was significant. Alcohol problems at Time 2 were lower when partners were matched on impulsivity (both low or both high) than when they were discrepant. The results of these analyses suggest that it is critical to consider both partners when examining alcohol outcomes in partnered participants.

0172

THE EFFECT OF ADOLESCENT BINGE CONSUMPTION OF CAFFEINATED ENERGY DRINKS ON ADULT ALCOHOL CONSUMPTION

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The consumption of alcohol in combination with caffeinated energy drinks (Vodka Redbull, FourLoko, etc.) has seen a huge increase in popularity, particularly among young adults, despite potential negative health effects of these drinks. This has led several states in the United States to start banning the sale of these types of alcoholic beverages. Current research shows that young adults that consume large amounts of energy drinks may be more at risk for alcohol abuse. However, little is known as to how energy drink consumption in adolescents could lead to changes in alcohol consumption later in life. We hypothesized that binge consumption of sucrose and caffeine could sensitize the mesolimbic reward system, thereby priming these subjects for future alcohol consumption. Here, we set out to investigate if the consumption of large quantities of highly caffeinated energy drinks during adolescence affected ethanol consumption during adulthood of mice. Consumption of caffeinated energy drinks (Red Bull, Monster, NOS) was achieved using both a continuous access and a limited (binge) access paradigm. Following their exposure to energy drinks as adolescents, the now young adult mice were given access to increasing concentrations of alcohol (3%, 6%, 12% and 20%) for an additional 20 days. The results showed that there was no increase in consumption or preference of alcohol between the caffeinated energy drink consumers and the controls. These results suggest that the exposure to large amounts of caffeine and sucrose during adolescence does not predispose mice to increase alcohol consumption in later life. It is possible that consumption of large amounts of energy drink and alcohol may be linked to an impulsive genotype. This will be a matter of future investigations.
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0173

ENERGY DRINK CONSUMPTION AND THE USE OF ALCOHOL, TOBACCO, AND DRUGS OF ABUSE AMONG DUTCH PARTYGOERS

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Introduction: Some surveys have raised concern about a possible association between energy drink consumption and alcohol and drug use. The aim of the current study was to determine if the quantity of alcohol and drug use on a night out differs between those who consume energy drinks and those who do not. In contrast to previous studies, which were all conducted in university students, the current study was conducted in partygoers who attended parties, clubs and discotheques.
Methods: N=5768 partygoers (18–30 years old) were recruited at parties, clubs and discotheques in The Netherlands. On premise, they completed a short interview (demographics). They were invited to complete a follow-up survey about their energy drink consumption, alcohol and drug use of that particular evening. The quantity of alcohol, tobacco, and drug use (before and during the night out) were statistically compared between those who mixed alcohol with energy drink (AMED) and those who consumed alcohol alone.
Results: A total of 1096 partygoers (19%) completed the follow-up survey. N=188 consumed AMED and N=699 consumed alcohol alone. No significant differences between the groups were found with regard to the use of alcohol, tobacco, and drugs, including cannabis, ecstasy, cocaine and amphetamines.
Conclusion: No difference was found regarding the consumption of alcohol, tobacco and drug use between those who consumed energy drinks that evening and those who did not. The current findings do not support the raised concerns about mixing energy drinks with alcohol.

0174

DUTCH STUDENT SURVEY: ALCOHOL AND ENERGY DRINK CONSUMPTION, ALCOHOL RELATED CONSEQUENCES AND RISK TAKING

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Introduction-Recent surveys raised concerns regarding alcohol mixed with energy drinks (AMED). Aim of this online survey among Dutch students was to assess drinking and mixing behavior, alcohol related consequences and level of risk taking behavior. Methods-Students were invited to complete an online survey assessing demographics, alcohol consumption (frequency and quantity), alcohol related consequences, and levels of risk taking behavior. Between-group analyses compared those who (1) occasionally consume AMED, (2) consume energy drinks but never mix with alcohol (AED), and those who consumed alcohol only (AO). Within-subjects comparisons (AMED-group) were conducted to determine if mixing with energy drinks has an effect on overall alcohol consumption and its consequences. Results-N=6002 students completed the survey, including N=1239 AMED, N=917 AED, and N=3185 AO consumers. Between-group analyses confirmed that the groups significantly differ on alcohol, drug, and tobacco use (AO<AED<AMED).This difference is reflected by their risk taking scores: AO (5.4)<AED(6.4)<AMED(7.2).
Within subject analyses in the AMED-group compared occasions when drinking alcohol alone with those when consuming alcohol mixed with energy drinks. Compared to alcohol only consumption, when consuming alcohol mixed with energy drinks students reported significantly ($p<0.001$) less alcohol consumption (5.4 versus 6.0 drinks), less drinking days (9.2 versus 1.9 days), and less occasions with more than 4 (women)/5 (men) alcoholic consumptions (4.7 versus 0.9). Past months maximum number of alcoholic drinks while mixing (4.5) was significantly ($p<0.001$) lower when compared to occasions when they consume alcohol alone (10.7). Accordingly, the average duration of alcohol consuming was significantly ($p<0.001$) shorter while mixing (6.0 vs. 4.0 hours). In line, past years maximum number of alcoholic drinks when combining (4.8) was significantly ($p<0.001$) lower when compared to occasions of alcohol consumption alone (14.6). Finally, in comparison to consuming alcohol only, when consuming alcohol mixed with energy drinks significantly ($p<0.001$) fewer alcohol related consequences were reported (4.9 vs. 2.6), including driving a car while intoxicated, taking risks, being injured or hurt. Conclusion-When consuming alcohol mixed with energy drinks less alcohol is consumed and less alcohol related consequences are experienced, suggesting energy drinks do not enhance alcohol consumption or alcohol related consequences.

0175

BEVERAGE TYPE AS A PREDICTOR OF ALCOHOL USE OUTCOMES AMONG UNDERGRADUATE STUDENTS

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Purpose: Studies have shown that both demographic variables (e.g., age, gender and Greek membership) and beverage type are associated with alcohol outcomes (Carter et al., 2010; Ham & Hope, 2003; Naimi, 2007). However, no studies to date have examined the *relative* contributions of beverage type and demographic variables to the prediction of alcohol outcomes.
Methods: Data were collected during the baseline assessment of an ongoing RCT testing web-based brief motivational interventions for college drinkers. Participants were a randomly selected sample of undergraduate students (N=350) who reported at least one drinking occasion in the past month. Predictor measures included a demographic questionnaire assessing Greek membership, legal drinking status (minors versus 21 years and older), and gender, as well as self-reported typical beverage type. Outcome measures included a quantity-frequency measure (Collins et al, 2002) and the Rutgers Alcohol Problem Index (White & Labouvie, 1989).
Results: Negative binomial models indicated that Greek membership was positively associated with all alcohol outcomes, whereas male gender and legal drinking status were positively associated with quantity and frequency, respectively. Model comparisons indicated that beverage type significantly contributed to the prediction of alcohol-related problems and typical quantity above and beyond the demographic variables. Specifically, beer and liquor consumption predicted greater alcohol-related problem experience, and liquor consumption alone predicted increased typical quantity.
Conclusions: Beer and liquor consumption are associated with riskier drinking, even after accounting for potential confounding variables such as legal drinking status, Greek membership and gender.

0176

PROSPECTIVE EXAMINATION OF THE LEVEL OF RESPONSE MODEL ON ALCOHOL PROBLEMS AMONG COLLEGE STUDENTS

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Schuckit and colleagues proposed a model in which level of response to alcohol (LR) is associated with alcohol outcomes directly and indirectly via mediation by alcohol expectancies, coping motives, and peer influences. The LR model has received general support in several cross-sectional studies but has only been examined in one prospective study, which also included laboratory assessment of LR and did not control for baseline LR – alcohol outcome relations. We seek to extend research on the LR model by prospective prediction of alcohol problems while controlling for baseline associations. Participants (N = 1,014) were recruited for a randomized alcohol prevention trial prior to college entry and were assessed via survey at baseline, 10-, 22-, and 46-months follow-ups. Retention rates were 90.8%, 84.0%, and 62.0%, respectively. Problems (PROBS) were assessed at each wave, with LR was assessed via the SRE (first 5 times drinking) at 22 mos, and alcohol expectancies (EXP), coping motives (COPE) and peer influences (PEER) at 46 mos. Unconditional model analyses supported a linear trajectory which demonstrated positive growth in problems. Intervention conditions and gender were then covaried and direct paths from LR to PROBS intercept and slope were estimated. Paths from LR to putative mediators (PEER, EXP, COPE) and from these factors to PROBS intercept and slope were estimated and indirect effects were tested. Additional LR model hypothesized paths were included. Model fit was acceptable (CFI=.91, RMSEA=.06, SRMR=.05). LR demonstrated significant positive associations ($p < .001$) with the intercept of problems such that a lower level of response was associated with more problems prior to college matriculation. However, LR demonstrated significant negative associations ($p < .01$) with the slope of problems indicating a lower level of response was associated with less growth in problems during college. LR was not associated with PEER, EXP, or COPE and all tests of indirect effects from LR to PROBS intercept and slope via PEER, EXP, and COPE were non-significant. PEER was positively associated with both the intercept ($p < .001$) and slope ($p < .01$). While observed LR – PROB intercept relations are consistent with the LR model no other hypothesized direct or indirect effects were observed. These prospective findings raise questions about the LR model, particularly with respect to measuring LR via the SRE. Supported by NIAAA R01AA013919.

0177

POSITIVE AND NEGATIVE EMOTIONAL EXPRESSION PREDICT POOR LONGITUDINAL DRINKING OUTCOMES AMONG ALCOHOLICS INTERVIEWED ABOUT DRINKING AND ITS CONSEQUENCES

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Higher levels of positive affect have been associated with good health outcomes and health-protective factors in the general population. This study investigated whether positive and negative emotions expressed during the baseline interview of a longitudinal survey of alcohol-dependent individuals might predict drinking outcomes over time. We hypothesized that positive emotional expression would predict better outcomes and negative expression worse outcomes.
Methods: 364 SCID-diagnosed alcoholics were recruited from treatment and non-treatment sources and followed for 2.5 to 3 years. At baseline, respondents were asked open-ended questions about their drinking (e.g., What made you seek help for your alcohol problem right now?) Interviews were audio-recorded and 56 were randomly selected and transcribed. Transcripts were analyzed by the Linguistic Inquiry and Word Count program to identify high content of positive- and negative-emotion words. The resulting ratios of emotion words as a function of total words were compared with baseline and longitudinal percent days abstinent (PDA), drinks per drinking day (DDD), and percent heavy drinking days (HDD). Partial correlations (controlling for age, gender, and baseline drinking severity) determined associations between affect expressions and drinking outcomes.
Results: Some positive emotions, such as joviality and well-being, as well as some negative emotions, such as guilt and stress, were associated with poor drinking outcomes. Joviality was associated with fewer PDA at baseline and 6 months, more DDD at 1 year and more HDD at baseline, 6 months, and 2 years. Well-being was associated with fewer PDA at 2 years, more DDD at 1 year and more HDD at baseline and 2 years. Self-assurance was associated with higher HDD at baseline. Stress and guilt were associated with fewer PDA and more HDD at 1 and 1.5 years. Stress was also associated with more DDD at 2 years. Some emotional states, such as anxiety, depression, anger, fatigue, fear, hostility, sadness, calmness, and serenity had no association with drinking.
Conclusions: While it is reasonable for alcoholics to express negative emotion while describing their drinking, it is noteworthy that both positive and negative emotional expressions were associated with poor longitudinal outcomes. These results suggest that affect examined as a predictor of outcomes for individuals with alcohol use disorders may be more complex than for individuals with other health challenges.

8. CONSEQUENCES OF ALCOHOL CONSUMPTION IN HUMANS

0178

PREDICTORS OF DRINKING AND DRIVING & RIDING WITH A DRINKING DRIVER AMONG UNDERAGE DRINKERS IN THE EMERGENCY DEPARTMENT

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This study evaluated the associations between demographics, alcohol use history, alcohol-related injuries, and drinking and driving (DD) and riding with a driver who has been drinking (RDD) among underage drinkers who presented in an emergency department setting. We utilized data collected from 1045 underage drinkers (age 16 to 20) who, as part of a randomized controlled trial, completed self-report measures assessing demographics, alcohol use, past-year injuries, past-year drinking and driving, and past-year occurrence of riding with a driver who had been drinking alcohol. One-quarter (25%) of participants endorsed DD behavior in the past year and 40% reported RDD in the same time period. Two parallel logistic regression analyses were conducted to examine correlates of past year DD and RDD based on demographics (race, gender, age, enrollment in school), age of first alcohol consumption, scores on the AUDIT-C, past-year alcohol-related injury, and ever having injured another person due to participants' own drinking. At the bivariate level, school enrollment, age of first alcohol consumption, AUDIT-C scores, alcohol-related injury, and having injured others due to one's own alcohol use were related to both DD and RDD; race was associated with RDD only and age was associated with DD only. Multivariate analyses revealed that participants who were of Caucasian race, enrolled in school, and who had initiated drinking at an older age had lower odds of both DD and RDD. History of past-year alcohol-related injury, higher scores on the AUDIT-C, and having previously injured others due to drinking were associated with increased odds of involvement in both DD and RDD. These findings indicate that, in addition to demographic and alcohol use factors, involvement in alcohol-related injuries are also associated with risky driving behaviors among underage drinkers. Given the rates of DD and RDD in this sample, and the relationships of both with alcohol use and injury history, our results suggest that the ED visit may provide an opportunity for interventions targeting reduction in both RDD and DD among underage drinkers. (Supported by NIAAA #018122).

0179

ATTRIBUTABLE FRACTION OF INJURY DUE TO ALCOHOL USE IN THE AMERICAS

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One particularly important outcome in the study of the burden of disease due to alcohol use is injury, typically associated with the acute effects of alcohol use. Recently, a great deal of work has been done to estimate the components of the Attributable Fraction (AF, the proportion of injury directly attributable to the use of alcohol) of injury due to alcohol; specifically, the Relative Risk (RR) of injury due to alcohol use. While RR estimates (and estimates of the prevalence of acute use) have been estimated for a number of countries around the world, estimates have been conspicuously absent for a number of countries in the Americas. The present work examines RR and AF estimates for 5 countries in the Central American and Caribbean countries, including the Dominican Republic, Guatemala, Guyana, Nicaragua, and Panama. Using, as the control period, the same 6 hour period the week prior and the definition of exposure as any drinking during this period, the overall RR estimate associated with any alcohol use 6 hours prior to the injury estimated combined across these 5 countries was 4.4. Along with the prevalence of drinking of any drinking 6 hours prior to the injury of 20.8%, the overall estimated AF of injury due to alcohol was 16.1%. RR estimates for each country separately were 3.3, 3.9, 4.2, 4.5, and 9.6 for Guyana, Panama, Nicaragua, Guatemala, and the Dominican Republic and prevalence estimates for the same countries were 21.0%, 20.8%, 21.5%, 21.1%, and 19.3%. The resulting AF estimates for these same countries were 14.7, 15.5, 16.3, 16.5, and 17.3. Although overall AF estimates were surprisingly similar across these countries, variation was seen in the RR and prevalence estimates which can have important implications for alcohol policy.

0180

UNDERAGE DRINKING AND UTILIZATION OF HEALTH CARE RESOURCES AT LEVEL I TRAUMA CENTERS

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Multiple studies have demonstrated that alcohol is associated with higher utilization of health care resources and especially imaging resources for adult trauma victims. The purpose of this study was to evaluate the association between positive blood alcohol concentration (BAC) and resource utilization for underage drinkers admitted to a level I trauma center. We performed a retrospective cohort study of injured patients, <21 years old, admitted to Harborview Medical Center (HMC) from 2005-2009. We linked the HMC trauma registry to HMC billing department data and extracted the following variables: age, gender, race/ethnicity, mechanism of injury, injury severity score (ISS), length of hospitalization, ICU admission, final disposition (dead vs. alive), year of admission, and (BAC). An injury was considered alcohol-related if the patient had a BAC>0. Children <13 years were excluded from analysis due to the minimal number in which BAC>0. Linear regression was used to evaluate the association between BAC and length of hospitalization. Logistic regression evaluated the association between BAC and the odds of ICU admission, discharge status (home with no help, skilled nursing facility, and jail) and death. Negative binomial regression evaluated the association between BAC and computed tomography (CT) utilization, the most commonly used advanced imaging technology. All analyses were adjusted for patient and injury-related variables that could potentially influence outcomes. A total of 2,435 patients, 13–20 years old were included in our final analysis. A positive BAC was reported in 20% of these patients. The presence of alcohol was associated with increased odds of ICU admission (OR: 1.47; 95% CI: 1.12–1.92), and discharge to jail (OR: 5.04; 95% CI: 2.21–11.49). In negative binomial analyses and after adjusting for gender, race, mechanism of injury, ISS, ICU admission and final disposition, alcohol was only associated with higher utilization of abdominal CTs (IRR: 1.23; 95% CI: 1.06–1.44). Similar to adult trauma victims, positive BAC is associated with increased utilization of health care resources in underage drinkers. However, the association with higher utilization of advanced imaging techniques, such as CT, is less significant in the younger population. This could be partially attributed to a higher threshold of physicians in utilizing CT, especially repeat CTs, because of the concern for potential carcinogenic consequences of radiation.

0181

PREDICTING DRIVING AFTER DRINKING OVER TIME AMONG COLLEGE STUDENTS
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Despite substantial prevention efforts, driving after drinking (DAD) is a prevalent high-risk behavior among college students and is a leading cause of death and injury. Greater exploration of factors predicting future DAD behavior is necessary to develop efficacious targeted interventions to reduce DAD among college students. The current study evaluated demographic, social cognitive and behavioral predictors of DAD using longitudinal data. Participants were 655 non-abstaining college students (67.2% female, 60.3% Caucasian, of mean age 19.3 years) who completed online surveys at two time points 12 months apart. Demographics, weekly alcohol consumption and family history of alcohol abuse or dependence were assessed at Time 1. At both time points, participants reported their rates of driving after drinking three or more drinks in the past three-month period, and the extent to which they (i.e. attitudes) and the typical student (i.e. injunctive norms) approved of driving a car after drinking. Results revealed that 27.9% of students reported engaging in DAD at either time point, with the proportion of students reporting DAD increasing significantly from Time 1 (15.7%) to Time 2 (21.1%), $Z = 2.29$, $p = .011$. At Time 1, the vast majority of students (86.1%) reported strongly disapproving of DAD; whereas just over half (50.2%) believed that the typical student strongly disapproved of DAD. Participants' attitudes and injunctive norms towards DAD did not change significantly from Time 1 to Time 2; however, at both time points, participants overestimated peers' DAD approval levels. Further, logistic regression findings showed that older age (*OR* = 1.49, *C.I.* = 1.16, 1.91), greater alcohol consumption (*OR* = 1.06, *C.I.* = 1.03, 1.09), greater perceived peer approval of DAD (*OR* = 1.28, *C.I.* = 1.03, 1.58), and past DAD behavior (*OR* = 4.18, *C.I.* = 2.50, 6.99), uniquely contributed to the prediction of DAD behavior 12 months later. These findings not only provide further support for the high prevalence rates of DAD among college students but also offer unique insights into the longitudinal predictors of DAD among this population. Findings indicate that DAD-reduction efforts among college students would benefit from targeting older students, and that interventions correcting DAD-related normative misperceptions may be especially beneficial among this population.

0182

DIFFERENCES IN SF-36 HEALTH SURVEY SUBSCALE SCORES AMONG DWI OFFENDERS
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Drawn from a large, federally-funded study to examine physical and mental health status in a population of DWI offenders (''Health Consequences Among DWI Offenders'', National Institutes of Health (R01 AA12567)), the purpose of this current study is to examine the hypothesis that there would be significant differences in scores obtained on the various subscales of the SF-36 Health Survey among demographic subgroups of a DWI population. The sample consists of 295 DWI offenders recruited from courts in Buffalo, NY and selected suburbs for the Erie County Study of Behavioral Health. Data collected includes demographics, alcohol and drug use, various risk-taking behaviors, and details regarding participants' (most recent) DWI arrest. The sample is about 75% male and 78% Caucasian, with a mean age of 32.3 (±11.4) years. Over 71% (n=210) of the subjects were first-time DWI offenders, over 50 subjects (18%) were second-time offenders, and the remaining 11% reported between three and seven DWIs in their lifetime. All eight SF-36 subscales were examined, comprised of measures of Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health. Statistically significant differences were found for the Physical Functioning subscale with regard to both age ($r=-.33$, $p<.001$) and ethnicity ($F=7.6$, $p<.01$), with younger subjects and Caucasians faring better than older subjects and non-Whites. Significant negative correlations were also found between age and the Role-Physical ($r=-.21$, $p<.001$) and Bodily Pain ($r=-.23$, $p<.001$) subscales. There were no significant results obtained for either gender or number of DWIs. While the investigators expected to see a larger number of significant differences in subscale scores among the various demographic subgroups, they will examine the possibility that, since age was found to have significant correlations with three of the subscales, significant differences in subscales scores will emerge for gender and number of DWIs when age is controlled for in further analysis (to be presented in the poster). Results have important implications for early intervention with DWI offenders who face both substance use and subsequent negative health issues.

0183

THE RELATIVE CRASH RISK OF DRUGGED AND DRINKING DRIVING: FATAL CRASHES (PRELIMINARY RESULTS)
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Aims: There is a growing interest in the extent to which the joint use of drugs and alcohol by drivers relates to crash involvement. We evaluated the hypotheses that drugged driving contributes to fatal crashes, but not as much as drinking and driving.
Methods: We matched the 1998–2009 Fatality Analysis Reporting System (FARS) and the 2007 National Roadside Survey. Only states in which more than 79% of the drivers in the FARS file were tested for drugs and had a known result were included. A (0,1) dummy variable identified the presence of any drug. A total of 1,068 fatally injured drivers and 3,139 non-crash involved roadside survey sampled drivers satisfied the matching criteria. We ran two separate logistic regressions (main effects only) to estimate relative-risk estimates for drug-involved driving alone, and/or with alcohol as a covariate, for different demographic groups. To account for crash-responsibility, only single-vehicle crashes were included.
Results: About 66% of the non-crash-involved drivers were negative for both alcohol and drugs; 7% were positive only for alcohol; and 2% were positive for both. For fatally injured drivers, the percentages were 11%, 55%, and 16%, respectively. The odds ratio (OR) for crash involvement was significantly higher for males and underage drivers than for females and drivers aged 21–34. Drugs contributed to crash risk (OR=1.68) when BAC was not included in the model. With alcohol in the model though, the contribution of drugs to crash risk was no longer significant.
Conclusions: These results present evidence in support of both hypotheses, namely that both drugs and alcohol contribute to crash risk, which such contribution being much higher for alcohol. Partition of the drug measure into components and the analyses of alcohol by drug interaction should add clarity to these results.

0184

DRINKING DRIVING AND FATAL CRASHES: ARE SOME RACIAL/ETHNIC GROUPS MORE AT RISK THAN OTHERS?
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Aims: Despite the gains made in traffic safety over the past 20 years, some racial/ethnic groups in the U.S. are overrepresented in alcohol-related motor vehicle fatalities. Several explanations have been offered. In this effort we evaluate if, at a given BAC level, some racial/ethnic groups face a higher crash risk than others.
Methods: We matched the 1998–2009 Fatality Analysis Reporting System (FARS) and the 2007 National Roadside Survey. Only states in which more than 79% of the drivers in the FARS file were tested for drugs and had a known result were included. A total of 1,068 fatally injured drivers and 3,139 non-crash involved roadside survey sampled drivers satisfied the matching criteria. Logistic regression was used to estimate relative-risk estimates. To account for crash-responsibility, only single-vehicle crashes were included. Interaction terms were used to examine whether race/ethnicity changes the RR curve as a function of BAC of a fatal crash for single- and all-vehicle crashes.
Results: As expected, alcohol was a significant contributor to crash risk. Also, non-Hispanic White and African-American drivers were less likely to be involved in a single-vehicle crash than Their White counterparts. The interaction term between BAC and race/ethnicity was however, statistically non-significant. In other words: at a given BAC level, all racial/ethnic groups are at the same crash risk.
Conclusions: Although rates of crash involvement differ across racial/ethnic groups, the impairing effects of alcohol on driving are similar to members of different racial/ethnic groups. Although culturally tailored, interventions should focus equally on reducing impaired driving across all groups.

0185

THE ROLE OF ALCOHOL USE AND AVOIDANT COPING IN THE RELATIONSHIP BETWEEN ASSAULT, PTSD, AND PHYSICAL HEALTH

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Trauma exposure and posttraumatic stress disorder (PTSD) are associated with poorer physical health in college students (Flood et al., 2009; Lawler et al., 2005). Theories suggest that psychological mechanisms, such as coping strategies, and behavioral mechanisms, such as health risk behaviors, may help account for this relationship (Schnurr & Green, 2004; Schnurr & Jankowski, 1999). The current study tested these two proposed explanations by examining both avoidant coping and alcohol use as mediators of the relationship between trauma exposure, PTSD, and physical health. We included both mechanisms in the same model to more clearly delineate the proposed psychological and behavioral pathways. We recruited 827 college women who reported heavy episodic drinking (≥4 drinks on one occasion) at least twice in the past month. We compared three groups: women with no trauma history, women who reported at least one experience of childhood or adult sexual assault that was not within the past 3 months but did not have current PTSD, and women who had experienced sexual assault and had current PTSD. Measures of avoidant coping, alcohol use, and physical health were included. To test mediation effects, we ran multiple mediation analyses with three path models, where assault group was the independent variable with three categories (no trauma, assault no PTSD, assault and PTSD). We found that PTSD, not trauma exposure, was significantly positively associated with alcohol use (range of βs = 1.90 - 2.92) and that both PTSD and trauma exposure significantly predicted increased avoidant coping (range of βs = .22 - .67). This suggests that PTSD in particular may be associated with heavy alcohol use, while assault history in and of itself, as well as PTSD, may be related to coping with avoidant strategies. We also found that avoidant coping, not alcohol use, mediated the relationship between trauma, PTSD and physical health (range of mediation effects 1.16 – 3.52). These findings suggest that for young women, avoidant coping may be more critical in the relationship between PTSD and physical health concerns than alcohol use. Thus, decreasing avoidant coping may be an important area of intervention for young trauma-exposed women to improve physical health.

0186

AMERICAN INDIAN WOMEN'S PERCEPTIONS OF PARTNER VIOLENCE AND ALCOHOLUSE ON RESERVATIONS

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Intimate partner violence (IPV) and alcohol use have impacted American Indian families and traditional indigenous communities. The current study examines the experiences of American Indian women and girls affected by IPV. In a mixed-methods study on the impact of IPV on mother-daughter attachment relationships within Northern Plains and Upper Midwest American Indian reservations, 50 semi-structured ethnographic interviews were conducted with 25 women and 25 girls from two reservations in the Northern Plains and Upper Midwest region of the United States. The ages of the women ranged from 29 to 54 and the girls' ages ranged from 12 to 18. Interview transcripts and session notes were coded for recurring themes, using the qualitative software (ATLAS.ti), then retrieving coded segments of text cross-referencing partner violence and alcohol/substance use. Approximately 46% (23) of the participants reported that they had been in relationships with a partner who used substances while being violent toward them. Additionally, 32% (16) of the participants reported being under the influence of substances during the occurrences of violent acts from a partner. The need for alcohol and substance use/abuse intervention emerged as an important issue for study participants. Participants frequently reported negative consequences affiliated with alcohol and substance use such as social service involvement, legal ramification, and even death within their respective communities. Additionally, participants identified the impact of substance use on their families functioning across generations. This context provides some insight on historical trauma and the participants' perspectives of potential contributing factors of family violence and abuse on their reservations. Finally, the reliance of family and spiritual support resonated with participants as a means of coping with trauma.The outcomes of this study provide insight into the development of culturally appropriate treatments as well as policies within reservations. Incorporating interventions in line with the communities' culture is essential, therefore an accurate ethnic identity assessments is warranted in treatment. Establishing protocols to identify and respond to IPV within smaller reservations will lead to better safeguards and trust among members. Additionally, by implementing substance use/abuse interventions that include components on IPV interventions will inform community members about dynamics of these factors.

0187

YOUNG WOMEN'S DESCRIPTIONS OF SITUATIONS AND BEHAVIORS THAT SIGNAL RISK FOR ALCOHOL-RELATED SEXUAL ASSAULT

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Five focus group discussions were conducted with 42 young (*M* = 24.9; *SD* = 2.7; range = 21–30 yrs), female, social drinkers to determine the situations and behavioral cues that they believe signal risk for sexual assault (SA). Women were recruited through advertisements in an entertainment newspaper and on Facebook. Two-thirds (66%) of the women were White, 24% Black, 5% of mixed race, 5% of another race, and 10% reported being Hispanic. Prior to discussions, women completed a brief questionnaire about their history of victimization and usual drinking patterns. Women reported consuming an average of 15.1 drinks (*SD* = 8.1) weekly, and heavy episodic drinking an average of 7 times (*SD* = 7.6) in a typical month. Rates of prior SA were high among the sample. Sixty-two percent reported some form of childhood SA. Less than half (43%, *n* = 18) of women had experienced adult SA as a result of physical force, while 63% (*n* = 26) had experienced SA due to incapacitation. Discussions were conducted until saturation was reached (i.e., new information was no longer emerging from discussions). Across the 5 groups, women agreed that certain settings and situations increased risk for SA, including: in bars when ''hanging out''; in public places (e.g., subways, events) or sporting events where crowd density was high; and at house parties that involved alcohol, over-crowding, or people ''crashing'' overnight. Women were asked to describe behaviors that men engage in that cause them to feel ''concerned or frightened'' for their sexual safety. A number of behaviors were described in all 5 discussions. These included certain types of touching, specifically a lingering, rubbing, stroking touch. Other situations that were of concern involved men who: become aggressive when told ''no,'' made unexpected sexual comments/jokes or compliments, encroached on one's personal space (following, cornering at the bathroom, restricting movement with his body), and ignored cues of disinterest. Women qualified their level of concern or fear with most of these behaviors. The most common qualifier was the degree of isolation the women felt in the situation, followed by the degree of persistence exhibited by the man. When isolation was high, all of these behaviors, with the exception of compliments, were seen as high risk for SA. These findings will be discussed in terms of the costs/benefits women appear to recognize and acknowledge when choosing to drink and become intoxicated when socializing with men.

0188

CHANGES IN EMOTIONAL REACTIVITY AND DISTRESS TOLERANCE AMONG HEAVY DRINKING ADOLESCENTS DURING SUSTAINED ABSTINENCE

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Objective: Negative affect and low distress tolerance have been associated with increased likelihood of alcohol consumption and relapse. This study utilized the Paced Auditory Serial Attention Test (PASAT-C) Computer Version to examine affective reactivity, cognitive performance, and distress tolerance during early abstinence among heavy drinking adolescents.
Method: Participants, ages 16–18 (50% female), were 23 heavy episodic drinking youth (HED) and 23 demographically-matched, non-drinking teens (CON). Both groups were drawn from the same schools and assessed at three time points: HED were first studied within 10 days (*M* = 4.26, *SD* = 4.4) of heavy episodic drinking and then at two 2-week intervals over four subsequent weeks of monitored abstinence. CON were studied at the same 2-week intervals.
Results: Findings indicate that HED responded with greater distress to the PASAT (i.e., greater increases in frustration and irritability and greater decreases in happiness) at the initial assessment, but their affective responses normalized with sustained abstinence. CON's and HED's task performance did not differ at the initial assessment or across time. HED showed faster quit times in the task at the first assessment, and both groups reduced quit times across testings. Among HED, greater lifetime and recent alcohol consumption, frequency of alcohol-induced blackouts, and withdrawal symptoms were associated with increases in negative affect with PASAT-C exposure. Earlier age of onset of alcohol use was linked to poorer performance.
Conclusion: Heavy episodic drinking adolescents demonstrated heightened emotional reactivity and poorer distress tolerance to a cognitively challenging task during early abstinence. The combination of elevated negative affect and low distress tolerance may place adolescents at a heightened risk for escalations in use or relapse.

0189

EARLY ADOLESCENT SUBSTANCE USE PREDICTS CONDUCT DISORDER SYMPTOMS BUT NOT DEPRESSIVE SYMPTOMS IN LATE ADOLESCENCE

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Adolescent substance use has been shown to increase risk of depressive (e.g., Mason et al., 2008) and conduct disorder symptoms (e.g., Wells et al., 2004) over and above prior symptoms. However, few studies have examined prospective links from mid- to late-adolescence or considered associations between substance use, depression and conduct disorder in the same model.

To examine whether early substance use increases risk of depressive and conduct disorder symptoms by late adolescence, we used the Developmental Pathways Project sample, which includes a cohort of 521 6th graders from the racially- and demographically-diverse Seattle Public Schools followed longitudinally for 6 years (91% retention). Participants were over-sampled for depression and conduct problems; sample weights were used to ensure generalizability. In 9th grade, adolescents reported their frequency of alcohol and marijuana use in the past 6 months, level of use-related impairment in the past 6 months, and DSM-IV depression and conduct disorder symptoms in the past year. Self-reported depression and conduct disorder symptoms were re-assessed in 12th grade.

The hypothesized structural equation model fit the data well, χ^2 (8) = 17.38, $p < .05$, RMSEA = .05, and CFI = .98. Latent substance use (Indicators: alcohol and marijuana use frequency, use-related impairment) in 9th grade significantly predicted 12th grade conduct disorder symptoms (β = .21, p < .01), over and above 9th grade conduct disorder (β = .66, p < .01) and depressive symptoms (β = -.07, p < .05), but did not predict 12th grade depressive symptoms (β = -.05, p > .10). Only 9th grade depressive symptoms significantly predicted depressive symptoms in 12th grade (β = .49, p < .01).

Our findings indicate that early substance use is a risk factor in the development of late adolescent conduct disorder symptoms, but not depressive symptoms. These results replicate the work of Mason and Windle (2002), who demonstrated that latent substance use predicts greater conduct problems by late adolescence, and extends it by highlighting that prospective risk exists over and above paths to depression. Importantly, our results suggest early substance use may not contribute to risk of adolescents developing depression, as has been suggested elsewhere (Hallfors et al., 2005), if prior depressive symptoms, and links with conduct problems, are taken into account.

0190

CHARACTERIZING THE NATURE AND FUNCTION OF SUBJECTIVE RESPONSES TO ALCOHOL AMONG ADOLESCENTS USING ECOLOGICAL MOMENTARY ASSESSMENT

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Animal models have identified unique patterns of acute reactivity to alcohol among adolescents, but it is unclear how directly these findings can be applied to humans. And while alcohol administration studies are widely used with adults, ethical and legal concerns preclude alcohol administration to underage drinkers in the laboratory. Our primary objective was to capture the real-time occurrence of adolescents' subjective responses to alcohol in their natural environments using ecological momentary assessment (EMA) methods. Specifically, our goals were to characterize the types and intensity of responses (e.g., sedative, stimulatory, craving) and to examine whether subjective responses predict clinically meaningful aspects of drinking behavior, such as the quantity and rapidity of alcohol consumption. Participants were 29 non-treatment seeking adolescents, ages 15 to 19 years, who consumed alcohol at least twice weekly in the past 30 days. The sample was 55% female, 69% Caucasian, and 83% non-Hispanic; the majority (72%) met criteria for an alcohol use disorder. Youth completed momentary assessments of mood and craving immediately before and after the first three drinks of a drinking episode for approximately 1 week (mean = 6.5 days; SD = 1.7). Given that subjective responses to alcohol are dose-dependent, we estimated blood alcohol concentrations (eBAC) at each drink report. Generalized estimating equations (GEE) showed that intoxication (i.e., eBAC) was positively associated with increases in subjective feelings of high and sedation as well as decreases in urge to drink and stimulation (p values < .05). Results also showed that greater levels of sedation and high following drinking were predictive of higher quantities of alcohol subsequently consumed that day (p values < .05). Similarly, subjective sedation and urge to drink predicted whether adolescents would subsequently engage in a heavy drinking episode as well as the latency between drinks (p values < .05). Findings from this study demonstrate the utility of EMA for capturing subjective responses to alcohol among adolescent drinkers, who cannot be assessed using alcohol administration methods in the laboratory. Moreover, this study is an initial step toward advancing our understanding of adolescents' responses to alcohol and thereby bridges an important translational gap between animal models and the clinical field.

0191

DRINKING MOTIVES MODERATE THE REAL-TIME ASSOCIATION BETWEEN EPISODIC MOOD AND DRINKING AMONG SUBSTANCE-USING YOUNG ADULTS

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Mood and motives have been separately linked to alcohol intake, particularly in cross-sectional data or reports of typical drinking. In this study, we used real-time data to explore the role of drinking motives as moderators of the relationship between mood and episodic drinking. We examined mood prior to drinking and subsequent alcohol intake among a sample (N = 92) of young adults (18–30 years; M = 22 years). Participants were regular users of both malt liquor (ML; i.e., 40 oz weekly) and marijuana (MJ; i.e., once/week). They were 73% male, 70% European American, and 50% were current students. They used cell phones and IVR technology to provide 21 days of prospective data, including initiating interviews *before* and *after* each episode of using alcohol and/or MJ. Current analyses were based on alcohol data, including positive (e.g., happy) and negative (e.g., sad) mood before drinking and alcohol intake (i.e., # standard drinks) per episode. We also examined the moderating effects of reasons for drinking, assessed by the Drinking Motives Questionnaire, on the within-person associations between mood and alcohol intake.

Participants reported on 606 drinking episodes (33% alcohol only, 66% both alcohol and MJ). They consumed an average of 6.05 standard drinks/episode (SD = 3.98). Using multilevel modeling, we examined participants' mood before drinking in relation to number of drinks per episode, controlling for gender, ethnicity, and day of the week. Within-person analyses showed that an increase in positive mood prior to drinking was significantly associated with heavier drinking. Similarly, an increase in negative mood prior to drinking was significantly associated with heavier drinking. Drinking motives moderated the mood-drinking relation. Specifically, the relation between positive mood and drinking was stronger ($p < .05$) among participants higher in social motives. The relation between negative mood and drinking tended to be stronger ($p = .07$) among participants higher in coping motives. Neither enhancement nor conformity motives moderated the mood-drinking relation.

Our results for mood and alcohol use are consistent with previous studies. In addition, drinking motives help explain how positive and negative mood before drinking influence subsequent alcohol intake. An episode-level understanding of the factors that contribute to heavy drinking among young adults can inform the development of effective interventions to reduce their alcohol intake.

0192

DEPRESSION, ALCOHOL USE DISORDERS AND SUBSTANCE USE DISORDERS MODERATE THE IMPULSIVITY LEVELS OF COLLEGE STUDENTS

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Impulsivity includes multiple constructs, including impulsive actions and decisions. Recent research found significant associations between depressive symptoms in college students and difficulty in controlling behavioral impulses; The current study assessed impulsivity in a college population in relation to substance/alcohol use, depression, and anxiety. College students(N=1839)from two demographically distinct Connecticut schools, aged 18–25, were assessed on the MINI interview for diagnosis of Axis I disorders, including alcohol and substance use disorders. Impulsivity was garnered through measures including the Zuckerman Sensation Seeking Scale(SSS), Barrett Impulsivity Scale(BIS-11)and Behavioral Inhibition Activation System Scale(BIS-BAS).

A multivariate general linear model analysis of variance(ANOVA)showed both significant main effects and interactions at a p<.05 level. Students with substance use disorders(SUD-abuse or dependence)had higher total scores on the Zuckerman, and higher scores on the BIS-11 Attentional and Motor Impulsivity sub-scales than students who did not. Students with alcohol use disorders(AUD-abuse or dependence)also had higher total scores on Zuckerman and all three BIS-11 impulsiveness sub-scales: Attentional, Motor, and Non-planning. Students with an anxiety disorder reported higher scores on the BIS-11 motor impulsiveness scale. Although students with depression showed no significant main impulsivity effects, depression had significant interaction effects in other areas. Students with both AUD and depression showed significant interaction effects with higher scores on the BIS-BAS Reward and BIS-11 non-planning impulsiveness scales. Significant interactions characterized students with AUD, SUD, and depression, who had higher total scores on BIS-11 attentional impulsiveness and non-planning impulsiveness.

These data help solidify existing research examining links between not only bipolar disorder, alcohol use and impulsivity, but also depression and substance use. SUD and AUD were both associated with higher sensation seeking scores, and attentional/motor impulsivity. When combined with current depression, subjects had higher scores for non-planning impulsivity, which supports the 'impulsive decisions' construct of impulsivity,(that posits that depressed individuals have trouble thinking through behavior before making decisions). This is a topic of interest, as specific impulsivity measures might predict future AUD/SUD.

0193

IMPULSIVITY MODERATES THE RELATIONSHIP BETWEEN PARTICIPATION IN DRINKING GAMES AND NEGATIVE ALCOHOL-RELATED CONSEQUENCES IN A FRESHMAN COLLEGE SAMPLE

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Drinking games endorse social drinking environments, but also promote participants to consume excessive amounts of alcohol (Grossbard, Geisner et al., 2007). Previous research reports drinking game participation in college-aged samples is associated with excessive alcohol consumption and subsequent negative alcohol-related consequences (Kenney & Hummer, 2006). Although several studies have examined this relationship, relatively few have examined the role of impulsivity. The current study aimed to assess how impulsivity moderates the relationship between participation in drinking games and negative consequences of drinking in a college population. Subjects were college freshmen (N=1392; 54.3% female) from two Connecticut academic institutions; one a small, private college and the other a larger, public university. Self-reported impulsivity scores were obtained using the Zuckerman Sensation Seeking Scale, the Barrett Impulsivity Scale (BIS-11), and the Behavioral Inhibition/ Activation System Scale (BIS-BAS). To measure negative alcohol-related consequences, items from the Brief Young Adult Alcohol Consumption Questionnaire (BYAACQ) were chosen based on how well they represented consequences of alcohol consumption. Measures of participation in drinking games were obtained via self report.
A univariate general linear model showed significant interaction effects on the above variables at a $p<0.05$ level. Scores on the Zuckerman and three BIS-11 sub-scales, Attentional ($F(1, 1391) = 28.450$, $p=0.000$), Motor ($F(1, 1391) = 8.037$, $p=0.005$), and Non-planning Impulsivity ($F(1, 1391) = 34.155$, $p=0.000$), positively moderated the relationship between participation in drinking games and negative alcohol-related consequences. Scores on the BIS-BAS sub-scale for Fun Seeking also positively moderated the relationship between participation in drinking games and negative alcohol-related consequences ($F(1, 1391) = 30.765$, $p=0.000$).
The above results add to the literature reporting that participating in drinking increases negative alcohol-related consequences. Study data extended previous findings by showing that self-reported impulsivity scores significantly moderated this relationship. Future research could assess impulsivity effects of participation in drinking games and negative alcohol-related consequences in high school populations.

0194

SOBER-TO-DRUNK PERSONALITY DIFFERENCES: REPORTS FROM TARGETS AND THEIR "DRINKING BUDDIES"

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Existing literature supports the use of the Five-Factor Model (FFM) personality dimensions (i.e. Emotional Stability, Extraversion, Agreeableness, Intellect, and Conscientiousness) as a comprehensive representation of stable aspects of mood, affect, and behavior. This study evaluated the use of the FFM as an organizational framework for understanding both self-perceptions of drunkenness (i.e. individual changes in mood, affect, and behavior associated with one's own intoxication), as well "drinking buddies"" perceptions of their friends' drunkenness (i.e., changes in mood, affect, and behavior associated with a friend's intoxication). Using cross-sectional data from a lab-based survey of college-student, drinking-buddy pairs at a large, mid-western university ($N = 184$ [92 pairs], 53% female), target participants reported on their sober and drunk "personalities," as well as the sober and drunk "personalities" of their accompanying drinking buddy using four 50-item questionnaires designed to assess levels of each of the five factors for themselves (sober and drunk) and their drinking buddy (sober and drunk). The drinking buddies completed parallel assessments for themselves and their friend in order to determine if one's self-reported sober-to-drunk personality differences were comparable to the sober-to-drunk personality differences that their drinking buddy reports witnessing in them. Differences between drunken and sober personality were pervasive for all five factors (as assessed through a three level hierarchical linear model) and demonstrated systematic differences between self-report and reports from drinking buddies as a function of specific personality scale, reported condition (drunk or sober), and the frequency of the individual's binge drinking. Findings support the use of multilevel modeling for dyadic data from self and collaborative reports, as well as the use of the FFM as a framework for organizing global changes in "personality" that occur under intoxication. Supported by NIAAA grants, T32 AA13526, R01 AA13987, R37 AA07231 and KO5 AA017242 to Kenneth J. Sher and P60 AA11998 to Andrew Heath

0195

SEX DIFFERENCES IN ALCOHOL'S EFFECT ON SMOKING CUE REACTIVITY IN NON-DEPENDENT SMOKERS

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Alcohol is known to increases tobacco cue sensitivity; with males tending to be more responsive to pharmacologic smoking cues and females to conditioned cues. Although these relationships are well established with dependent smokers, non-dependent smokers have rarely been the focus of controlled research studies. Male and female non-dependent smokers (n = 57) who were moderate drinkers were recruited from the general population, and randomly assigned to an alcohol (target BAC 0.06%), placebo, or a control beverage condition as well as a video condition involving the presentation of neutral and/or smoking imagery 20 and 80 minutes following beverage administration. After each video presentation, participants rated their subjective state and desire to smoke using visual analogue scales, questionnaire of smoking urges (brief), and the biphasic alcohol effects scale. Analyses revealed that smoking cues increased desire to smoke in both males and females relative to neutral cues. As well, sex x beverage x video x time interactions revealed that alcohol lead to an increased desire to smoke for overall craving to smoke in women relative to men when the smoking cue was presented during the ascending limb of alcohol absorption. Moreover females also endorsed increased excitatory properties and general intoxication during the ascending limb of alcohol absorption compared to males, although their blood alcohol level and reported use of alcohol and tobacco were not different from their male counterparts. These finding suggest that alcohol may differentially affect male and female non-dependent smokers' responsiveness to tobacco salient stimuli and female smokers may be especially vulnerable to such cues when they are presented early during alcohol absorption.

0196

ALCOHOL, MENTAL HEALTH, AND SEXUAL VICTIMIZATION AFFECT WOMEN'S MOOD AND SEXUAL AFFECT IN A HYPOTHETICAL SEXUAL SCENARIO

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Recent research suggests that alcohol, mental health, and sexual victimization are associated with women's sexual emotional responding. However, these factors have rarely been studied during an imagined sexual interaction presented in a controlled laboratory setting. This study sought to examine acute alcohol intoxication effects on positive mood, negative mood, subjective sexual arousal, and sexual desire at 4 times during a hypothetical risky sex scenario. Relationship potential with a potential sexual partner was also manipulated, and sexual victimization history and current mental health were assessed prior to the experimental protocol. Participants were 435 female heavy episodic drinkers, aged 21–30, at elevated risk for sexually transmitted infections. They completed a computerized background questionnaire, a standard alcohol administration protocol (target BAL=.010%), and then projected themselves into an experimental sexual scenario. Positive and negative mood and sexual arousal and desire were assessed at 4 story breaks: 1) prior to any sexual activity; 2) after kissing; 3) after sexual touching; and 4) after realizing that no condom was available. Sexual desire and positive mood peaked (and negative mood was lowest) at break 3, but sexual arousal continued to increase throughout the story. Intoxicated women reported higher positive and lower negative mood, but less sexual desire, than sober women. Further, intoxicated women who were less bothered by anxiety symptoms had a stronger decline in sexual desire from breaks 3 to 4 compared with sober women and intoxicated women more bothered by anxiety symptoms. Sexual arousal varied less for intoxicated women than sober women. Intoxicated women reported higher sexual arousal at breaks 1 and 2 than sober women, but sober women who were less bothered by depression symptoms reported higher arousal than intoxicated women and sober women more bothered by depression symptoms at breaks 3 and 4. Further, throughout the scenario, lower positive mood and higher negative mood were associated with sexual victimization history, more depression, anxiety, and trauma symptoms, and low relationship potential with the male character. This study suggests that alcohol affects women's in-the-moment sexual responding and that personal factors may interact with alcohol intoxication. Sexual risk prevention programs should highlight alcohol and mental health influences on women's mood and affect during sexual situations.

0197

STRESSING THE IMPORTANCE OF ANXIETY IN ALCOHOLISM

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The role of stress in alcohol use generally and relapse among alcoholics is clear. However, recent preclinical research implicates stress neuroadaptation following chronic alcohol use as a key etiologic mechanism in alcoholism. However, stress is a broad and often ill-defined construct in human research. This may have slowed progress on translating research on stress neuroadaptation from animal models to humans.

Recent affective neuroscience research suggests that the negative affective response to stressors can be parsed into the components of *fear* vs. *anxiety* by manipulating time course of threat (phasic vs. sustained, respectively). Cues which reliably predict the occurrence of threats elicit fear, whereas cues that signal uncertain threat elicit anxiety. Previous research from our lab has established that alcohol intoxication selectively dampens anxiety to uncertain threat but not fear to certain threat. Based on extant theory about neuroadaptive responses to repeated heavy alcohol use, we hypothesized that recently detoxified alcoholics would demonstrate increased negative affective response to uncertain threat.

We examined the negative affective response to certain and uncertain stressors in recently (1–8 weeks) sober alcoholics vs. healthy controls. Using a cued threat task adapted from preclinical research, participants viewed a series of cues that predicted shock administration (100% shock probability at cue offset). In certain threat blocks, all cues lasted 5 seconds resulting in imminent, certain threats. In uncertain threat blocks, participants were instructed that cue duration would vary unpredictably from 5 seconds to 3 minutes. Startle potentiation relative to no shock blocks provided the measure of negative affective response.

Startle potentiation was analyzed in a General Linear Model with Group as a between-subjects factor and Threat (certain vs. uncertain) as a within-subjects factor. At N=50, abstinent alcoholics displayed greater startle potentiation relative to controls during both threat types. The Group X Threat interaction was not significant but the Group difference was descriptively largest during uncertain threat.

These results suggest chronic alcohol use may produce stress neuroadaptation that manifests as increased negative affect to both uncertain and certain stress when abstinent. This heightened response to stressors may account for the increased urge to drink and risk for relapse during stress among alcoholics.

0198

ACTION FOCUSED COPING AS A MEDIATOR BETWEEN SOCIAL SUPPORT AND DEPRESSION IN AN ALCOHOL DEPENDENT IN-PATIENT TREATMENT SAMPLE

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The objective of this study was to examine the mediating role action-focused coping plays between social support and symptoms of depression in an alcohol-dependent population. Participants were 44 men and 42 women, 17–65 (M = 34.99, SD = 10.12) residing in a residential substance abuse treatment facility for alcohol dependence. The number of previous treatment attempts ranged from 0–10 (M = 1.48, SD = 2.04), and the number of days clean and sober ranged from 2–120 (M = 45.36, SD = 56.74) at the time of data collection. Participants completed a battery of self-report measures, including the Beck Depression Inventory (BDI-II; M = 15.44, SD = 13.29), the Social Support Questionnaire (SSQ; M = 2.80, SD = 2.13), and the COPE (M = 152.35, SD = 20.56). Mean number of people in social support network predicted action-focused coping (path a; β = 2.51, p < .05) and symptoms of depression (path c; β = -2.16, p < .01). Additionally, action-focused coping reliably predicted depressive symptomatology (path b, β= -0.33, p < .001).When action-focused coping was controlled, social support no longer predicted symptoms of depression (path c'; β = -1.34,*ns*). These results indicate that among alcohol dependent patients, action-focused coping (CI= -2.09, -.15), but not emotion-focused coping (CI= .97,.01), fully mediated the relationship between the number of people in a support group network and reporting of symptoms of depression. Treatment implications are that focusing on increasing social support may decrease depressive symptoms via an increase in action-focused coping. It may be that the more supportive people a person perceives in their life, the more able they are to reach out to those people during an urge to drink and/or during times of stress.

0199

EXPLORING COLLEGE STUDENTS' PERCEPTIONS OF DEPRESSED MOOD AND THE RELATIONSHIP OF THESE PERCEPTIONS TO ALCOHOL USE AND PROBLEMS

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This study examines college students' perceptions of depressed mood rates on campus (depressed norms), and the relationship to the student's own drinking and mood. There is ample information about students' misperceptions of alcohol use and how these are linked to drinking and problems. This study extends the construct of normative perceptions to depressed mood assessing whether students accurately assessed how sad, depressed, and suicidal others were on their campus. We also examine whether one's own mood, drinking, and drinking problems are related to one's perceptions of other's mood.

Method: Participants included 982 undergraduates (56% female; 59% Caucasian) at a large public university. Students completed a brief web-based survey in Autumn of 2011 with measures of alcohol consumption (Quantity/Frequency), alcohol-related severity (AUDIT), and depressed mood (Beck Depression Inventory-BDI). Depression norms were assessed using a 9-item measure on perceptions of sadness, depression, and suicidality in typical students (e.g., What percent of students do you think felt sad, down or "blue" in past two weeks?), and asked students about their own experiences (e.g., Do you feel sad, down, or "blue"?).

Results revealed that students significantly underestimated the % of typical students who feel sad (est. 50%, actual 67%; t(970) = 5.65, p < .001), overestimated the % of depressed students (est. 31%, actual 28%; t(969) = 4.64, p < .001), and overestimated the % of students feeling suicidal (est. 8.8%, actual 3%; t(975) = 17.03, p < .001). Students own mood (total BDI) was significantly positively related to their perceptions of others' sadness, depression, and suicidality (r's = .16, .22, and .22 respectively; p < .001). Students own drinking quantities (peak drinking in past month, typical weekend drinking, or drinking days per week) were not related to perceptions of mood, depression, or suicidality. However, drinking severity (total AUDIT) was significantly positively related to their perceived rate of depressed students (r = .05, p < .05).

Conclusion: Normative misperceptions of sadness, depression, and suicidality exist, however without a clear direction. These misperceptions appear related to students' own mood and alcohol severity while being unrelated to alcohol use. Further research is needed to understand the accuracy of mood perceptions and the variables affecting them as well as the extent to which alcohol problems are related to these impressions.

0200

HIGH RISK ALCOHOL USE IS ASSOCIATED WITH DEPRESSION AND ANXIETY SYMPTOMS IN ACUTE AND EARLY HIV INFECTION

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Alcohol use is a known risk factor for HIV transmission and may exacerbate neuropsychiatic complications in chronic infection, but little is known about the correlates of high risk alcohol use in acute and early HIV infection (AEH). Forty-six AEH men were included in the current study, with an average of 32.2 years of age (SD = 10.6) and 14.5 years of education (SD = 2.2), with a median estimated HIV infection duration of 77 days [IQR = 25, 89]. As part of a comprehensive evaluation, participants completed psychiatric, neuropsychological, and neuromedical assessments. Participants also completed self-report measures regarding substance use disorders, including the Alcohol Use Disorders Identification Test (AUDIT) and Drug Abuse Screening Test (DAST) focused specifically on methamphetamine (MA) use. High-risk alcohol use, as defined by the AUDIT, was associated with younger age (p = .03), higher score on the DAST (MA; p = .03), and increased anxiety (p = .005) and depression (p = .04) on the Profile of Mood States (POMS). In contrast, there were no associations between alcohol-use and neuropsychological performance, other psychiatric symptoms (e.g., fatigue), or HIV disease factors (e.g., current and nadir CD4 count, plasma and CSF viral load, duration of infection) (all ps > .05). In a multiple regression analysis predicting anxiety and depression severity, a significant and independent effect of the AUDIT score emerged even when age and DAST (MA) score were included in the model. These results suggest that high risk alcohol use is associated with elevated psychiatric distress in individuals with AEH, in whom such symptoms are quite prevalent and clinically relevant. Alcohol use screening in AEH individuals may therefore be important because treatment of alcohol use disorders may also alleviate anxiety and depression in this population.

0201

THE EFFECT OF ALCOHOL ON THE WHITE MEMBERS OF INTERRACIAL GROUPS
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White individuals often report monitoring their thoughts and behavior during interracial interactions. While theories of prejudice suggest that controlled self-monitoring suppresses expressions of prejudice, recent studies indicate that, regardless of underlying prejudice, the act of self-monitoring during interracial interactions may be disruptive and lead to anxiety. Alcohol is known to impair controlled self-monitoring processes and affect self-performance evaluation, and thus may affect the experience of Whites during interracial interactions. Using an interactive social paradigm and behavioral-expressive measures of affect, we examined the effects of alcohol on the socio-emotional experiences of Whites during either all-White or interracial social interactions.
METHOD: Ninety-two White men and women consumed a moderate dose of alcohol, a placebo, or a non-alcoholic control beverage over the course of 36 minutes in groups of three unacquainted individuals. Participants interacted with either two other Whites or one White and one Black individual. We used the Facial Action Coding System and comprehensive content-free speech analysis to examine affective and behavioral dynamics during these exchanges.
RESULTS: Hierarchical Generalized Linear Modeling accounted for the clustering of observations within individuals and individuals within groups. Analyses revealed significant beverage by group racial composition interactions predicting measures of discomfort thought to be associated with self-monitoring (both ''dampened smiles'' and speech pauses). Beverage did not interact with group racial composition to predict negative affective displays.
DISCUSSION: Whites assigned to interracial groups displayed more speech and facial signs of discomfort than those interacting in all-White groups. Alcohol consumption reduced differences between Whites assigned to interracial and all-White groups in displays of discomfort. Alcohol did not, however, increase displays of ''negative'' facial expressions related to disgust, contempt, or fear among Whites assigned to interracial groups. Using a novel social paradigm, this study suggests that the discomfort experienced by Whites during interracial interactions is attributable to negative-self evaluation. It also offers new directions for alcohol researchers by identifying those social situations (e.g., heterogeneous interactions) in which alcohol consumption is likely to be particularly reinforcing.

0202

EFFECTS OF ALCOHOL CONSUMPTION ON TWO COMPONENTS OF IMPULSIVE BEHAVIOR IN BINGE AND NONBINGE DRINKERS
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Impulsivity has been clearly related to alcohol use in epidemiological and correlational studies. Impulsivity appears to play a particularly important role in binging. While self-reported impulsive personality traits are typically higher among binge compared to non-binge drinkers, it is unclear if these ratings are elevated as a behavioral consequence of acute alcohol intoxication. It has been hypothesized that binge drinkers experience disproportionate increases in impulsivity during the initial period of drinking, leading to a loss of control over further drinking, and one preliminary study supports this possibility. In this study, Binge (n=49) and NonBinge (n=34) drinkers performed two distinct types of impulsivity tasks at baseline and after consuming alcohol. The two tasks included a continuous performance test (Immediate Memory Task; IMT) and a stop-signal task (GoStop Impulsivity Paradigm). Each task type corresponds to two different components of impulsivity: response initiation (IMT, rapid responses that occur before stimulus processing is complete) and response inhibition (GoStop, failures to inhibit responses, despite new information). Task performance was assessed in both groups before alcohol consumption and again after a simulated binge alcohol (0.9 g/kg, 95% alcohol) procedure. It was expected that impulsive responding on IMT and GoStop would be increased in both groups after alcohol administration, but the effect would be greater in the Binge drinker group. We found that (1) Binge and NonBinge drinkers did not differ in their impulsive responding in either of the 2 impulsivity measures before alcohol; (2) alcohol consumption produced significantly increased impulsive responding in both the IMT and the GoStop relative to baseline performance, with the effect size being significantly larger for the GoStop relative to the IMT; and (3) the increased impulsive responding on IMT was only found to be significant in the Binge group. This study demonstrated that impulsivity of Binge and NonBinge drinkers are not different at baseline, but Binge drinkers are even more impulsive after alcohol consumption. These data have implications for identifying underlying behavioral mechanisms contributing to different patterns of alcohol consumption in populations vulnerable to alcohol-use disorders.

0203

READINESS TO CHANGE AND BRAIN DAMAGE IN PATIENTS WITH CHRONIC ALCOHOLISM
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High motivation to change is a crucial triggering factor to patients' engagement in clinical treatment. It happens that alcohol-dependent patients come to treatment without being genuinely ready to abstain from alcohol. The main objective of the present study is to investigate whether the low readiness to change observed in some alcoholic inpatients at treatment entry could, at least partially, be explained by macrostructural gray matter abnormalities in critical brain regions involved in cognitive, emotional and social skills. Thirty-one recently detoxified alcoholic patients and 27 age-matched healthy controls underwent 1.5-T magnetic resonance imaging. An adapted version of the Readiness To Change Questionnaire was completed by patients at alcohol treatment entry. This tool is designed to assess the three main stages of motivation to change alcohol consumption: Precontemplation (substance abuse and no intention to stop drinking), Contemplation (strong intention to change habits but ambivalent behaviour) and Action (cessation of excessive alcohol consumption and behavioural changes for healthier habits) stages. Alcoholic patients were divided into ''Action'' (i.e. patients in action stage) and ''PreAction'' (i.e. patients in precontemplation or contemplation stages) subgroups. The PreAction subgroup, but not the Action subgroup, had gray matter volume deficits compared with controls ($p<0.005$, FDR corrected). Unlike the patients in the Action subgroup, the PreAction patients had gray matter abnormalities in the cerebellum (Crus I) and fusiform gyri, and widespread structural damage in the frontal cortex, including the lateral orbitofrontal cortex, the ventromedial, dorsomedial, dorsolateral prefrontal cortices and the rostral cingulate zone ($p<0.001$ uncorrected). The scant motivation to modify inappropriate drinking behaviour observed in some alcoholic patients at treatment entry could be related to macrostructural brain abnormalities in regions subtending cognitive, emotional and social abilities. These regional volume deficits may prevent some patients from resolving their ambivalence and applying the processes of change that are a prerequisite for moving towards a healthier lifestyle according to the Transtheoretical Model.
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0204

THE EFFECTS OF SELF-CONTROL CONSTRUCTS ON ALCOHOL-RELATED PROBLEMS VIA AFFECTIVE LABILITY
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Although heavy alcohol use often results in alcohol problems, several putative antecedents seem to be directly related to alcohol problems even after controlling for use. Based on the affective processing model of negative reinforcement (Baker et al., 2004), one may expect that an overreliance on an affective system can lead to the development of addictive behaviors. Affective lability, or the rate and intensity at which one's moods oscillates, has been shown to predict alcohol problems both cross-sectionally and prospectively among college students (Simons, Carey, & Wills, 2009). In the present study, several putative antecedents to alcohol-related problems were examined including neuroticism, positive urgency, negative urgency, good behavioral self-control, poor behavioral self-control, good emotional self-control, and poor emotional self-control. A sample of 307 college students completed a battery of surveys at one time point. Affective lability was modeled as a mediator of the effects of each self-control construct on alcohol problems while controlling for use. Specifically, using structural equation modeling, the total, indirect, and direct effects of each self-control construct on alcohol problems was estimated based on 5000 bootstrapped samples. Consistent with previous research, each self-control construct had a significant direct effect on alcohol problems even when controlling for use: neuroticism ($b=.28, p<.001$), positive urgency ($b=.33, p<.001$), negative urgency ($b=.42, p<.001$), good behavioral self-control ($b=-.27, p<.001$), poor behavioral self-control ($b=.44, p<.001$), good emotional self-control ($b=-.31, p<.001$), and poor emotional self-control ($b=.36, p<.001$). The indirect effect via affective lability was significant for each of these constructs: neuroticism ($b=.17, p<.001$), positive urgency ($b=.135, p=.001$), negative urgency ($b=.16, p<.001$), good behavioral self-control ($b=-.13, p<.001$), poor behavioral self-control ($b=.20, p=.001$), good emotional self-control ($b=-.19, p<.001$), and poor emotional self-control ($b=.21, p<.001$). In the face of heterogeneous measures of self-control, affective lability was found to be a robust mediator such that it partially or fully mediated the predictive effects of each self-control construct. The theoretical importance of affective lability is discussed in terms of the affective processing model of negative reinforcement, and the implications for future research are considered.

0205

ECOLOGICALLY ASSESSED AFFECTIVE OUTCOMES OF ALCOHOL CONSUMPTION: DO EXPECTANCIES MATCH EXPERIENCE?

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Regulation of affect has long been considered a key factor motivating alcohol use. Drinkers report using alcohol to enhance positive affect and to relieve negative affect (Cooper, et al., 1995), and field studies have shown positive and negative affect are associated with increased urges to drink and drinking levels (Schroder & Perrine, 2007; Simons, et al., 2005). Some ecological studies have shown that individual differences in the anticipated outcomes of drinking (i.e., alcohol outcome expectancies) moderate the affect-drinking relationship (Armeli, et al., 2000, 2005). However, the effect of affect on drinking is typically examined rather than whether alcohol use results in affect change (Cheetham, et al., 2010). The present study is unique in that both affect states and appraisals of affect change were assessed during the drinking episode. Current drinkers ($N = 404$) completed electronic diary reports for 21 days, resulting in 11,840 drink reports. Participants rated their PA and NA and whether their last drink was ''pleasurable,'' ''relieved unpleasant feelings or symptoms,'' and ''made me feel worse.'' Three-level linear mixed models with moments (L1) nested within drinking episodes (L2), nested within participants (L3) were estimated. Analyses included all CEOA subscales to test the unique effect of expectancy subtypes on specific affective outcomes and controlled for day of week, gender, weight, and drinks consumed. Stronger sociability expectancies were associated with greater PA (enthusiasm: $\beta = .12$, $p = .009$; happiness: $\beta = .13$, $p = .001$; excitement: $\beta = .12$, $p = .004$) and less NA (sadness: $\beta = -.09$, $p = .03$). In contrast, stronger tension reduction expectancies were associated with less PA (happiness: $\beta = -.06$, $p = .036$) and greater NA (sadness: $\beta = .08$, $p = .007$; distress: $\beta = .08$, $p = .004$). Stronger sociability expectancies were associated with increased appraisals of pleasure, $\beta = .11$, $p = .015$. Stronger tension reduction expectancies were associated with increased appraisals of relief, $\beta = .08$, $p = .022$. Results suggest that individuals with strong expectancies for negative affect relief from drinking experience *more* sadness and distress while drinking and *less* happiness and excitement. At the same time, these individuals' subjective appraisals suggest that they experience increased relief from drinking. Findings suggest that expectancies can operate outside of direct experience and may color perceptions of the affective outcomes of drinking.

9. PREVENTION

0206

THE ALCOHOL POLICY LANDSCAPE: PRICING LEVERS TO REDRESS EXCESSIVE ALCOHOL CONSUMPTION AND RELATED HARMS

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Increasing community and political concern about excessive alcohol consumption and related harms, particularly among young adults, has prompted recent calls for the introduction of tighter regulatory controls. From a research perspective, measures which increase alcohol prices are considered most effective in reducing alcohol consumption and related harms. This paper presents a timely review of two pricing policy levers that have been considered and/or implemented internationally: minimum pricing and bans on price discounts/promotions. Minimum pricing has received considerable attention in recent years, particularly in the UK. Minimum pricing sets a floor price per unit of pure alcohol or per standard drink below which it would be illegal to sell alcohol. It cannot be circumvented by supermarket deep discounting, adaptive marketing or below-cost sales strategies commonly used by retailers. In the only empirical study of its kind, recent longitudinal analyses indicate that minimum pricing was associated with substantial declines in alcohol consumption in British Columbia, Canada. Albeit subject to initial legal challenges, minimum pricing is likely to be introduced in Scotland in 2012, and intense discussion and debate is underway in the UK government about how the policy could be introduced south of the Scottish border. In Australia, government reluctance to alter extant alcohol taxation arrangements due to a wine glut and industry restructuring has renewed interest in minimum pricing amongst public health advocates. Conversely, insufficient empirical research and policy advocacy attention has been devoted to alcohol promotions and discounts (e.g., happy hour), which are designed to markedly reduce the cost of drinking the more alcohol consumed. Available evidence from the USA highlights significant associations between price specials and binge drinking. Bans/guidelines on alcohol promotions are in place in several EU member states and in most Australian states/territories, however little empirical research has examined the impact of such regulations and compliance checking varies. Anecdotal evidence indicates recent legislation banning quantity discounts and promotions in Scotland has been undermined by adaptive marketing measures by the alcohol industry; to circumvent such practices, minimum pricing is needed as a complementary policy. In unison, both policies hold promise of making inroads in curbing excessive alcohol consumption and related harms.

0207

THE ASSOCIATION BETWEEN STATE ALCOHOL POLICIES AND ADOLESCENT ALCOHOL USE

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Little is known about the effects of state alcohol policies on adolescent alcohol abuse and related consequences. We examined the relationship between the stringency of 14 policies across the 51 states and the District of Columbia, as rated by the Alcohol Policy Information System (APIS) and a variety of youth outcomes as assessed by two prominent national surveys. We updated state policy ratings using 2007 APIS data, and obtained state-level alcohol use and related outcomes and attitudinal variables from the 2009 NSDUH and YRBS surveys. State demographic characteristics related to alcohol policies and underage drinking were retrieved from the 2010 U.S. census. Pearson correlations determined alcohol policies and demographics related to drinking outcomes and we ran linear regression models to determine if policy ratings were related to outcomes when controlling for demographics also related to these outcomes. At the standard level of statistical significance ($p < .05$), state control of alcohol sales (i.e., whether the state restricts sales of liquor only, sales of wine and liquor, or has no statewide restrictions) was associated with at least 4 of 11 youth alcohol-related outcomes. At a less conservative criterion of significance ($p < .10$), age for on-premise sellers and keg registration were also associated with 4 outcomes. All behavioral associations were in the expected direction insofar as higher policy ratings corresponded with lower prevalence of alcohol-related behaviors. With respect to attitude-related associations, states with stronger policies exhibited higher perceived risk of harm from drinking and greater levels of disapproval of alcohol use by same-age peers. In general, study findings provide preliminary support for the utility of state policies designed to reduce adolescent alcohol use and related consequences. However, factors contemporaneous with adoption, such as environmental strategies to reduce adolescents' access to alcohol including monitoring and enforcement, could also have contributed to these outcomes. The strongest relationships found supported the importance of state control of alcohol sales and retailer support provisions for false IDs, and state policies were consistently related to lower levels of youth alcohol-related outcomes. However, some findings may have occurred by chance, and the cross-sectional nature of the data precludes attributions of causality. Policy advocates should use study findings with caution.

0208

USE OF UNDERAGE COMPLIANCE CHECKS AMONG LOCAL LAW ENFORCEMENT AGENCIES IN U.S.

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A number of studies have found that underage compliance checks at alcohol establishments are effective in reducing the likelihood of selling alcohol to persons under the legal drinking age. Less is known, however, about the extent to which law enforcement agencies are conducting compliance checks. We assessed the prevalence of use of compliance checks among local law enforcement agencies across the U.S. We obtained a list of all local law enforcement agencies (n=15,833) from the U.S. Bureau of Justice Statistics. We randomly sampled from this list, stratifying based on size of state (number of agencies per state) and selecting 40 agencies from larger states and 20 from smaller states. Within state, we also stratified by size of agency (number of officers per agency) and the ratio of police agencies to sheriff agencies. Finally, to ensure representation of larger metropolitan areas we added law enforcement agencies from the top three largest cities in each state (if these agencies had not been randomly sampled). Our final sample was 1,632 agencies. We attempted to interview the staff person at each agency who was most knowledgeable about alcohol enforcement strategies within the agency. We assessed whether the agency conducted compliance checks, and if so, other aspects of the implementation process. We also compared responses across several agency/jurisdiction characteristics. Our response rate was 66.3% (1,082/1632). We found that 39% (n=422) of agencies conducted compliance checks at alcohol establishments in the past year. Among agencies that did checks, 57% conducted checks at all establishments in their jurisdiction, 24% conducted checks at least 3–4 times per year, 36% conducted a follow-up check within three months if an establishment failed a check, and 63% penalized the licensee of the establishment (vs. only the server/seller) if an establishment failed a check; however, only 5% (n=21) of agencies reported doing all four of these recommended actions. Larger agencies (>15 officers) and agencies in larger towns (>50,000 population) were more likely to conduct compliance checks and to do checks more frequently. We conclude that because less than half of the local law enforcement agencies are conducting compliance checks, sales to underage persons may be reduced by broader adoption of this effective strategy. In addition, among agencies conducting compliance checks, nearly all could improve on at least some aspect of their implementation process.

0209

DO NEIGHBORHOOD ATTRIBUTES MODERATE THE RELATIONSHIP BETWEEN ALCOHOL OUTLET DENSITY AND CRIME?

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In two very recent studies, we found positive associations between alcohol outlet density and several violent and nonviolent crime outcomes across neighborhoods in Minneapolis, MN (Toomey et al., 2011; in press). In this study we assess whether various neighborhood attributes moderate these associations between density and crime. Data are from 2009 and were analyzed at the neighborhood level (n=84 neighborhoods). Our outcomes, obtained through the City of Minneapolis, include four categories of violent crime incidence (assault, rape, robbery, total violent crime) and five categories of non-violent crime incidence (vandalism, nuisance crime, public alcohol consumption, driving while intoxicated, underage alcohol possession/consumption). We identified seven potential moderating variables, including four types of neighborhood physical structures (non-alcohol businesses, schools, parks, and religious institutions) and three other neighborhood characteristics (neighborhood activism, overall neighborhood quality, and number of condemned buildings). Data for moderating variables were collected via archival data sources, observations at parks, and surveys of neighborhood associations. We hypothesized that some attributes may be potential assets (e.g., neighborhood activism, religious institutions) and hence would decrease the association between alcohol outlets and crime, while others may be liabilities (e.g., number of condemned buildings, poor neighborhood quality) that may increase the association between outlets and crime. For each crime outcome, we created a geospatial model accounting for spatial auto-correlation and controlling for relevant neighborhood demographics (e.g., percent living in poverty; percent unemployed), with an interaction term (moderator X density) included for each potential moderating effect. We found that very few interaction terms were significant and we observed no clear patterns across crime outcomes with regard to potential moderating effects. We conclude that the lack of moderating effects of neighborhood attributes suggests that the addition of alcohol outlets to any neighborhood regardless of the possible assets or liabilities in a given neighborhood could result in an increase in a wide range of crime.

0210

SPATIAL DIFFUSION EFFECTS OF POLICE COMPLIANCE CHECKS

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Studies have established that underage compliance checks by police reduce the likelihood of underage sales, consumption, and related consequences. Theory suggests that similar and proximal establishments share communication networks and it is hypothesized that these networks act as conduits for disseminating information about compliance checks (e.g., warning neighboring establishments that compliance checks are being conducted in area). The goal of the current study was to examine whether the effects of police compliance checks diffuse to neighboring establishments. This study was a secondary analysis of the Complying with the Minimum Drinking Age trial and included over 2000 police compliance checks conducted at over 900 alcohol establishments. The primary outcome was sale of alcohol to a pseudo-underage buyer without the need for age identification. A multilevel logistic regression was used to model the effect of a compliance check at each establishment as well as the effect of compliance checks at neighboring establishments within 500 meters (stratified into four equal-radius concentric rings). Covariates included buyer age and gender, license type of each establishment (full liquor versus beer or wine only), area (urban versus suburban), and establishment type (on-sale versus off-sale). Number of neighboring establishments was included as an offset, and random intercepts were included for buyer and establishment. Establishments that had a police compliance check in the past 30 days were less likely to sell to the pseudo-underage buyer (OR = .39, 95% CI = .24, .64). In contrast, a police compliance check between 31 and 90 days prior had no observable effect (OR = .82, 95% CI = .60, 1.11). Establishments with neighboring establishments within 125 meters who were checked by police within the prior 90 days had an additional reduction in the likelihood (OR = .69, 95% CI = .52, .91). Police compliance checks on neighboring establishments in the other three rings (126 to 500 meters) had no additional effect. Sensitivity analyses suggest this neighboring effect is stronger in areas with higher density of establishments. Results confirm the hypothesis - protective effects of police compliance checks do spill over to neighboring establishments. Although this effect was smaller than the effect on the checked establishment and limited to close neighbors, these findings have implications for the development of an optimal schedule of police compliance checks.

0211

ALCOHOL OUTLET DENSITIES AND PRICE IN THE CONTEXT OF PRIVATIZATION

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Alcohol beverage prices or taxes have been shown be related to alcohol sales and use and related problems. Greater numbers of alcohol outlets per geographic area or population have also been shown to be related to greater alcohol sales, survey measures of alcohol use, driving after drinking and problems. What is not clear are the mechanisms underlying these relationships. One possible mechanism is that alcohol outlet densities operate via marketing systems with higher densities linked to lower prices and subsequently increased levels of consumption and resulting public health outcomes. This study examines the relationship between alcohol outlet density under conditions of the partial privatization of off-premise consumption in British Columbia occurring over the past decade. Two hypotheses are tested. First, reflecting basic supply-demand principles, greater densities of alcohol outlets will be directly related to reductions in beverage prices in response to greater geographic competition. Second, reflecting the effects of niche marketing and resulting market stratification, increased densities of private liquor stores will be especially related to reductions in beverage prices within this outlet category. The hypothesized price effects may take the form of either charging a different price for the same beverage or the substitution of relatively inferior (cheaper in price terms) for relatively superior (more expensive in price terms) beverages. Data were collected from: (1) a survey of BC private store prices and practices, (2) alcohol outlet location information and (3) data on demographic characteristics. Multi level models examine the relationships between prices at individual private liquor stores and the densities of government liquor stores, private liquor stores, bars and restaurants, controlling for background demographics and geographic unit level effects. Spatial dependences were also examined. Increased densities of private liquor stores were associated with lower mean prices of beer and all alcohol aggregated across brands at the store level. However, increased numbers of bars, restaurants and government liquor stores were not associated with such lower prices similarly indexed. There appeared to be no outlet level effect on discounting patterns, however, with the mean-price differences apparently reflecting differences in the quality of brands carried rather than unequal prices for any given brand.

0212

MEASURING IMPACTS OF ALCOHOL OUTLETS ON ASSAULTS AND MOTOR VEHICLE CRASHES ACROSS 50 CALIFORNIA CITIES

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Prior research has demonstrated that alcohol outlet densities are related to rates of both violent assault and motor vehicle crashes. The vast majority of these studies have focused upon establishing effects within differently defined geographic areas: counties, zip codes, Census tracts, block groups and blocks. However, the selection of different geographic areas for analysis has well known impacts upon observed outlet effects. This observation suggests that analysis strategies be adapted to different levels of geographic resolution provided by these sources.

The current study relies upon data recently made available from 50 medium-sized cities in California in 2008. These data allow us to examine outlet effects at the Census block group level and specify statistical models suitable for analyses of outlet effects on assaults and crashes. Central to these models is the hypothesis that, although alcohol related assaults may be prevalent within analysis units, alcohol related motor vehicle crashes demonstrate spatial lag effects. We provide methods to assess these different spatial relationships between outlets and problems and show that different model specifications are required to assess the full impacts of alcohol outlets in community settings. These analyses are conducted using Bayesian spatial models that directly measure the effects of spatial lags (i.e., problem risks in a given block group being affected by outlet densities in neighboring block groups) while also controlling for spatial autocorrelation of the error term (i.e., unexplained similarity of residuals between adjacent block groups). These cross-sectional block-group findings are compared to Bayesian space-time results at the lower-resolution zip-code level throughout California for the years 1999 through 2008.

Preliminary results indicate that local risks of violent assault are positively related to local densities of both bars and off-premise outlets, and also to spatially-lagged bar densities. The risk of injury crashes being categorized as drinking-related by police was positively related to local but not lagged bar densities, while being positively related to lagged but not local densities of restaurants and off-premise outlets. These results suggest that assaults and motor vehicle crashes in a given geographical unit are affected by outlet densities both within that unit and in neighboring areas.

0213

A NATIONAL EVALUATION OF GRADUATED DRIVING LICENSING LAWS
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Graduated driver licensing (GDL) laws now exist in all 50 States and the District of Columbia. These laws generally require three-staged licensing for novice drivers: (1) a learner's permit; (2) an intermediate or provisional stage where the novice can drive solo, but only under certain conditions; and finally (3) a full license with no restrictions. These GDL systems reduce the exposure of young novice drivers to risky situations (such as driving late at night and driving with several distracting teens in the car). Logistic regression methods were used to conduct a national evaluation of GDL law effectiveness on reducing fatal crash involvements of 16- and 17-year-old drivers. Results indicated that states that adopt a basic GDL law can expect a decrease of 8% to 14% in the proportion of 16- and 17-year-old drivers involved in fatal crashes (relative to 21- to 25-year-old drivers), depending upon the state's other existing laws that affect novice drivers. Nighttime restrictions were found to reduce 16- and 17-year-old driver involvements in nighttime fatal crashes by an estimated 10% and 16- and 17-year-old drinking driver involvements in nighttime fatal crashes by 13%. Passenger restrictions were found to reduce 16- and 17-year-old driver involvements in fatal crashes with teen passengers by an estimated 9%. Overall, GDL reductions were largest for young White drivers, followed by African-Americans, and then Asians, with no significant reductions for young Hispanics. GDL laws also had no apparent effect on speeding-related fatal crashes for any of these novice drivers but they did on alcohol-related fatal crashes. The effect of GDL laws on the likelihood of alcohol-impaired driving was observed through a delay in full licensure and a reduction in drinking and driving by 16- and 17-year-old drivers, with the effect being greater on young male drivers compared to young female drivers. States without potent nighttime and passenger restrictions in their GDL laws should strongly consider adopting them.

0214

REQUIRING INTERLOCKS TO REINSTATE: 50% EFFECTIVE
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While a large number of studies have demonstrated that vehicle alcohol interlocks are effective in reducing recidivism, a major problem in their overall effectiveness is (1) the ability of convicted impaired driving offenders (DWI offenders) to avoid installing them by claiming not to own a car; or (2) DWI offenders who accept license suspension rather than the interlock sanction but continue to drive illicitly. One policy for forcing DWI offenders to install interlocks currently being implemented in a number of states is to require a minimum period on the interlock as a condition for license reinstatement.
The state of Florida was among the first states to implement such a program. This study reports on the first decade of that policy, covering the percentage of 225,000 DWI offenders who installed interlocks in order to reinstate their licenses.
From 40% to 60% of the DWI offenders, depending on whether they were first-time or repeat offenders, spent some time on the interlock. The percentage of all the time the 225,000 drivers spent on the interlock during their sanction period was between 15% and 20%. Requiring an interlock as a condition for driver's license reinstatement increases the interlock installation rate from 20% to 50% but still covers only a small portion of the time that DWI offenders are barred from driving.

0215

WHY DO IGNITION INTERLOCKS ONLY TEMPORARILY REDUCE IMPAIRED DRIVING? A LIKELY EXPLANATION FROM ALCOHOL BIOMARKER DATA
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A long standing puzzle for ignition interlock research has been: why would DUI offenders who are required to use an interlock revert to control levels of impaired driving once the interlock is removed from the car? During the interlock drivers reduce drinking driving by over 60% relative to non-interlock control offenders (as measured by recidivism likelihood). Reversion to control rates of recidivism once interlocks are removed has been reported in many studies. This study attempts to address that question. 302 first and repeat DUI offenders used an interlock for an average 8 months, provided blood for measurement of %CDT, GGT, γCDT, PEth, ALT, AST and gave interviews for AUDIT, TLFB, DRINC at device installation and 8 months later (usually at removal). As reported in 2010, baseline levels of alcohol biomarkers strongly predict rates of failed interlock BAC tests (a predictor of recidivism) over 8 months. Vehicle starts held constant at about 175/month and as is commonly reported in interlock studies, during the interlock period the rates of failed BAC tests dropped by half. Nonetheless, there were no changes in levels of 6 alcohol biomarker over the 8 months from baseline to study end. By contrast, among 15 pre-post subscales of standard psychometric assessments, the majority (77% of subscales) of drinking, and drinking related consequences, reported strongly significant reductions in drinking. All within-subjects findings were nearly identical whether evaluated with parametric or non-parametric analyses. Simply enough, the biomarker data are at odds with the self-report data. However, the biomarker data is more concordant with the expected resumption of post-interlock recidivism data than is the information acquired through the assessments. The failure to find a reduction in drinking via alcohol biomarker was consistent across all three interlock risk groups (those with zero interlock failed BAC tests, those with low rates, and those with high rates). Evidently study subjects with interlocks find ways to drink more strategically, reducing drinking-driving, without necessarily reducing total drinking, despite their reports to the contrary. If valid, this serves as an explanation why recidivism can be reduced during the interlock control period, but without the interlock the apparent self-control and strategic drinking does not last and old habits reassert themselves.
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0216

SMOKE-FREE BAR POLICIES PREDICT DRINKING BEHAVIORS AND ALCOHOL USE DISORDERS IN A LONGITUDINAL U.S. SAMPLE
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Background: Smokefree legislation prohibiting smoking in indoor public venues, including bars and pubs, is an effective means of reducing tobacco consumption and tobacco-related disease in both non-smokers and smokers. Given the high comorbidity between alcohol consumption and tobacco use, it is possible that the public health benefits of smokefree policies may extend beyond smoking-related outcomes to drinking behaviors. However, little research has examined whether tobacco legislation reduces alcohol consumption and rates of alcohol use disorders (AUDs). The current study addresses this gap in the literature using a large, prospective, nationally representative U.S. sample.
Methods: Using Waves I (2001–2002) and II (2004–2005) of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC), we examined the predictive relationship of the implementation of state-wide smokefree legislation in bars between Waves I and II and changes in alcohol consumption (drinking frequency, drinks per episode, and binge drinking) and DSM-IV AUD status among individuals who reported drinking in public at least once a month (n=5913). Specifically we investigated whether the effects of smokefree policies would be most evident among Wave I smokers and heavy drinkers. General estimating equations (GEE) were used to account for clustering of individuals within states.
Results: Smokefree policies were associated with significantly decreased frequency of alcohol consumption and binge drinking among current smokers or hazardous drinkers at Wave I. Moreover, compared with individuals in states without smokefree policies, those with a current AUD at Wave I were significantly less likely to continue to meet AUD criteria at Wave II if they lived in a state that adopted smokefree bar policies. This finding was particularly robust among current smokers at Wave I. Smokefree bar legislation was not associated with changes in drinking quantity nor AUD onset among those with or without a lifetime history of AUD.
Conclusion: These results capture the beneficial effects of smokefree policies on drinking outcomes among individuals at greatest risk for alcohol-related health problems and represent an innovative legislative approach to decrease morbidity and mortality associated with alcohol consumption. Current findings can inform policy debates to more fully capture the public health benefits of implementing smokefree legislation.

0217

IS STANDARD DRINK SIZE INFORMATION ENOUGH TO CURB DRINKERS' ENTHUSIASM? FINDINGS FROM A FIELD INTERVENTION AMONG BAR GOERS

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Purpose: Test the disclosure of standard size information (SSI) to bar goers as they order drinks. Standard sizes have been proposed as a more accurate measure to assess alcohol consumption, which, if adopted by drinkers, could potentially reduce the risk for alcohol abuse (NIAAA, 2005). We tested the effect of SSI on natural consumption behavior. Because we expected that SSI alone would not be enough to reduce drinking, we combined it with other information and tested several experimental conditions: (1) SSI only, (2) SSI + guidelines, (3) SSI + guidelines + argument for moderate drinking, and (4) SSI + guidelines + argument + recommendations tailored to participants' gender and drinking styles. The design also included control participants.
Methods: This intervention was tested among 953 bar goers (21 years of age and older; 65.8% male) recruited as they walked to bars and restaurants at night. After answering a few baseline questions, they were presented with a bar menu in which the information was embedded. Participants were asked to indicate what they would be ordering from the menu (foods and drinks) for the rest of the night if this was the only menu they could order from. Participants were asked to return to our staff once they were done visiting bars/restaurants for the night, in order to complete a brief questionnaire on the events and alcohol-related behaviors that occurred since the first contact with the staff. Breath alcohol concentrations (BACs) were collected both at entrance (first contact) and exit (second contact).
Results: Outliers (3 standard deviations above/below the mean on BACs or orders) were removed from the analyses. Analyses of variance were conducted on the amount of alcohol that participants ordered (converted in standard drinks) and BAC difference scores with the condition and gender as predictors. Women ordered significantly less alcohol than men ($p < .001$). The effect of the condition was significant on BAC difference scores only ($p < .001$). Pairwise comparisons revealed that the increase in BACs was the greatest in condition 3 (ps < .000). In all other conditions, the increase in BACs was similar to that of control participants.
Conclusion: SSI may fail to reduce alcohol ordering and consumption. There may be some boomerang effect resulting in greater alcohol consumption when the menus contained standard sizes, guidelines, and a persuasive argument to promote moderation in drinking.

0218

THE TRANSLATIONAL PARADIGM IN ADDICTION GENOMICS RESEARCH: A MODEL OF BEST FIT?

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Translating scientific discoveries to improve population health is a top NIH priority. This goal is central to the field of public health genomics, which seeks to identify risk factors for prevention and treatment. However, this new emphasis on translational research may present challenges for scientists who find themselves under increasing pressure to demonstrate the translational value of their research to obtain funding. We conducted semi-structured interviews of a sample of 20 addiction scientists, including those engaged in alcoholism research, and asked them how they think genetic research addresses addiction as a public health problem and how their own research fits within the translational spectrum. Interview transcripts were qualitatively analyzed. We found that some scientists could describe the impact their research may have upon addiction treatment or prevention while others struggled to posit public health benefits and expressed doubts about the utility of genetic research in clinical practice. One scientist stated: ''I think that the basic science that we have uncovered in clinical research with regard to brain changes, cognitive changes, psyche-testing results has been very important in trying to help people educate the public on what the consequences of drugs are.'' Other scientists believed that there was too much focus on translating findings into practice: ''I think that the promise at this stage has less to do with public health more to do with eventual understanding of basic process that is underlying the development of addiction.'' Another stated: ''It would be nice if we all had either clearly clinical drug development focuses or just looking at neurobiology…rather than people misrepresenting the data as being genuinely potentially translational just because that is what you have to say to get money.'' While the ''bedside'' application of research is important, we question whether it is reasonable to place so much emphasis on the translation of genetic research into medical and public health practice if doing so hinders the work of basic science at ''the bench.'' Our findings air the conflicting perspectives of scientists who explore the etiology of addiction. Some think the NIH may push too hard for translation. Rather than expecting all researchers to conceptualize their work using the translational paradigm, in some cases it would be better to allow the translational value of their work to emerge on its own.

0219

PATTERNS OF SELECTED ALCOHOL CONTROL POLICIES ACROSS U.S. STATES

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We will describe preliminary results from a process to identify and weight essential provisions of state alcohol control policies. The weights for each provision were assigned based on the relative importance for policy implementation, empirical evidence and theory as determined by a panel of alcohol policy experts. We used a criterion-based scale for each policy that had a 0.0– 1.0 range. We assessed the presence or absence of 47 policies and provisions within each policy in 50 US states and the District of Columbia for 1999–2011 using the Alcohol Policy Information Systems (APIS) and other data sources. We will present data for taxes on alcohol (TAX), restrictions on hours of sale (HOS), graduated driver licensing laws (GDL), keg registration policies (KEG), and house party laws (HPL). In 2011, states varied in their mean rating score for HOS (mean=0.53; standard deviation = 0.31), HPL (mean=0.32; s.d. = 0.29), KEG (mean 0.18; s.d. = 0.20) and GDL (mean=0.42; s.d.=0.16). TAX was examined using a continuous variable of dollars/drink based on excise, ad valorem and sales taxes for beer (and for beer, wine and spirits in states without government monopoly). The mean state tax per drink on beer was $0.104 (range $0.008–0.30). The restrictiveness ratings of the five policies were not strongly correlated with one another at the state level. For example, TAX was not associated with ratings for HOS (r=-0.03), HPL (r=0.03), KEG (r=0.01) and GDL (r=0.16). We observed similar findings between KEG and HOS (r=0.18), HPL (r=0.16), and GDL (r=0.10). Three of five policies became more restrictive between 1999 and 2011, with significant change in policy scores for HPL (β=0.012; p<0.001), KEG (β=0.009; p<0.001), and GDL (β=0.016; p<0.001). In future work we will assess and aggregate policies by state to obtain an overall policy environment rating by year. We will use these ratings to assess whether the policy environment accounts for state-level variation in alcohol consumption and alcohol-impaired driving behavior among youth and adults.

0220

COMPARATIVE ASSESSMENT OF STATE ALCOHOL CONTROL POLICIES

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Assessing the state alcohol policy environment requires identifying effective policies and understanding their relative effectiveness. We will present policy effectiveness ratings from a Delphi Panel of experts on alcohol control policy. We grouped 47 alcohol policies identified as effective into four domains to compare whether ratings differed by policy type: (1) pricing, (2) physical availability, (3) drinking and driving, and (4) promotion. Experts rated the effectiveness of 47 alcohol control policies by target behavior and population: (1) binge drinking among adults, (2) binge drinking among youth, (3) impaired-driving among adults, and (4) impaired-driving among youth. The average effectiveness ratings across the four groups was 2.5 to 2.8 - a rating between ''somewhat effective'' (a score of 2) and ''effective'' (a score of 3). Pricing policies had the highest ratings (3.7–4.0), with alcohol excise taxes receiving the highest ratings in all four contexts (4.5–4.7). Effectiveness for reducing binge drinking (r = 0.50) and impaired driving between adults and youth (r = 0.45) between adults and youth were positively correlated. The correlation for reducing binge drinking and impaired driving were very strong among both adults (r = 0.88) and youth (r = 0.85). Policies targeting the general population are rated as effective for reducing binge drinking and impaired driving among youth, although the converse was not also true. Comparative policy analyses can help policymakers to prioritize efforts to reduce excessive drinking and related harms and are also useful for policy research.

0221

RELATIONSHIP BETWEEN YOUTH AND ADULT BINGE DRINKING IN THE US

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A common policy response by state legislatures to address excessive drinking among youth is to enact restrictions on drinking that exclusively focus on youth. However the sole focus on youth does not account for the possible relationship between youth and adult drinking at the population level. Little is known about the relationship between state-level adult binge drinking prevalence and youth alcohol use. We studied alcohol consumption behaviors among students in the biennial state-based Youth Risk Behavior Surveys and adult binge drinking prevalence from the Behavioral Risk Factor Surveillance System survey during 1999–2009 to assess the effect of a five percentage point difference in adult binge drinking on alcohol-related behaviors among youth, adjusting for age, sex, racial/ethnic composition, income, educational attainment, religious affiliation, consumer price index, urbanization, alcohol treatment characteristics, and enforcement. We observed that a 5% higher state-level adult binge drinking prevalence was associated with a 5% (95% CI: 1.03, 1.07) greater odds of binge drinking and a 6% (95% CI: 1.03, 1.08) greater odds of drinking and driving among youth. Binge drinking by adults predicts alcohol consumption and drinking and driving among youth in the same state.

0222

PROVISION OF ALCOHOL TO UNDERAGE YOUTH BY YOUNG ADULTS

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Purpose: It is well known that a significant proportion of underage drinkers obtain alcohol from family, friends, and/or other acquaintances. This study aimed to understand the attitudes and behaviors of young adults regarding provision of alcohol to underage drinkers.
Method: Participants were 1,014 individuals who were originally enrolled as first-year college students in an ongoing prospective study of health risk behaviors. Participants turned 21 during Years 2–4 of the study, after which (Years 6–7) they were asked a series of questions regarding: 1) whether or not they had ever provided alcohol to someone who was a) 18–20 or b) under 18, and their relationship to the underage person(s); 2) their perception of the legal and health risks of doing so; and 3) whether or not they had been approached to provide alcohol to someone underage. Descriptive statistics were used to analyze the data.
Results: In total, 67% of the sample had provided alcohol to someone underage, including 16% who ever provided to someone under 18 and 65% who provided to someone between the ages of 18–20. Among individuals who had been approached for alcohol by someone under 18, 39% had provided alcohol. The vast majority (87%) of individuals who had been approached by an older minor (ages 18–20) provided alcohol. Legal reasons appeared to be more salient motives than health reasons for not providing alcohol to underage drinkers. Participants expressed more permissive views about providing alcohol to a family member than to a friend, for recipients under age 18. For example, 41% of the sample reported that it was okay to provide alcohol to a family member under the age of 18, but only 15% reported that it was okay to provide alcohol to a friend under the age of 18.
Conclusion: The study findings highlight that young adults represent a new prevention target for strategies to reduce underage drinking. More research is needed to understand the characteristics of these young adults who provide alcohol to underage drinkers.

0223

MOTIVATION-ENHANCING INTERVENTION FOR OPERATING UNDER THE INFLUENCE OFFENDERS: THREE YEAR RECIDIVISM COMPARED TO AN ALTERNATIVE PROGRAM

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Many states use group-delivered interventions with people arrested for operating a motor vehicle under the influence of alcohol or drugs (OUI). However, few provide information about program effectiveness in reducing recidivism, especially in a comparison group design. This study utilizes the State of Maine's transition from one OUI program to another to assess differences in recidivism. Our purpose was to examine the OUI recidivism rates between when Maine's OUI offender program used a motivation-enhancing intervention, PRIME For Life (PFL) to when it previously used a different intervention approach. Using data collected by the state, we compared three year recidivism rates between two time periods. The first (Cohort 1, n = 4,922, 9/1/1999-8/31/2000) was when Maine's program used the Substance Abuse Life Circumstance Evaluation (SALCE) and the Weekend Intervention Program (WIP) as the core interventions. The second (Cohort 2, n = 5,262, 9/1/2002-8/31/2003) was when the state used PFL as the core intervention. In both cohorts, offenders were required to participate either in the core program or – among those with signs of increased risk of negative consequences – the core program plus further substance use treatment. We categorized participants into three intervention categories: did not complete, completed the core program, and completed the core program plus treatment. Logistic regression predictors included intervention category, cohort (1 vs. 2), and their interaction; and controlled for age, gender, and prior OUI. The intervention type X cohort interaction was statistically significant (p = .009), meaning that the recidivism rates for PFL differed from those for WIP/SALCE. Adjusted for the control variables, recidivism rates for Cohort 1 (12.7%) and Cohort 2 (13.4%) noncompleters did not significantly differ (OR = 0.94, ns). In contrast, more WIP/SALCE program completers had a subsequent OUI than PFL completers (11.8% and 9.4%, respectively, OR = 1.28, p = .04). The same pattern was found among people required to take these programs plus subsequent substance use treatment (16.3% and 11.4%, OR = 1.51, $p < .001$). The results suggest that while subsequent OUI rates remained consistent for noncompleters across these two time frames, Maine's use of a motivation-enhancing program (PFL) led to lower recidivism rates compared to the earlier program.

0224

FEASIBILITY OF USING IPADS FOR DATA COLLECTION AT COLLEGE PARTIES

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Purpose: Tablet computers operating on a wireless network can run web-surveys with complicated skip logic in a variety of environments proximal to behavior of interest. The purpose of this study was to compare the use of tablets with paper and pencil surveys at college parties.
Methods: Two college parties were identified by driving a route around campus and partygoers were recruitedonce permission was granted from the party host. Participants were interviewed using an online survey via ipad and 3G subscription or a paper-and-pencil version of the study. All subjects were asked to give a breath sample to analyze current breath alcohol concentration (BrAC) after completing the survey. Subjects were recruited into a follow-up phone survey and received a $5 gift card for participation in each survey.
Results: All participants who were approached to participate agreed: final sample included 18 participants, 9 from each party. Eight subjects were interviewed using the online version of the survey, and ten subjects were interviewed using the paper-and-pencil form. All participants were current college students: 35.3% were freshmen, 29.4% were sophomores, 11.8% were juniors, and 23.5% were seniors. More than two-thirds (77.8%) of participants were underage drinkers. Participants represented both genders (61.1% male). BrAC values ranged from 0.045 to 0.182 with a mean BrAC of 0.093 (SD 0.038). No differences were noted in the gender, age, reported drinking, or BrAC values between those who completed the electronic versus paper-and-pencil version of this survey.
Conclusions: iPads appear to be a feasible method of data collection in the field. Given the interviewer format of these surveys, no differences on major items were observed. Anecdotally, there may be slowed response from the internet network when a party is ending, as students use their wireless devices to begin looking for the next party location.

0225

CONGRUENCY IN PARENT- AND STUDENT-REPORTED DATA ON PARENTING BEHAVIOR: WHICH IS A BETTER PREDICTOR OF COLLEGE STUDENT DRINKING?

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Background**:** Recent efforts to reduce college student heavy episodic drinking have included parent-based interventions (PBIs). PBIs have been developed and continue to be refined based on research documenting associations between protective parenting (e.g., monitoring) and lower levels of drinking and between risky parenting (e.g., permissiveness) and higher levels of drinking. This area of research has primarily relied on student-reported data on parenting which is often cited as a limitation of this work. However, the degree to which parent- and student-reported data correspond is not known. In addition, there is a gap in the literature with respect to the comparative predictive utility of parent- and student-reported data. Objective: The goal of the present study was to determine the level of agreement between parent- and student-reported data on a range of parenting behaviors. The secondary goal was to determine whether parent- or student-reported data on parenting better predicts college student drinking at a longitudinal follow up.
Method: Data were collected from a sample of 145 parent-student dyads at a large public northeastern university at two time points. At the first time point (the spring of the freshman year of college) parents and students reported on parental monitoring, expertise, trust, access, approval of moderate and heavy drinking, and permissiveness. At follow up in the fall of the sophomore year, students reported on their typical weekly drinking. Parents' and students' reports of parenting behavior at time 1 were compared. Two separate regression models analyzed whether parent- or student-reported parenting data better predicted student drinking at follow up.
Results: Agreement between parents' and students' reports of parenting was low to moderate, with intraclass correlation coefficients ranging from .13 (for expertise) to .62 (for permissiveness). Results from the regressions indicated that the model using student-reported data better predicted college student drinking (R^2 for students=.30; R^2 for parents=.20).
Discussion: Findings suggest that student-reported data on parenting is a stronger predictor of college student drinking than parents' self-reported data. Studies on parent influences on college student drinking, including research on PBIs, may benefit from using student-reported data, as it appears to be more strongly associated with college drinking.

0226

EVALUATING A PROTECTIVE BEHAVIORAL STRATEGIES SKILLS TRAINING INTERVENTION IN REDUCING RISKY ALCOHOL OUTCOMES AMONG STUDENTS WITH POORER MENTAL HEALTH

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Students with poorer mental health (anxiety, depression, increased levels of distress in comparison to their peers) are at risk for elevated alcohol related consequences (Park & Grant, 2005). Surprisingly few studies, however, have investigated ways to reduce risk in this population. The current study evaluated the efficacy of a Protective Behavioral Strategy (PBS; e.g., Martens et al., 2005) cognitive-behavioral skills training with personalized feedback (PBS-STPF) intervention in increasing PBS and reducing risky drinking and consequences among students seeking services from a college counseling center. Participants (N = 142) were randomized to either the PBS-STPF intervention or health information control condition. The 30 minute, one-on-one intervention utilized skills training, with the aid of a personalized PBS feedback sheet, to reinforce current PBS and encourage the use of new PBS. Participants completed 1-month follow-up surveys. Repeated measures ANOVAs were conducted to explore intervention effects. Treatment participants reported significantly larger increases in PBS use relative to control participants (p = .002). Males reported significantly greater decreases in typical weekly drinking (p = .05) and past two week binge drinking events (p =.03). Results for females revealed that intervention condition interactions with primary drinking outcomes were trending towards significance. For both males and females, intervention condition interactions with alcohol consequences were trending towards significance. After completion of data collection we expect that the larger sample size will confirm the significance of these interactions. Further, 6-month follow-up data will be reported and discussed at the symposium. This project demonstrated the preliminary efficacy of a cognitive behavioral based PBS intervention among students with poorer mental health in increasing PBS use and reducing risky alcohol outcomes. Given that students with poor mental health are an at-risk population for negative alcohol-related consequences, the results present a novel and practical intervention addressing the needs of this population.

0227

RELATIONSHIP OF PROTECTIVE BEHAVIORAL STRATEGIES TO ALCOHOL CONSEQUENCES AMONG SWEDISH HIGH SCHOOL SENIORS: MODERATING ROLE OF CONDUCT DISORDER SYMPTOMS

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Protective Behavioral Strategies (PBS) may decrease harmful consequences of drinking by reducing risky alcohol use. Several studies have found an inverse relationship between PBS and alcohol consequences, but others have found no relationship. Research indicates anxiety, depression, and conduct disorder symptoms are associated with greater risk of alcohol-related problems among young adults. The current study evaluates the extent to which the relationship between PBS and alcohol consequences in young adults is moderated by mental health (anxiety and depression) symptoms, conduct disorder symptoms, and gender. We hypothesized PBS would be less effective for those with higher conduct and mental symptoms, as the majority of PBS do not address coping drinking situations. Data are from baseline assessment of a longitudinal study of alcohol use and consequences among high school seniors. Participants (N=2230; age range: 17–19) at 17 high schools in Sweden completed surveys during fall of their senior year. Results indicated individuals with higher conduct problem scores drank on significantly more occasions, had more alcohol consequences and used fewer PBS. Individuals with more mental symptoms had significantly more alcohol consequences but there was no association between these symptoms and quantity/frequency of drinking or use of PBS. The main effects of conduct problems in predicting drinking and PBS were qualified by a significant interaction between conduct problems and PBS in predicting drinking consequences, drinking frequency (but not quantity), and total AUDIT scores. Simple slopes showed PBS scores were weakly and positively associated with drinking and alcohol consequences for those without conduct problems, but significantly negatively associated with drinking and related consequences among those with higher conduct problems. Findings were not significantly moderated by gender nor mental health symptoms. In contrast to our hypothesis, findings suggest individuals with a history of conduct disorder may benefit more from using PBS, and may be a particularly appropriate group to target for skills-training interventions given their lower natural use of PBS. Findings also suggest anxious or depressed individuals may require additional interventions, as similar use of PBS strategies did not lead to reduced consequences compared to those with fewer symptoms. This research was supported by NIAAA #U01 AA018276 awarded to Drs. Larimer & Berglund.

0228

EXAMINING PROTECTIVE BEHAVIORAL STRATEGIES IN YOUNG ADULTS: WHICH STRATEGIES ARE ASSOCIATED WITH HEAVIER DRINKING AND NEGATIVE CONSEQUENCES?

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Protective behavioral strategies (PBS) are a common component of interventions for young adult drinking. Research indicates that some strategies, including those that can be utilized while drinking, are directly correlated with lower drinking levels (Cf. Martens et al., 2005). Other strategies, however, may be indirectly related to drinking, and instead be more closely associated with alcohol-related consequences. Two studies assessed the Protective Strategies Questionnaire (PSQ; Palmer, 2004), which may be well-suited to the assessment of direct and indirect strategies. In Study 1, data from a sample of undergraduate drinkers (N = 374) was used to conduct principle components analysis (PCA) and confirmatory factor analysis (CFA). In Study 2, data from a clinical sample of young adult heavy drinkers (N = 173) was used to replicate the CFA model. In both studies, relationships among the factors, alcohol use and consequences were examined. PCA and CFA in split halves of the undergraduate sample and CFA in the clinical sample confirmed two factors: a Direct Strategies (e.g. ''space drinks out over time'') factor and an Indirect Strategies (e.g. ''have a designated driver'') factor. Path analysis results indicated that, in both samples, Direct Strategies were significantly associated with lower alcohol consumption. Indirect Strategies were less strongly associated with drinking but were significantly associated with fewer alcohol-related consequences. Indirect effects testing also revealed, in both samples, a significant indirect path from Direct Strategies through alcohol consumption to consequences. In contrast, the indirect path from Indirect Strategies through drinking to consequences was not significant. This information could be used to tailor clinical interventions for young adult drinkers. Patients with varying characteristics may be more amenable to different types of strategies. Patients with less motivation to change drinking may benefit from an increased focus on the use of Indirect Strategies.

0229

PROTECTIVE BEHAVIORAL STRATEGIES AS A MEDIATOR OF THE RELATIONSHIP BETWEEN ANXIETY AND HIGH-RISK DRINKING

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Alcohol use disorders and anxiety disorders co-occur, and lesbian and bisexual women appear at higher risk for both alcohol and anxiety disorders (Cochran et al., 2003; King et al., 2008). Because of high personal and societal costs of alcohol use, researchers and clinicians have aimed to identify factors that might reduce both alcohol consumption and negative alcohol-related consequences. Protective behavioral strategies (PBS; e.g., Martens et al., 2005, 2007; Sugarman & Carey, 2007) are cognitive-behavioral strategies students can engage in when consuming alcohol. Although research has found direct effects of increased PBS on decreasing alcohol use and alcohol-related negative consequences, it is unclear whether anxiety influences the use of such strategies, which in turn predict alcohol consumption and related consequences. The present study examined the mediating role of PBS on the relationships between both generalized anxiety and social anxiety with alcohol consumption and consequences. A national sample of 1,090 Lesbian and Bisexual women between the ages of 18–25 completed an online survey that assessed the constructs of interest. The findings demonstrated that generalized anxiety was associated with heavier alcohol consumption and experiencing more consequences. Furthermore, results showed support for mediation such that individuals who reported having higher levels of anxiety were less likely to use PBS, which in turn led to higher levels of alcohol consumption as well as negative consequences. When examining the mediating role of PBS on the relationships between social anxiety and drinking behavior, no evidence of mediation was found. As found in previous research, social anxiety was negatively associated with alcohol consumption and positively associated with negative consequences (Lewis et al., 2009). However, social anxiety was not associated with use of PBS. These findings highlight the importance of examining who is at risk as well as why they are at risk. It is important to note that the mediating role of PBS was found for generalized anxiety but not for social anxiety. Future research should examine additional factors that may help to explain these findings, such as drinking motivations. The results from the current study suggest that when addressing high-risk drinking among sexual minority women, clinicians may need to pay closer attention to individuals higher in self-reported generalized anxiety and to help increase use of PBS.

10. TREATMENT / RECOVERY

0230

PATIENT COMMITMENT STRENGTH DURING MI, HEALTHCALL PARTICIPATION, AND DRINKING OUTCOMES: RESULTS FROM A RANDOMIZED TRIAL OF HIV PRIMARY CARE PATIENTS

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AIM: Strengthening patient commitment to change health behaviors is a central goal of motivational interviewing (MI). The strength of patients' language indicating commitment to change (e.g., substance use) in manualized treatment sessions, especially the latter portions of a session, has repeatedly been shown to predict treatment outcomes in treatment-seeking patient samples. Heavy drinking in HIV-infected patients predicts mortality and risk behaviors. The relationship between in-session commitment language to drinking outcomes among HIV primary care patients recruited via screening is unknown.
METHOD: Urban English- or Spanish-speaking HIV primary care patients who drank ≥4 drinks at least once in the prior 30 days participated in a MI session aimed at drinking reduction. Patients were randomly assigned to HealthCall (brief daily calls to an interactive voice response system to enhance drinking self-monitoring for 60 days) or not. The outcome variable was drinks per day, last 30 days. Patients' utterances related to change across MI session deciles (commitment strength) were coded by trained raters with the DARNC system (Amrhein et al., 2003). The relationship of patient commitment strength during the MI to the outcome, and its interaction with HealthCall assignment, was tested with a generalized linear model for an outcome with a negative binomial distribution.
RESULTS: MI sessions of 141 patients were recorded (121 English; 20 Spanish). The two coders were highly reliable (ICC=.71). Greater commitment strength in the second half of the MI session predicted decreased drinking at 60 days, controlling for baseline drinking ($p< 005$). HealthCall assignment interacted with commitment strength ($p<.09$), suggesting that among patients not assigned to HealthCall, commitment MI strength robustly predicted drinking outcomes, while among patients assigned to HealthCall, commitment strength had less effect.
CONCLUSION: Strength of commitment to change at the end of MI is an important predictor of drinking reduction after brief intervention among non-treatment seeking patients identified through screening in HIV primary care. Participation in a low-cost enhancement of MI may offer added benefit to patients with lower commitment to change at the end of a brief MI. Results should be replicated.

0231

HIV RISK BEHAVIORS AMONG WOMEN IN SUBSTANCE ABUSE TREATMENT: CORRELATES AND PREDICTORS OF CHANGE

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This observational study sought to improve our understanding of factors that contribute to risky sexual behavior among women seeking treatment for alcohol and other substance use disorders. Women were recruited at the start of outpatient (n=236) or inpatient (n=166) treatment. At intake, a Timeline Follow-back interview was used to obtain retrospective reports of daily drinking, drug use, and sexual behavior for a 90-day pre-treatment baseline period. Additional interview and questionnaire measures also were obtained. Measures were re-administered at four 90-day follow-up interviews. Among women who reported sex with a primary partner during baseline (n=261), 15% reported consistent condom use for all events with this partner, whereas 80% reported no condom use with this partner. Among women who reported sex with a non-primary partner (n=159; doesn't include commercial sex trading), 26% reported consistent condom use and 45% reported no condom use with such partners. Significant correlates of non-use of condoms included negative beliefs and attitudes and low self-efficacy regarding condom use and AIDS prevention, as well as psychological distress, sexual impulsiveness and sensation seeking, history of severe assault by a male partner, and (with primary partners) negative partner attitudes toward condom use. Some of these correlates also predicted unprotected sex with a primary partner during the first 90 days after treatment entry, after controlling for baseline. However, unsafe sex with a non-primary partner during follow-up was most notably associated with follow-up levels of substance use, i.e., more drinks per drinking day and greater frequency of alcohol, marijuana, and cocaine use. In sum, preliminary analyses of baseline and follow-up data indicate a high prevalence of unprotected sex in this population. Identification of factors related to baseline and follow-up levels of risky behavior may suggest targets for future intervention development.

0232

IS EMPATHIC SPEECH RELATED TO CHANGE TALK? EXPLORING IN-SESSION BEHAVIOR IN MOTIVAITONAL INTERVIEWING FOR ALCOHOL & SUBSTANCE USE DISORDERS

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Clinician empathy is a central component in psychotherapy and has been cited as an important factor of successful treatment for clients with alcohol and substance use disorders (AUDs/SUDs). Within motivational interviewing (MI), empathy has been described as functioning to create an environment where clients can freely explore their ambivalence towards change (Miller & Rose, 2009); and although empathy has been identified as part of MI's relational component, research has not explored the empathic content of clinician speech and its relation to client behaviors such as client change talk (CT) and sustain talk (ST). This study is a secondary analysis of previously coded MI sessions for clients with AUDs/SUDs. Sessions (n = 150) were reanalyzed to measure the quantity and frequency of clinician empathic speech (ES). A coding system was developed which measured the presence of ES, providing measures of empathic speech frequency (ESF) and empathic speech quantity (ESQ). It was hypothesized that both ESF and ESQ would significantly correlate with client CT, but would not significantly correlate with client ST. Results found that ESF correlated with CT ($r = .23$, $p < .01$) as well as ST ($r = .35$, $p < .001$); and ESQ correlated with ST ($r = .17$, $p < .05$) but not CT ($r = .12$, $p > .05$). Step-wise and bootstrapping mediation analyses found that clinician variables of total reflections (REF-T), reflections of change talk (REF+), and MI-consistent behaviors (MICO) each were significant mediators of the relationship between ESF and CT. The mediation model that used reflections of change talk as a mediator accounted for the most variance in the relationship between empathic speech frequency and change talk ($R^2 = .61$). This study showed that ESF, rather than ESQ, had a stronger relationship with both client CT and ST. The relationship between ESF and CT was mediated by reflections and other MI-consistent clinician behaviors which have previously been shown to elicit CT from clients (Moyers et al., 2009). Results suggest that clients receiving MI for alcohol and drug use are more likely to offer more CT and ST to clinicians who offer more frequent instances of empathic speech rather than a greater quantity of empathic speech. These findings are important for those looking to improve their ability to train or practice MI with AUD/SUD clients.

0233

A NEW APPROACH TO CODING SPEECH IN MOTIVATIONAL INTERVIEWING

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Signal processing techniques have been used recently for automatic emotion recognition of speech. Features of speech such as pitch and frequency can be used reliably to discriminate not only between emotional and non-emotional speech, but also between specific affective content (Sato & Obuchi, 2008). In the present study we apply these techniques to explore utterances of change talk (CT: speech favoring change) and sustain talk (ST: speech favoring the status quo) recorded during motivational interviewing (MI) sessions with ambivalent alcohol users.

All procedures were approved by the local IRB. Participants were alcohol users who responded to an advertisement for non-treatment-seeking problem drinkers. Data were collected as part of a study examining a potential neural substrate for change talk in MI using magnetoencephalography (Houck, Moyers, & Tesche, 2011).

The Mel scale approximates the human auditory system's pitch response (Stevens, 1937), and can be more appropriate for speech analysis than is the raw frequency scale (i.e., Hz). Mel frequency cepstral coefficients (MFCC: Davis & Mermelstein, 1980) were extracted as the principal feature for this analysis. All speech recordings had precise onsets and offsets to facilitate their use in the parent study and were ideally suited for this application. Analysis was performed using the RASTAMAT toolbox (Ellis, 2005). Each recording was subdivided using a 25 ms sliding window. These frames were transformed to the frequency domain using a fast Fourier transformation. Sub-band energies were computed using a Mel filterbank and log-transformed. MFCCs were computed by taking the inverse Fourier transformation of the transformed sub-band energies.

The first 20 MFCCs for each utterance were averaged across frames, and the output analyzed using HLM 7. 20 MFCCs were entered at level 1, nested within utterances at level 2, with speech category (CT or ST) entered as a categorical variable, nested within participants at level 3. Results indicated a trend toward significance (p = .10).

These preliminary results suggest that auditory features of speech may be used to differentiate CT and ST utterances. Such features are commonly used by automatic classifiers, either offline or in real time, to categorize speech. If replicated in a larger sample, our results could be used in such classifiers to augment process coding of therapy sessions, or to provide real-time feedback to clinicians to highlight salient client speech.

0234

WINDOWS OF OPPORTUNITY: SEQUENTIAL ANALYSIS OF CLIENT-CLINICIAN INTERACTION USING TIME WINDOWS

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Time window sequential analysis (Bakeman & Quera, 1995) allows researchers to explore whether a target behavior is contingent upon a given behavior in a behavior stream. Both behaviors must occur within a specified time window, but one need not *immediately* precede the other or occur at a specified lag. This flexible analysis strategy permits the exploration of the immediate effects of specific kinds of speech within treatment sessions. Motivational interviewing clinicians directly influence client speech during MI sessions (Moyers & Martin, 2006; Glynn & Moyers, 2010), both change talk (CT: speech favoring change) and sustain talk (ST: speech favoring the status quo)., and that this speech mediates between therapist behavior and alcohol use outcomes (Moyers et al, 2009). Lag sequential analysis has shown that clinicians trained to selectively reinforce client change talk will will more effectively elicit and respond to CT from their clients (Moyers et al, 2011). The present study uses time window sequential analysis to evaluate the immediate influences upon CT and ST in front-line settings. Participants were 190 substance use clinicians randomized to MIU or MI+ training workshops. Up to five work samples could be submitted in the year following the training workshop. Recordings were coded using an objective behavior rating system using specialized coding software. A 30-second window was applied before and after each utterance. Transition probabilities were computed using GSEQ (Bakeman & Quera, 1995). Results indicate immediate effects of therapist behaviors on CT. Consistent with prior research, these results suggest that behaviors of theoretical interest MI have an immediate and robust effect on client speech. Client speech also appears to have an immediate effect upon clinician behavior. These short windows of opportunity during sessions may represent the best time for clinicians to influence client speech, and through speech to have an impact on alcohol use outcomes.

0235

EFFICACY OF WEB INTERVENTION FOR MALE AND FEMALE DRINKERS WITH AND WITHOUT A RECENT IN-PERSON TREATMENT HISTORY

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Purpose: Evaluation of Web-based interventions needs to consider which populations or sub-groups can benefit the most and under what circumstances. Using a Web-based intervention for veterans returning from Iraq and Afghanistan with risky drinking and PTSD symptoms, we examined differences in efficacy for veterans who received in-person treatment for substance abuse and/or other mental health disorders as compared to veterans who did not receive this type of treatment within the last three months.

Methods: Veterans were randomized to either an Immediate Intervention Group (IIG) or a Delayed Intervention Group (DIG). The DIG received treatment after an additional assessment which occurred at the same time as the post-intervention assessment for the IIG, thus serving as a no-treatment comparison.

Results: 304 participants (13.4% women) completed the assessments. At baseline for internet treatment, risky drinkers in treatment had more severe problems than risky drinkers not in treatment, as evidenced by higher scores on the Short Inventory of Problems (SIP) ($F(1,303)=4.62$, $p=.032$) and the PTSD Checklist ($F(1,303) =63.76$, $p=.000$) as well as more exposure to combat situations on the Combat Experiences Scale ($F(1,303)=4.78$, $p=.030$). The two groups did not differ on demographic variables, AUDIT scores, or alcohol consumption. At follow-up there was a significant decrease in Drinks per Drinking Day (DDD), Average Weekly Drinking (AWD), and Percent Heavy Drinking Days (HDD) in the IIG compared to the DIG (Multivariate $F= 4.99$, $p=.000$). For male veterans, there was no difference in these three drinking measures regardless of in-person treatment status.. The picture was more complicated for female veterans. Women in treatment within the last three months showed little effect of the web intervention on DDD and AWD while women not in treatment showed a larger decrease ($F(1,38)=3.3$, $p=.075$ and $F(1.38)=4.8$, $p=.038$ respectively).

Conclusions: Web-based programs can be effective for male risky drinkers, whether or not they are in treatment for alcohol or other mental health disorders. Participants who had more severe alcohol and trauma-related problems were already in treatment outside the intervention, and apparently were using the web-based intervention as adjunct treatment. The sample size for women was too small to draw firm conclusions, but points to the need to evaluate the effect of web-based interventions separately for men and women.

0236

CLIENT LANGUAGE ASSESSMENT PROXIMAL/DISTAL (CLA-PD): OVERVIEW AND PILOT RELIABILTY

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The present work provides an overview and pilot reliability for the Client Language Assessment – Proximal/Distal (CLA-PD). The CLA-PD is intended for assessing client change language within behavioral treatment sessions. The five language dimensions for "change talk" are derived from those within the Motivational Interviewing Skill Code (MISC; Miller et al., 2003; 2008; see also CLAMI, Moyers et al., 2006), and adapted to distinguish "proximal" from "distal" targeted behavior change. In other words, the system includes 21 language codes (five positive and five negative: Reason, Ability, Commitment, Taking Steps, and Other statements) in relation to the primary behavior change target (distal change) and in relation to the coping behaviors or life changes (proximal change) intended to facilitate that behavior change, as well as one additional neutral language code. The coding manual was developed to include examples that encompass a broad range of content which may be covered in behavioral treatments for alcohol or other substance use. In the present work, two independent raters received approximately 40 hours of training on the use of the CLA-PD system by the first author. Coding of seven pilot cases from a Project MATCH clinical research site showed good reliability for the majority of language codes. Specifically, 2-way mixed Intraclass Coefficients (ICC; single measure, consistency) ranged from .72 to .96 for positive distal statements, .53 to .94 for negative distal statements, .61 to .92 for positive proximal statements, and .61 to .84 for negative proximal statements. As is typically the case, "poor" agreement items were those with low frequency of occurrence in the data: for positive statements these were taking steps-distal and ability-proximal, for negative statements these were ability-distal, other-distal, ability-proximal, and other-proximal. The CLA-PD has demonstrated pilot interrater reliability for 15 of 21 language codes; all items will be subjected to additional testing within a larger sample. When behavioral alcohol or other substance use treatments are multi-session and skill-based, the CLA-PD may provide further detail in relation to client change language, and therefore processes of decision-making, commitment, and maintenance of behavior change.

0237

THE ALCOHOL INTERVENTION MECHANISMS SCALE (AIMS): OVERVIEW AND PILOT RELIABILTY

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The present work provides an overview and pilot reliability for the Alcohol Intervention Mechanisms Scale (AIMS). The AIMS measures therapist interventions that occur broadly across modalities of behavioral treatment for alcohol use disorders. It was developed based on identified commonalities in the *function* rather than *content* of therapist speech in observed therapy sessions [e.g., Cognitive Behavioral Therapies, Motivational Therapies, and Disease Model approaches], as well as from existing observer rating systems. In the AIMs, the primary function areas are: Explore (four codes), Teach (five codes), and Connect (three codes). The intent is to capture the exploratory and didactic nature of behavioral alcohol treatment while also measuring the relational/interpersonal capacities of the therapist and/or therapy. In addition, three codes do not fall under a primary function: confront/challenge, general information, and neutral/facilitate. Therapist behavior counts provide a frequency rating of occurrence. The three functions (Explore, Teach, Connect) are then rated on global skillfulness, which provide a quality valence to the overall session. Two independent raters received roughly 30 hours of training on the use of the AIMS system by the first author. Coding of seven pilot cases from a Project MATCH clinical research site showed generally high reliability of the measure. Specifically, 2-way mixed Intraclass Coefficients (ICC; single measure, absolute agreement) ranged from .87 to .96 for the Explore Function codes (explore change question and reflection, general assessment, goal setting), .86 to .98 for Teach Function codes (homework - teach, teach/advise, structure, self-disclosure), .87 to .92 for the Connect Function codes (affirm/self-efficacy, empathy/support, emphasize control/collaborate) and .98 for the confront/challenge code. ''Fair'' agreement codes were homework - explore (Teach Function) with ICC = .42 and general information with ICC = .42. Having demonstrated interrater reliability in this pilot sample, the AIMS is a promising observer rating measure of common factors and putative mechanisms of action in behavioral alcohol treatment.

0238

IS THERE A DIFFERENCE? A MULTIVARIATE DISTINCTION OF TWO BRIEF INTERVENTIONS

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When conducting clinical trials assessing the impact of interventions on alcohol use outcomes, it is important to include measures of treatment fidelity. Measuring theoretically relevant constructs allows the researcher to confirm that a treatment was delivered in accord with theoretical principles. Also, it can be used to show that two different treatments were not operating via the same mechanisms. The current study seeks to differentiate two brief interventions (BI) using summary scores from the Motivational Treatment Integrity Code (MITI), a treatment fidelity measure based on Motivational Interviewing (MI) principles.
Data for the current study was collected as part of a larger trial investigating two BIs for trauma patients with alcohol use disorders. Injured patients admitted to a level-one trauma center were randomized into a brief motivational interview (BMI), brief surgeon advice (BSA), or a standard care (SC) condition. BMI and BSA interventions were performed and audio-recorded while the participants were still in the hospital. Treatment fidelity and the difference between BIs was evaluated with a MANOVA using seven summary scores derived from the MITI: MI Spirit, Empathy, Direction, Percent MI-Consistent behaviors, Percent Open Questions, Percent Complex Reflections, and Reflection to Question Ratio.
A total of 78 sessions (BMI n = 40, BSA n = 38) were coded using the MITI by coders blind to treatment condition. A total of 14 sessions (18%) were double coded, and a two-way mixed intraclass correlation was used to assess the reliability of MITI measures, all of which fell in the ''good'' to ''excellent'' range. There was a significant omnibus MANOVA for BI condition (Wilks' λ = .461, F(7,70) = 11.67, p < .001), and all univariate F-tests, except for percent open questions, showed group differences in the expected direction. A Roy-Bargman Stepdown test was then used due to the correlation among MITI summary scores. Results from this analysis suggest that BMI and BSA interventions differed on four summary scores.

0239

PROLONGED EXPOSURE FOR THE TREATMENT OF PTSD IN A PTSD-ALCOHOL DEPENDENT SAMPLE

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Posttraumatic stress disorder (PTSD) is one of the most frequently co-occurring disorders in persons seeking treatment for alcohol dependence (AD; e.g., Brady, Back, & Coffey, 2004). Unfortunately, PTSD is associated with negative outcomes and substantial suffering in AD patients (Ouimette & Brown, 2003). Despite this grim outlook, there is clear evidence that trauma-focused Prolonged Exposure (PE) is an effective treatment for PTSD (e.g., Foa et al., 2005; Taylor et al., 2003) and early evidence suggests that PE may be effective at treating PTSD in substance abusers (e.g., Brady et al., 2001; Riggs et al., 2008). To more fully test PE in AD patients with PTSD, a RCT of PE vs. an active control treatment (Healthy Lifestyles; HLS) is being conducted. Current data represents outcomes from 100 subjects with current PTSD and AD receiving treatment as usual in a community treatment center. A significant Group x Time interaction was revealed for PTSD symptoms, F=3.86, p=.027, as measured by the Impact of Event Scale-Revised. In addition, a significant main effect for time was found, F=91.85, p<.001. Groups did not differ at baseline (PE, M=52.55 vs. HLS, M=50.78) but did differ significantly at 3-mo (PE, M=14.10 vs. HLS, M=24.28) and 6-mo follow-up (PE, M=14.88 vs. HLS, M=27.44). Six-month outcomes represented a 72% PTSD symptom reduction for PE and a 46% reduction for HLS. For depressive symptoms measured by the Beck Depression Inventory-II, a main effect for group, F=9.69, p=.004, and time was revealed, F=27.81, p<.001. Groups did not differ at baseline (PE, M=30.68 vs. HLS, M=31.20) but did differ at 3-mo (PE, M=6.91 vs. HLS, M=15.90) and 6-mo follow-up (PE, M=8.00 vs. HLS, M=18.10). Percent days abstinent from alcohol, as measured by a 90-day Timeline Follow Back did not differ between groups at any time point and indicated excellent treatment outcomes for both PE and HLS groups (baseline: M=43.40, M=54.36; 3-mo: M=95.00; M=96.67; 6-mo: M=87.71, M=90.66; respectively). Importantly, effective PTSD treatment did not appear to harm drinking outcomes. These data suggest that PTSD can be effectively treated in patients with co-occurring PTSD and AD using an existing and widely available evidence-based treatment (Foa et al., 2007). In addition, treatment provided by a PTSD specialist during standard early AD treatment, rather than a single therapist attempting to treat both PTSD and AD, may speed implementation of PE in standard AD treatment.

0240

COMPARISON OF STRATEGIES FOR REDUCING CUE-ELICITED CRAVING FOR ALCOHOL

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Craving, typically defined as a strong or persistent desire for a substance, is a commonly reported as a motivating factor in deciding to use a substance. Research has shown that, among heavy social drinkers, urge/craving is one of the most common reasons reported as the basis for drinking. In those with alcohol use disorders (AUDs) cravings to drink can maintain problematic alcohol use and can trigger a relapse from sobriety. Recently, mindfulness-based strategies have been applied to the treatment of addictive behavior, mainly in the form of targeting urges to use a substance. Mindfulness techniques involve focusing attention to the present and accepting experiences non-judgmentally. One goal of this detached observation to create a ''space'' between what people experience (e.g., cravings to drink) and how they respond to it (e.g., giving in/succumbing to desire). Nonetheless, little methodologically rigorous clinical and experimental research has been done to examine the effectiveness of mindfulness-based strategies on cravings to use a substance. The goal of the current study was to see how mindfulness strategies compared to other strategies when experiencing cue-elicited cravings. Specifically, individuals using a mindfulness-based coping strategy were compared to individuals who were asked to distract themselves from urges to drink, and to a control group not given any particular strategy. Individuals in this study (N=86) were heavy drinkers (male criterion: 14+ drinks/week; female criterion: 7+ drinks/week) who were recruited from the community. An in-vivo exposure to alcohol cues was used to assess increases and decreases in craving subsequent to participant attempts to use mindfulness skills, distraction skills, or coping as usual. Although no significant group differences existed at baseline, during the extinction period in which individuals applied their assigned strategies, groups reported significantly different levels of craving (Fs= 6.0–14.1, ps <.01). Nonetheless, the strategy that appeared most effective in reducing acute craving was distraction rather than mindfulness. In this study, observing and accepting cravings did not appear particularly successful as a means to reduce urge to drink in at-risk heavy drinkers.

0241

AN IVR MULTI-SESSION TREATMENT PROGRAM FOR RISKY DRINKERS: INITIAL EFFICACY

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Purpose: This study provides an initial test of a totally automated, multi-session treatment for problem drinkers in the community using a sophisticated Interactive Voice Response (IVR) system with speech recognition. The IVR is controlled by a computer system that emulates validated treatment strategies and the style of experienced clinicians. Simple IVR systems have been used in alcohol treatment research primarily to monitor daily drinking, to deliver assessments, and for brief intervention. To our knowledge, this is the first study to deliver a full alcohol treatment program using a sophisticated computer-controlled IVR system.
Methods: We adapted Miller and Munoz's self-help book, ''Controlling Your Drinking: Tools to Make Moderation Work for You'' (2005), into a computer-controlled IVR system that incorporated Miller and Munoz's strategies while enhancing the motivational aspects of the program. Participants could participate in up to 26 calls over 13 weeks. Participants were recruited via ads in newspapers and on Craigslist. 47 participants were randomized to receive either the IVR program or an informational pamphlet in the mail, with 3 and 6 month follow-up.
Results: The average age was 57, with a range of 28–81 years. 59.6% of participants were male and 40.4% were female; 83% were Caucasian and 13% were African-American. There were no significant differences between groups at baseline on demographics or drinking variables. Due to the small sample size, effect sizes of moderate or at least moderate size are reported, with p values for ANCOVAs when the results were significantly different between groups. The number of heavy drinking days per month decreased for the intervention group over time, with an effect size of -0.44 at 3 months and -0.74 (p=.02) at 6 months. Percent days abstinent per month increased over time, with an effect size of 0.64 (p=.04) at 3 months and 0.45 at 6 month follow-up. A moderate effect size for drinks per drinking day was found at 6 months (-0.49).
Conclusions: This initial test of a full computer-controlled IVR treatment program indicates positive changes in drinking can be achieved. The sample recruited was older than expected, and the results suggest that older adults in particular will use a totally automated IVR alcohol treatment system to change their drinking behavior.

0242

ASSOCIATION BETWEEN PATIENT BELIEFS REGARDING ASSIGNED TREATMENT AND CLINICAL RESPONSE AMONG VERY HEAVY DRINKERS AT 6-12 MONTH FOLLOW-UP

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Although the association between perceived treatment condition and reductions in drinking is well established, positive responses in the placebo group are not necessarily a long-term effect.This NIAAA-funded study explores differences between RCT patients according to their perceived treatment condition (active or placebo) to examine possible short- and long-term placebo effects on drinking patterns. The sample for this study was drawn from a large-scale, multi-site RCT of quetiapine fumerate extended release for the treatment of alcohol dependence. Qualitative interviews and quantitative surveys were conducted with 39 patients after the end of the original trial. All patients in this sample were assigned to the placebo condition and were interviewed 6–12 months after the trial (n=39). Drinking patterns and patient beliefs regarding assigned treatment were assessed. To examine possible short- and long-term placebo effects, drinking patterns before, during, and after the drug trial among those who believed they received the active drug (Perceived-Active group) are compared to those who believed they received the placebo drug (Perceived-Placebo group). Even though all the patients in this sample were actually assigned to the placebo condition during the RCT, 53% (21/39) believed they were or might have been assigned to the active drug condition when they were in the RCT. Almost a third of the Perceived-Active group (29%; 6/21) were abstinent at the time of follow-up compared to 17% (3/18) of the Perceived-Placebo group. Based on the drinking pattern they recalled having during the trial, 81% (17/21) of the Perceived-Active group appeared to have reduced their alcohol use during the RCT compared to 61% (11/18) in the Perceived-Placebo group. The Perceived Active group was also three times more likely to be among those who had maintained reduced drinking patterns at follow-up (77%; 3/13) compared to the Perceived-Placebo group (23%; 3/13). Results from this study lend themselves to short- and long-term placebo effects: Compared to the Perceived-Placebo group, the Perceived-Active group appeared more likely to reduce their drinking during the RCT and to maintain those changes at follow-up. These findings call for additional programmatic research of the biopsychosocial mechanisms underlying specific and non-specific (placebo) treatment effects associated with long-term reductions in alcohol use.

0243

IN SEARCH OF LONG-TERM TREATMENT EFFECTS: ANALYSIS OF DATA FROM THE COMBINED PHARMACO-THERAPIES AND BEHAVIORAL INTERVENTIONS STUDY

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Patients assigned to randomized controlled trials (RCT) often experience positive changes from baseline; however, long-term treatment outcomes and the processes of change are two areas of alcohol research that remain poorly understood. To examine long-term treatment effects and the underlying processes of change, patients who had changes in their drinking status in the past 12 months (Recent Changers) were compared to those who were abstinent for the past 12 months (Abstainers).This NIAAA-funded study sample was drawn from a large-scale, multi-site RCT for the treatment of alcohol dependence (COMBINE). Using a quantitative, self-administered questionnaire, patients were categorized as either recent changers or abstinent in the past 12 months. Using qualitative data from telephone interviews, patients (n=61) were compared on measures of drinking patterns and processes of change at 5- to 9-year follow-up. Among Abstainers, periods of sobriety lasted 1.5 to 10 years, an average of 6.5 years of continuous sobriety. Binge drinking in the past year was reported in 92% of the Recent Changers group. Participation in Alcoholics Anonymous (AA) was reported 5 times more often by Abstainers compared to Recent Changers (44% vs. 8%). Getting social support from family/friends was reported by 25% of Abstainers compared to none of the Recent Changers. Compared to the Recent Changers, Abstainers were 2–3 times more likely to have ever had alcohol-related legal problems (60% vs. 22%) and problems at work or school (84% vs. 33%). Abstainers also appeared twice as likely to be able to pinpoint and articulate the moment of clarity in which they experienced a significant increase in their desire to cut down on their alcohol use or to achieve sobriety (e.g., the ''ah-ha moment,'' ''turning point'') compared to the Recent Changers (76% vs. 36%). Abstainers were also twice as likely to have multiple episodes of treatment compared to the Recent Changers (48% vs. 25%). Results of this long-term follow-up study suggest patients with 12 or more months of abstinence from alcohol may have different processes of change than those with more recent changes in their drinking status, to include having negative consequences from drinking, participating in formal and informal treatment, and recalling pivotal turning points in their recovery.

0244

THE EFFECTS OF COUNSELOR CHARACTERISTICS ON WITHIN-SESSION PROCESSES AND OUTCOMES IN A BRIEF MOTIVATIONAL INTERVENTION FOR HEAVY DRINKING

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This study aims at better understanding the mechanisms of alcohol brief motivational interventions (BMI) by investigating the influence of counselors' individual characteristics and within-session behaviors.
The sample included 216 young men screened as heavy drinkers and randomly selected to receive a single BMI conducted by one of 18 counselors performing 12 BMIs each. Counselors were selected to maximize differences in several of their characteristics (e.g. background and training, clinical and MI experience). We tested the links between counselors' individual characteristics, counselors within-session behaviors (measured as the frequency of MI-consistent [MICO] and MI-inconsistent [MIIN] behaviors), and alcohol use outcomes at 3-month follow-up using regression analyses.
In relation to alcohol outcomes, experience in the field of addiction was significantly associated with less frequent binge drinking episodes. The extent to which the counselors viewed themselves as trained to conduct BMI and effective in doing so was significantly related to less drinking days at follow-up. No counselor personal characteristics predicted change in drinks per drinking days or in number of alcohol related negative consequences. Counselors' personal characteristics were strongly related to within-session MI behaviors. More MICO skill was related to counselors being women, psychologists (vs. physicians), trained in MI, having more clinical and addiction experience, viewing themselves as more trained and more effective in BMI, and believing in BMI effectiveness. More MIIN behavior was related to counselors being older, physicians (vs. psychologists), and having more clinical experience, whereas less MIIN was related to counselors having more experience in the addiction field, being trained in MI, and believing more in BMI effectiveness. Counselors' within-sessions behaviors did not significantly predict alcohol or consequence outcomes. Counselor addiction experience and attitudes toward BMI were associated with change in alcohol use at 3 month follow-up. This influence, however, does not appear to be transmitted through within-session MI-behaviors, even if counselor characteristics were strongly related to counselor within-session behaviors. More research is needed to understand counselor influence on BMI outcomes, using more complex analyses, and integrating client personal characteristics and within-session behaviors as potential mediators and/or moderators.

0245

PREDICTIORS AND THREE-YEAR DRINKING OUTCOMES OF CONTINUED TREATMENT AMONG INDIVIDUALS IN REMISSION FROM ALCOHOL DEPENDENCE

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Background: While the effect of treatment on remitting from alcohol problems has been well established, less is known about the effects of continued treatment among individuals who are already in remission, specifically in regard to predictors of continued treatment and subsequent relapse rates.
Methods: Data are from Waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). The sample was restricted to persons in remission from alcohol dependence, with 2,574 individuals identified meeting DSM-IV criteria for alcohol dependence at some time prior to, but not within the last 12 months at the Wave 1 (baseline) interview. These baseline remitted individuals were divided into three groups: those who never went to treatment (natural remission, N=1,888), those been to treatment prior to, but not within the last 12 months at Wave 1 (prior-treatment remission, N=473) and those been to treatment both prior to and within the last 12 months (continued-treatment remission, N=273).
Results: Structural equation models showed severity of prior lifetime alcohol problems was the most important predictor of treatment vs. natural remission and among treatment remission, continued-treatment vs. prior-treatment. The prevailing current treatment type for continued treatment seekers was AA, attended by 87% of the group, followed by counseling from a physician/psychiatrist (20%). Baseline remitted individuals undergoing continued treatment were more likely to be abstainers during the 3-year period following Wave 1 (68%) compared to the prior-treatment (39%) and natural remitted group (20%). However, among those who drank during this follow-up period, continued treatment individuals were more likely to become alcohol dependent and engaged in risky drinking compared to the other two groups. Conclusions: The study findings suggest that individuals with a history of severe alcohol problems are more apt to seek, and benefit from, continued treatment. Moreover, abstention may be the best strategy for avoiding future risky drinking and dependence for this group with severe prior problems. (Supported by grant R01 AA017197 from NIAAA)

0246

TRANSTHEORETICAL MODEL CONSTRUCT PROFILES OF WOMEN WHO REDUCED ALCOHOL CONSUMPTION IN PROJECT CHOICES: ROADMAP TO SUCCESS

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The Transtheoretical Model of Change (TTM) provides researchers and clinicians with a heuristic for understanding a process of intentional behavior change. The model's constructs can provide indicators of an individual's progression from problem recognition and contemplation, through preparation and commitment, to observable changes in a target behavior. The TTM constructs predict outcomes (Carbonari & DiClemente, 2000) and explain the mechanisms through which interventions work to facilitate behavior change (Pinto, Marcus, DePue, Goldstein, 2001; Stotts, DeLaune, Schmitz, & Grabowski 2004). TTM profiles can provide clinicians a guide to target interventions to an individual's status of change as indicated by his/her level of motivational readiness to change, decisional considerations, self-efficacy and temptation, and the use of the experiential and behavioral processes of change (Velasquez, Maurer-Gaddy, Crouch, & DiClemente, 2001). The current study used data from Project CHOICES Efficacy Trial, a multisite study to test an intervention for the prevention of alcohol-exposed pregnancy. A Profile Analysis was conducted to compare TTM construct profiles of women at the 3month post-treatment assessment who reduced their drinking to below risk levels (less than 5 drinks a day and less than 8 drinks per week) and women who continued to drink at risk levels at 9 months post treatment. The TTM construct profiles in the current study consisted of the women's reported use of the experiential and behavioral processes, pros and cons for changing the drinking behavior to below risk levels, and the situational confidence and temptation associated with changing their drinking. There was a significant parallelism effect ($p<.001$) and levels effect ($p=.024$). Each of the TTM constructs in the post-treatment profile was significantly different for the women who successfully reduced their drinking at 9 months versus those who did not. Women who successfully reduced their alcohol use had greater reported use of the experiential ($p<.001$) and behavioral processes ($p<.001$), greater pros ($p<.001$) and lower cons ($p=.012$) for changing drinking, greater confidence ($p=.030$) and lower temptation ($p<.001$) than women who continued to drink at risk levels at 9 months. Clinicians can use TTM construct profiles to provide targeted interventions to improve the probability of an individual achieving successful change in alcohol behavior.

0247

TOBACCO TREATMENT EFFECTS ON LONG-TERM ABSTINENCE FROM ALCOHOL AND ILLICIT DRUGS: A META-ANALYSIS

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This update of a 2004 meta-analysis (Prochaska, Delucchi, Hall, JCCP) examined tobacco treatment effects on long-term abstinence from alcohol and illicit drugs. Fifteen new studies were identified for a total of 34 randomized controlled trials meeting review criteria; 28 of the 34 trials were conducted with participants with alcohol use disorders.
Two individuals independently and systematically reviewed the studies with one reviewer blinded to authorship, affiliation, funding source, and journal. Smoking and alcohol/drug use outcomes at posttreatment and long-term follow-up ($\geq$ 6 months) were abstracted and summarized with a random effects model.
Intervention effects for smoking cessation were significant at posttreatment and comparable for participants in addictions treatment (Relative Risk [RR]=1.73, 95% CI 1.19, 2.53, I2=2.46) and recovery (RR=1.54, 95% CI 1.21, 1.96, I2=0), but not significant at long-term follow-up. Posttreatment tobacco effects were strong both for cessation pharmacotherapy (RR=1.59, 95% CI 1.23, 2.06, I2=5.80) and behavioral interventions without medication (RR=2.02, 95% CI 0.88, 4.67, I2=14.81). Posttreatment tobacco effects were stronger for participants with alcohol use disorders (RR=1.70, 95% CI 1.31, 2.20, I2=4.95), than participants with illicit drug use disorders (RR=1.22, 95% CI 0.55, 2.71, I2=9.73).
Tobacco treatment effect on long-term abstinence from alcohol/illicit drugs was significant for studies published prior to 2004 (RR=1.25, 95% CI 1.07, 1.46, I2=0), but not for studies published more recently (RR=0.88, 95% CI 0.75, 1.03, I2=9.19). Behavioral treatments alone demonstrated a positive effect on long-term sobriety (RR=1.41, 95% CI 1.17, 1.71, I2=0), while the use of cessation pharmacotherapy did not (RR=0.89, 95% CI 0.79, 1.10, I2=0).
This meta-analysis of tobacco treatment in smokers with co-occurring addictive disorders indicates significant short-term smoking cessation effects that are not maintained long-term. Most interventions targeted tobacco separately from other substances. In terms of future directions, investigation of more extended tobacco treatment integrated within alcohol and drug treatment services appears warranted. The effect of tobacco treatment on sobriety also needs further study, especially the potentially moderating effects of cessation pharmacotherapy.
Supported by the California Tobacco-Related Disease Research Program (No. 17RT-0077) and the National Institute on Drug Abuse (P50 DA09253)

0248

WITHDRAWN

0249

PREDICTORS OF FIRST ENTRY INTO TREATMENT IN A LONGITUDINAL HIGH-RISK SAMPLE

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Factors influencing initial treatment entry can provide important information about potential early intervention strategies, yet limited information exists about such predictors for individuals with hazardous alcohol and/or drug use or a substance use disorder (SUD) diagnosis. Short term prospective studies suggest that treatment is more likely utilized by men and by those with lower income, with more psychopathology and less social capital. However, a large number of social factors, and other potential influences associated with alcohol problems have yet to be examined. The present study attempts to identify factors present prior to first treatment entry (either formal treatment or self-help), that predict who among risky drinkers seeks out treatment. Data are from the Michigan Longitudinal Study, a prospective study of families at high-risk for SUDs and matched controls. The sample included 489 (135 women; 354 men) participants who indicated "at-risk" drinking as defined by NIAAA criteria (for men, this involved consuming 5 or more drinks on any day or 14/week; for women, this involved consuming 4 or more drinks on any day or 7/ week) at any assessment point spanning eleven years. Seventeen percent of the at-risk drinkers sought treatment, with the first treatment episode occurring between ages 15 and 27 years (M = 20 years). Correlational analyses indicated that lower IQ, greater externalizing behavior in earlier life, greater peer substance use, more positive alcohol expectancies, and higher self and parent lifetime alcohol problems all predicted treatment entry. Binary logistic regression analysis was used to predict first treatment entry from significant associated predictors assessed at time-points prior to treatment initiation. Results showed that higher rates of peer substance use and greater parent lifetime alcohol use disorder scores were predictive of at-risk drinker's first treatment entry. Findings are informative for early screening and intervention strategies for at-risk drinkers who might benefit from treatment, including focusing on peer influences as a method for encouraging treatment seeking. Further, results suggest that at-risk drinkers with parents who exhibit less severe alcohol problems may be less likely to initiate treatment, even when it might be beneficial. Thus, intervention strategies should not be limited to at-risk drinkers with a positive family history of alcoholism. (Support: R37 AA0706: RA Zucker; T32 DA007267: M Gnegy)

0250

TREATMENT SETTINGS FOR ALCOHOLICS: A PARTIAL REPLICATION IN A COMMUNITY SETTING

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The purpose of this study was to replicate and extend, to a community setting, previous work conducted in a tightly controlled clinical research environment. The prior study found that (a) individuals with more severe alcohol problems benefitted more from inpatient than outpatient care relative to those with a less severe problem, and (b) those with lower cognitive functioning also benefited more from inpatient than outpatient treatment. To test the replicability of these findings in a real-world treatment environment, 176 individuals presenting with alcohol problems in the outpatient and detoxification units of a large, community-based treatment program were randomly assigned within Inpatient Need Group (i.e., Need for Inpatient versus No Need for Inpatient) to either inpatient or outpatient care. Need group cut-points were derived in the prior study. Clients assigned to inpatient were scheduled for 21-days of inpatient care, followed by up to 24 outpatient sessions over a 6-month aftercare. Those assigned to outpatient were allowed up to 30 outpatient sessions across a combined 21-day primary, and 6-month continuing care period. Results indicated that, over an 18-month post-primary care followup, inpatients initially had a significantly higher percentage of days abstinent than outpatients, but this effect dissipated within the first 6 months. However, inpatients, relative to outpatients, consumed a significantly lower amount of alcohol on days in which they did drink, and this did not vary with time. Contrary to the prior findings, problem severity did not moderate treatment effects on percentage of abstinent days. However, severity did moderate effects on alcohol consumption on drinking days. Consistent with the prior work, clients with more severe problems who received inpatient care, relative to outpatient care, drank significantly less alcohol on the days they drank. Cognitive functioning did not moderate treatment effects. Exploratory findings suggest that treatment expectancies also moderated treatment effects. Expectancy was positively associated with percentage of days abstinent in inpatient, but not outpatient care. At high expectancy levels, inpatients had a significantly higher percentage of days abstinent than did outpatients. These preliminary results partially replicate prior findings. Inpatient treatment may be best for clients with more severe alcohol problems, or high expectancies for success in the inpatient setting.

0251

MULTIVARIATE MEDIATIONAL ANALYSES OF DISTAL AND PROXIMAL FACTORS RELATED TO PARTNER VIOLENCE: IMPORTANCE OF CHILDHOOD AGGRESSION HISTORY

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Biopsychosocial developmental models of partner violence emphasize the role of distal developmental as well as proximal factors related to violence risk. This study examined the relationships among distal factors (parental history of alcohol use problems, childhood aggression frequency and conduct problems), and more proximal factors (psychiatric distress, alcohol-, cocaine- and marijuana consequences) and partner violence perpetration (PVP) among a Substance Use Disorder (SUD) treatment sample.
This sample included 193 participants reporting past year violence who were recruited from SUD treatment programs (ages 17–63; 76% female; 49% Caucasian, 37% African American). Baseline assessments included distal [paternal and maternal alcohol misuse, childhood aggression frequency (CAF) and conduct problems] and proximal factors (alcohol-, marijuana- and cocaine- consequences, psychiatric distress) as well as past year PVP. Bivariate correlations were conducted among the study variables. The primary analysis involved multivariate, multiple mediation analyses conducted using Hayes and Preacher's (2011) approach (SPSS MEDIATE macro) in order to examine the relationships among distal and proximal risk factors and PVP. According to correlational analyses, CAF, alcohol consequences and psychiatric distress were associated with partner violence. In the multivariate analysis, among analyses involving only demographics and distal factors, CAF and both maternal and paternal alcohol problems were related to partner violence. Several distal factors also were related to proximal factors (e.g., CAF and conduct problems were related to cocaine consequences and psychiatric distress). However, in the final model accounting for both distal and proximal factors and their inter-relationships, only CAF was related to partner violence perpetration. The findings highlight the relative importance of childhood aggression frequency (CAF) as an indicator of problems with PVP. Although there were bivariate associations between more proximal risk factors and PVP (alcohol consequences, psychiatric distress), CAF was a primary factor related to PVP and also was related to cocaine consequences and psychiatric distress. The findings suggest a need for early identification and intervention for childhood aggression, and have implications for assessment and treatment of individuals in SUD treatment involved with PVP. (Supported by NIDA R01 DA017295 and T32 DA007267)

0252

RELATIONSHIPS BETWEEN SPECIFIC COPING STRATEGIES AND VICTIMIZATION AMONG ALCOHOL AND DRUG USERS IN RESIDENTIAL TREATMENT

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Objective: This study evaluated associations between coping styles, alcohol and drug use, and violence victimization among 322 individuals entering a residential substance use disorder (SUD) treatment program.
Method: At treatment entry, participants completed measures of demographics, alcohol and drug use history, violence victimization by partners and non-partners, and general coping skills. Using scores from a modified Conflict Tactics Scale, participants were categorized into groups based on having either 1) no past year violence victimization, 2) past year violence victimization by a partner, 3) past year violence victimization by a non-partner, or 4) past-year violence victimization by both a partner and a non-partner. Parallel multinomial logistic analyses examined the relationships between demographics (race/ethnicity, gender, age), frequency of alcohol, heroin, cocaine, and marijuana use, and frequency of use of three coping styles (emotion-focused, problem-focused, avoidant) with victimization type.
Results: In multivariate models controlling for demographic characteristics, emotion-focused coping was not associated with violence victimization. However, both problem-focused and avoidant coping were related to the odds of victimization by both partners and non-partners. Specifically, more frequent problem-focused coping was related to decreased odds of victimization whereas more frequent avoidant coping was related to increased odds of victimization.
Conclusions: These findings indicate that among individuals in SUD treatment, use of problem-focused coping strategies (e.g., get help and advice from people) was associated with less frequent victimization by both partners and non-partners, and more frequent avoidant coping (e.g., giving up efforts to cope) was associated with more frequent victimization from both partners and non-partners. With the cross sectional design of the present study, it is not possible to infer the causal relationships between coping styles and victimization. Nevertheless, the findings suggest a need for additional longitudinal research to better understand the inter-relationships over time between coping and victimization.

0253

ATTRITION IN DRUG COURT RESEARCH: EXAMINING PARTICIPANT CHARACTERISTICS AND RECOMMENDATIONS FOR FOLLOW-UP

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Drug court research has gained considerable momentum over the past 20 years. Although some of the empirical literature has explored methodology relative to study design and participant recruitment to minimize attrition (e.g., Hagedorn & Willenbring, 2003; Joosen et al. 2005; Mateyoke-Scrivner et al. 2004), less is known about the individual characteristics that predict attrition in drug court settings. The Drug Court Enrollee Study had the primary aim of examining the relationship between psychosocial predictor variables and drug and alcohol use frequency over 3 months. As a first step toward understanding participant attrition, these exploratory analyses examine whether any of the following factors are predictive of study dropout: (1) demographics; (2) alcohol/drug use frequency; (3) treatment history; (4) criminal justice history; and (5) trauma symptoms. Eighty participants were screened for eligibility, 55 participants completed the baseline survey, and 26 participants completed the 3 month follow-up. To be eligible, study participants had to be 18 years of age or older, understand English, and score 6 or higher on either the Alcohol Use Disorders Identification Test (Saunders et.al., 1993) or the Drug Abuse Screening Test (Skinner, 1982). Measures exploring predictive factors included the Quick Drinking Screen (Sobell, et al., 2003), a criminal justice history measure (CALDAR, 2010), the Treatment Services Review (McLellan, et al., 1992), and the Modified PTSD Symptom Scale Self-Report (Resick, et al., 1991). Analyses involved nonparametric tests (i.e., Chi square and Kruskal-Wallis) to examine the differences between groups. For baseline and completer groups, significant differences found across baseline survey measures were systematically entered into logistic regressions predicting study dropout. After listwise deletion, the final model with 3 predictors (n=28) showed that traumatic experience (OR = 54.89, $p < .05$) and symptoms of PTSD (OR = 6.72, $p < .05$) indicated higher likelihoods of dropout. In addition, participants' medical problems trended toward significance as a predictor (OR = 11.86, $p = .07$). Although sample size is a limitation, these results suggest that researchers may consider increasing efforts to engage drug court enrollees in research, especially those with trauma histories and/or symptoms, and perhaps those with significant medical problems.

0254

MODELS OF ADDICTION AND RECOVERY UTILIZED BY ALCOHOL AND DRUG ABUSE TREATMENT PROGRAMS IN MIAMI

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The primary objectives of this study were: 1) to increase knowledge regarding the models of addiction and recovery utilized in AOD (alcohol and other drug) treatment programs; and 2) to better understand the impact of these models on treatment outcomes. Qualitative data were gathered in 2003 at two residential AOD treatment programs in Miami-Dade County. The author (a project researcher) conducted participant observation of each treatment program 3–4 days per week over a period of roughly 2 months. Research activities included observation of all treatment activities and informal interviewing of staff and clients at each facility. Observations and interactions were recorded in the form of ethnographic field notes. Other research team members carried out semi-structured, digitally recorded interviews with the program directors (n=3). All protocols received IRB approval. Program 1 was community-based, and its clients (n=60) were predominantly English-speaking African-American and white men and women. Program 2 was a faith-based, monolingual Spanish program serving Latino men (n=35). Following initial review of field notes and interview transcripts, major themes were identified and the research team constructed a codebook. Next, the team coded study data using NVivo qualitative data analysis software. Thematic analysis revealed three major aspects of addiction/recovery models that were particularly contested within the treatment environments: the "addict" identity, the locus of addiction, and conceptions of a higher power. Study findings are as follows: 1) treatment staff in both programs utilized elements of the disease model of addiction and the spiritual/moral model of addiction; 2) the community-based program relied more heavily on the disease model, while the faith-based program emphasized the spiritual/moral model; 3) rather than passively accepting treatment staff's ideas about addiction and recovery, clients actively negotiated these models with staff and among themselves; 4) mismatch between client and staff ideas regarding addiction and recovery negatively affected some clients' perceptions of their programs. The author concludes that a significant degree of mismatch between clients' and program staff's ideas about addiction and its treatment may present an obstacle to recovery from AOD abuse.

0255

USING MULTIPLE RECRUITING SOURCES TO REACH UNTAPPED SEGMENTS OF THE RECOVERY COMMUNITY IN RESEARCH

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The broad construct of addiction recovery is increasingly guiding substance use services and policy. However, the knowledge base on recovery experiences, definition and paths remains small, hindering service development. Existing studies are localized and often focus on treatment populations that represent only a restricted segment of the recovery community. Preparatory to developing a recovery scale, we used a multi-source recruiting strategy to maximize the diversity of individuals surveyed about their recovery paths and experiences. Recruiting was conducted via general media (e.g, Craig's List: 42%), treatment alumni groups and recovery services (17%) grassroots recovery organizations (e.g., Faces & Voices of Recovery-31%) and word of mouth (10%). Demographics, recovery paths and definitions were examined as a function of recruiting source. The sample represented 27 states from all US regions and was diverse in gender (47% male), age (range: 18 – 65), education (25% HS only, 39% some college, 36% college grads), and residential setting (42% urban, 46% suburban, 12% rural dwellers); 23% were African American, 7% Hispanic. In terms of recovery paths, 70% had gone to both treatment and 12 step, 15% to 12-step only, 3% treatment only, and 12% reported neither. Key differences were observed across recruiting sources in terms of (a) Demographics including race (e.g., more non-whites recruited through grassroots organizations) and age (e.g., greater percentage of persons <35 recruited through media); (b) Recovery paths- e.g., 79% of those who reported neither treatment nor 12-step (a rarely tapped recovery segment) were media recruited while 68% of the grassroots-recruited subjects had gone to both treatment and 12-step; and (c) Recovery definition: Significantly fewer of the media recruited (65%) selected total abstinence from alcohol and drugs as their recovery definition (vs. more moderate goals) than did persons recruited through other sources (85%); 100% of those recruited through alumni organizations/recovery supports selected total abstinence as their definition. Key sample characteristics differ across recruiting sources; in particular, general media recruiting reached an untapped segment of the recovery community; this it represents a cost effective strategy worth incorporating in future recovery studies to maximize the diversity of experiences surveyed. Funded by R01 AA017954

0256

CHARACTERISTICS AND TREATMENT RESPONSE IN ADOLESCENTS WITH AND WITHOUT FAMILY HISTORY OF ALCOHOL AND DRUG USE DISORDER

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Background: Family history (FH+) of alcohol and other drug use disorders (AOD) is associated with a fourfold increased risk for development of these same disorders in offspring but little is known about the characteristics of adolescents treated for AOD who are FH+. Also, there have been mixed findings regarding whether FH+ status influences treatment response and outcome. To inform this clinical area, this study assessed the proportion of patients in outpatient AOD treatment who were FH+, and compared them to FH negative (FH-) on demographic and clinical characteristics, and treatment response and outcomes.
Method: Adolescents (N=127; M age 16.7, range 14–19; 24% female; 87% White) participating in an outpatient treatment effectiveness study were assessed at intake and 3, 6, and 12 months later.
Results: Three quarters (75.6%) were FH+ for AOD. At baseline, there were no differences between FH+ and FH- in demographic variables, or in rates of comorbid conduct, oppositional defiant, attention deficit and hyperactivity, or major depressive, disorders. Groups did not differ either in mean age of first use or regular use of alcohol or marijuana and there were no differences in heavy drinking days (HDD) in the 90 days before intake; FH+ participants, however, reported higher percent days abstinent (PDA; $p< 0.01$). Regarding 12-step participation, FH+ participants reported more lifetime AA meetings at baseline ($p< 0.02$) and more AA meetings ($p< 0.02$) and NA meetings ($p< 0.05$) in the 90 days prior to treatment. With regard to treatment response, the two groups did not differ on PDA and HDD at 3-, 6-, and 12-month follow-up. Also there were no differences for 12-step attendance across the 3 time points, except FH+ attended more NA meetings in the past 6 months at 12-month follow-up ($p< 0.04$).
Conclusions: Consistent with prior clinical studies of AOD heritability, most study participants were FH+. We expected to find between-group differences in age of first use/regular use of alcohol and marijuana since it is more likely that FH+ individuals could be exposed to environmental alcohol/drug cues earlier, or possess genetic vulnerability that may accelerate the transition from initial to regular use. There were no differences between groups on PDA and HDD across follow-up, indicating other bio-behavioral or environmental factors may be more influential. The observed differences in 12-step attendance may be due to FH+ participants having an allied family history of 12-step involvement.

0257

SUSTAINED RECOVERY FROM ALCOHOL USE DISORDERS: FINDINGS FROM THE 30-YEAR FOLLOWUP OF THE SAN DIEGO PROSPECTIVE STUDY

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Many individuals who report problematic drinking early in life recover from their alcohol-related disorders over time. While characteristics that are associated with developing alcohol use disorders (AUDs) have been identified (e.g. family history of alcoholism [FH] and the genetically-influenced low level of response [LR]to alcohol) less is known about which factors measured prior to AUD onset and across adulthood relate to recovery from AUDs.
The current study examined a subsample of 114 probands from the San Diego Prospective Study who met criteria for an AUD (66% were dependent) at the 10-year followup, when the average age was ~31. Followup data collected every 5 years for ~25 years assessed alcohol use behaviors and problems as well as demographics and other relevant risk and protective factors. Discrete-time survival analysis (DTSA) was used to first evaluate whether premorbid characteristics seen at study entry, such as FH and LR, predicted ''sustained remission'' from AUDs through the 30-year followup (average age ~52 years). We then examined the association of time-varying covariates (i.e. marital/parental status; treatment) to remission. 43% of this sample met criteria for sustained remission at the age ~ 50 follow-up, about half of whom remitted at the first assessment (at ~ age 35) following initial diagnosis (10-year). 65% reported using AA at least once and 61% received treatment for alcohol-related problems; those with sustained recovery reported similar rates of ever using AA and formal treatment to those who had not recovered. Results from the DTSA showed that having less educated parents (B= -.19, p<.01), lower drinking frequency (B= -.41, p<.001), and having a child (B= .21, p=.06) at baseline predicted sustained remission from AUD. Having formal treatment for alcohol problems was positively related to remission at the ~age 30 follow-up (B=.16, p<.05) but was negatively related to remission at the ~age 50 follow-up (B=-.90, p<.001). Involvement in AA was unrelated to remission, as was marital and parental status across time.
Overall, these findings provide preliminary evidence for both premorbid and time-specific characteristics that relate to sustained remission from AUDs using data from a 30 year longitudinal study.

0258

THE RELATIONSHIP BETWEEN ALCOHOL PROBLEM RECOGNITION AND THE COURSE OF ALCOHOL RELATED DIFFICULTIES

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Some existing qualitative studies have found that recognition of alcohol problems precedes reductions in alcohol related difficulties. However, it is unclear what self-reported problem recognition reflects. If problem recognition reflects insight and motivation to change, endorsement of problem recognition may predict lower levels of alcohol-related difficulties. On the other hand, if problem recognition reflects non-ignorable problem severity or is an epiphenomenal aspect of problems, endorsement of problem recognition may predict higher levels of future alcohol-related difficulties. We analyzed prospective data from a community sample assessing 489 college freshmen who were followed from ages 18 to 34, half of which had familial history of alcohol use disorder. Multinomial logistic regression was performed to predict level of alcohol-related difficulties at ages 19, 20, 21, 24, 29, and 35 from the presence or absence of problem recognition at the previous wave. Our findings indicate that compared to individuals who did not endorse problem recognition, individuals who reported problem recognition had an increased probability of having higher levels of difficulties at the subsequent wave. After adjusting for concurrent alcohol related difficulties, problem recognition was no longer a significant predictor of higher levels of alcohol related difficulties at ages 18, 19, and 29 but remained a significant predictor at ages 20, 21, and 24. These findings suggest that problem recognition may be an indicator of more severe alcohol-related difficulties, that does not appear to presage a resolution of alcohol-related difficulties.
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0259

EVALUATION OF AN ATTENTIONAL TRAINING TASK WITH HEAVY DRINKING UNIVERSITY STUDENTS

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Research has suggested that attentional bias to drug-related stimuli – an automatic process in which one's attention is captured and held by substance-related stimuli – contributes to the development and maintenance of substance use. Therefore, interventions designed to reduce attentional bias may help decrease the likelihood of heavy drinking. Studies have found that multiple-session attentional training tasks, in which participants repeatedly practice directing their attention away from alcohol-related stimuli, were effective in reducing attentional bias. Although inexpensive, practical, and acceptable to young drinkers, the impact of single-session attentional training has had only limited impact on attentional bias and craving. Therefore, the current study was designed to examine the effects of a novel, single-session attentional training task on attentional bias, craving, and preference for alcoholic beverages. Following assessment of attentional bias using the dot probe task, 60 heavy-drinking university students were randomly assigned to one of three training conditions during which they practiced breaking their attention from single photographs representing each of the following central stimuli: (1) alcohol-related photographs, (2) nonalcoholic beverage-related photographs, or (3) irrelevant symbols. Following training, participants received a post-training dot probe, a battery of questionnaires, and a preference task in which they were asked whether they would take home an alcoholic or nonalcoholic beverage if given the opportunity to do so. Contrary to expectations, attentional training did not produce significant differences in attentional bias among the three conditions. In addition, there were no significant differences among the conditions in subjective craving, nor were there differences in the proportion of participants who preferred to take home an alcoholic beverage following participation. These findings are consistent with previous studies that have employed other single-session attentional training tasks. There are several potential explanations for the limited impact of the training in the present study: (a) a relatively small number of training trials, (b) the use of a non-clinical sample, (c) unintentional alcohol-related cue exposure in the alcohol photo condition, and (d) the complexity of the alcohol-related photos during training.

11. EPIDEMIOLOGY

0260

SPATIAL PATTERNS OF DRINKING IN MANDATED COLLEGE STUDENTS

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College student drinking is a significant and prevalent issue and is associated with both short and long-term health and behavioral consequences. In an effort to reduce negative consequences from underage drinking, universities have begun citing students who violate school alcohol policies. These alcohol citations include, but are not limited to, possession of alcohol, being in the presence of alcohol, behavioral problems while intoxicated, and receiving medical treatment due to intoxication. A number of environmental factors are associated with heavy drinking in college students, including alcohol access and price.
This study examined the density of alcohol retailers within a two mile radius of a campus in the Northeast. Alcohol retailers were identified by federal SIC or NAICS codes using ArcGIS, a spatial analysis computer program. Then, retailer addresses were geocoded and plotted onto a map of a 2 mile radius around the university. Participants were drawn from 364 students who were referred to the campus counseling center as a result of alcohol or drug use policy violation. Students filled out an ''event description'' form detailing the specifics of their citation. Spatial data such as names of residence halls, on-campus buildings, off-campus locations, and liquor stores were collected from these forms. Students did not consistently identify specific locations which resulted in incomplete data. Only students who identified an initial drinking location and location of their write-up were included in the spatial-analysis. Chi-Square analyses were run on both the location where students began drinking and location where write-up occurred. Findings indicated that low alcohol density off-campus with high on-campus drinking suggests that limited access to alcohol off-campus may contribute to high consumption on campus. Additionally, particular dorms had higher rates of alcohol consumption than others, and students rarely described staying in one location for their drinking. Rather, they traveled between rooms within dorms, between dorms, and in and out of the campus. Some of the more colorful locations students report drinking include: the library, on the campus shuttle, and outside in the woods. Examining the spatial data provided by the students provided a more in depth and descriptive picture of on campus drinking, and these findings are discussed in the context of campus and environmental prevention efforts.

0261

GENDER DIFFERENCES IN COLLEGE STUDENT ADHERENCE TO NIAAA DAILY AND WEEKLY DRINKING GUIDELINES

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Objective: The NIAAA drinking guidelines set limits for both daily and weekly amounts of alcohol consumption. Although these guidelines are gender-specific, the ratio for daily and weekly limits varies considerably (i.e., 4:3 vs. 14:7). It is unclear how well college student drinkers adhere to these guidelines, or if their drinking is in line with the widening gap between gender-specific guidelines for daily vs. weekly drinking.
Method: This study used a daily-level, academic-year-long, multi-site sample to describe adherence to NIAAA daily and weekly drinking guidelines in first year college students. Three cohorts of first-year college students (n=992; 58% female) reported daily drinking on a biweekly basis using web-based surveys throughout their first year of college (18 biweekly reports in total).
Results: Across the year, 65.6% of males and 66.3% of females exceeded NIAAA drinking guidelines at least once. Women exceed daily limits equally frequently as men (65.5% vs. 65.6%), but more commonly exceed weekly limits (55.6% vs. 47.2%). Similarly, in any given week, a smaller proportion of females (0.29 [0.26–0.31]) exceeded daily limits than males (0.32 [0.28–0.35]), while a larger proportion exceeded weekly limits (0.21 [0.18–0.32] vs. 0.16 [0.13–0.18]). In a GEE analysis across all 18 weeks, which controlled for race, age, school, age at first drink, drinking intentions (daily and weekly) and time as covariates, females were 1.68 [1.24–2.29] times as likely to exceed weekly NIAAA guidelines compared to males. Gender differences in exceeding daily limits were not significant.
Conclusions: These findings show that female college students are at greater risk of exceeding NIAAA recommended weekly drinking limits than their male counterparts. Typical college student drinking interventions (e.g., including norms perception, motivational interviewing and educational approaches) do not typically educate students about weekly drinking limits. The observed disparity in risk for long-term health consequences may represent a missed opportunity for education and intervention.

0262

ALCOHOL EXPERIMENTS IN THE FIELD: THE HIGH ECOLOGICAL SURVEY OF RISKY BEHAVIOR

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The research examined the feasibility of a new methodology¯the High Ecological Validity Survey of Risky Behavior (HEVSORB)¯for conducting field experiments in real-world drinking environments. The method adapts portal surveys, typically conducted at the entrances to drinking environments, to college campuses. A sample of people walking on campus on weekend nights (often going to drinking locations) is recruited. Participants are interviewed and breathalyzed and can be randomly assigned to receive a brief informational or motivational intervention. The same participants later are resampled and re-breathalyzed for the 'exit' portion of the survey. Significant differences in exit breath-alcohol concentrations (BrACs) between conditions can be attributed to the experimental manipulations. Importantly, the method allows researchers to test whether theorized causal relationships persist in natural drinking environments.The current feasibility study (n=736) had a 61.4% return rate for the exit part of the survey. However, return rates varied significantly as a function of the incentive given, ranging from 79.5% to 36.9%. Return rates also differed significantly as a function of race and whether participants were fraternity members, lived on campus, or consumed alcohol earlier in the evening. A total of 37.9% of participants tested positive for alcohol during the initial breath test (mean BrAC = .022) while 49.5% tested positive at exit (mean BrAC = .035). Of those who consumed alcohol the mean exit BrAC was .076. Participant BrACs varied significantly as a function of the location on campus where participants were recruited.This feasibility study used a version of the *Safe Nights* intervention (Kelley-Baker et al., 2012) to demonstrate the brief interventions could be administered and evaluated using the HEVSORB. The intervention included providing some participant groups with information on strategies to stay safe while at parties and bars (e.g., walking in well-lit areas, staying with your group, etc.), and we measured participants' negative experiences during the exit interview. Participants who received the intervention were significantly less likely to report experiencing aggression or hostility towards them, and had marginally lower exit BrACs.The research suggests that the HEVSORB is a feasible method for administering individual/group interventions to students and evaluating their impact on alcohol consumption and other behaviors.

0263

PREGAMING IN ENTERING COLLEGE FRESHMEN

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Research has identified pregaming, the practice of drinking before going out for an occasion where alcohol may or may not be served, as a common high-risk drinking behavior among college students with as many as 85% of college drinkers engaging in this practice. Pregaming has also been reported in high school students, but at lower prevalence, and it is unclear if pregaming escalates upon college entry or during the transition between high school and college. This study examined pregaming during this transition and determined whether this behavior represents a unique risk for problematic use above-and-beyond traditional measures of consumption (i.e., quantity/frequency: QFV, and heavy episodic drinking: HED). An additional objective was to identify characteristics of entering students who pregame based on risk factors identified in prior high school and college pregaming studies. Data were collected from entering freshmen during orientation activities across three years (2008–2010). Students with prior alcohol use (N=1250) completed a questionnaire assessing drinking in the three months prior to starting college including: overall use (quantity, frequency), HED incidence in past two weeks, pregaming (quantity, frequency), drinking game participation, alcohol-related problems and expectancies as measured by the Alcohol Expectancy Inventory (AEI). Analyses indicated that 64% of the sample and averaged three drinks in 27 minutes (mean BAC =.09). Regression analyses revealed that overall drinking (QFV) and demographic risk factors (e.g., gender, ethnicity, and Greek affiliation) explained 34% of the variance in overall problems; however, pregaming frequency explained an additional 6.0% of variance in problems above-and-beyond overall use and demographics (Overall R^2=.40). A separate analysis identified seven characteristics associated with pregaming frequency during this developmental transition including demographics (gender, ethnicity, Greek affiliation), heavy drinking, drinking game frequency, and two scales of the AEI (Attractive, and Egotistical) (all p<.01). Findings revealed that pregaming appears to escalate in the transition to college, and that this practice contributes additive risk in problematic use in this population. This study highlights the importance of assessing high risk drinking styles in college students as well as the need for additional studies examining pregaming trajectories across the freshman year and throughout college.

0264

CO-OCCURRING BINGE DRINKING AND EATING BEHAVIORS

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PURPOSE: The purpose of this study was to investigate binge drinking and binge eating behaviors in college students who report these activities and to identify potential covariates, behavioral triggers, and modifiable targets for intervention.
METHODS: A web-based survey was conducted (12/11), using both closed and open-ended questions to seek detailed information on student's drinking and eating behaviors. Binge drinking was defined as having drunk 4 or more alcoholic beverages (women) or 5 or more (men) alcoholic beverages in a 2-hour period. Binge eating was defined as eating in a discrete period of time, any amount of food that is definitely greater than most people eat in a similar period of time (e.g. within a 2 hour period) while feeling a loss of control regarding what you are eating or how much you are eating. Descriptive analyses were conducted to describe the sample and major study variables. Content analysis was used to interpret the qualitative data.
RESULTS: The sample was restricted to undergraduate students (N=113) whose mean age was 19.76 yrs (S.D.=1.17). The sample was predominately Caucasian (88.6%) and 65% female. Alcohol use was common (86%), while 63% of female students and 66% of male students endorsed binge drinking (BD) behaviors. Binge eating (BE) was reported by nearly a quarter (24.7%) of students and co-occurring behaviors were reported by 16% of the sample. No significant gender differences were noted in rates of binge drinking ($\chi 2$=0.07; p≤0.79), binge eating ($\chi 2$= 1.29; p ≤0.26) or co-occurring behaviors ($\chi 2$=0.57; p≤0.45). Nearly half of binge eaters (47.8%) reported that their BE episodes were related to alcohol or drug use. Content analysis revealed that binge drinking episodes were frequently associated with social activities (e.g., parties, football games) and that binge eating episodes were more likely associated with stressful events, boredom, or holiday celebrations. For co-occurring behaviors, binge eating frequently followed binge drinking episodes.
CONCLUSIONS: The results of this study extend previous findings regarding binge drinking and binge eating behaviors in college students, highlight potential prevention and early intervention strategies, and identify potential targets for intervention development. Additional cycles of enrollment in 2/12 will permit analysis of predictors of co-occurrence.
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0265

PATTERNS OF USE AND MOTIVATIONS FOR CO-INGESTION OF ALCOHOL MIXED WITH ENERGY DRINKS

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Use of alcohol mixed with energy drinks (AmED) is an increasingly prevalent trend causing concern due to potential increased alcohol consumption and engagement in risk-behaviour post-ingestion. While the majority of research has been focused on AmED use outcomes, there is a current paucity of data on the patterns of AmED use and motives for consumption, particularly beyond a regional college student sample. Consequently, the aim of the present study was to establish the consumption patterns and motivations for AmED use in a sample of AmED users drawn from the general population. Four-hundred and three Australians (*n*=244 females) aged between 18 and 35 who had consumed alcohol mixed simultaneously with energy drinks in the preceding six months completed a 10–30 minute online survey about their use of energy drinks, alcohol, and AmED. While AmED sessions reportedly occurred relatively infrequently compared to alcohol sessions, the quantity of alcohol consumed in AmED sessions was significantly greater than that ingested in alcohol sessions. Dominant drink preferences were evident for AmED sessions, with participants identifying alcohol spirits (particularly vodka) and Red Bull as their respective alcohol and ED mixers of choice. Reports of AmED use context indicated that participants typically consumed AmED whilst engaging in heavy drinking sessions in public venues (i.e., nightclubs, bars, pubs). The combined taste, functional outcomes (i.e., increased energy, ability to stay out later), and situational context of use (i.e., peer drink preferences, drink availability and price) were primary AmED use motives for over half the sample, with motivations related to novelty/impulsivity, interactive alcohol and ED effects, and increased sociability and positive mood demonstrating more equivocal endorsement. Thus, it appears that AmED users may be co-ingesting in a context and at a quantity which enhances the possibility of risky alcohol outcomes, despite users predominantly consuming AmED for the taste and increased energy.

0266

EXAMINING TRANSTHEORETICAL MODEL VARIABLES AND PATTERNS OF THURSDAY DRINKING ACROSS AN ACADEMIC SEMESTER AMONG COLLEGE WOMEN

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A common intervention model for substance abuse is the Transtheoretical Model (TTM) that suggests that there are levels of readiness to change one's substance abuse. College student alcohol consumption remains a problem on college campuses despite current prevention/intervention efforts as many students report that they are not ready to change their behavior. As a result of high-risk drinking, college students experience a variety of alcohol-related problems. Drinking patterns among college students vary according to calendar events (e.g. days of the week or week in the semester). Traditionally, researchers have examined drinking across the week (Monday through Sunday) on the weekends (Friday and Saturday) or on a weekday (Monday through Thursday). However, many students report treating Thursday as the start of the "weekend." The purpose of the current project was to identify subgroups of female college students that are characterized by the presence or absence of Thursday drinking across the fall semester and to examine these subgroups with respect to TTM variables. Female undergraduates (n=424) were recruited for a 10-week study. Over 93% of the sample reported consuming alcohol previously. A series of repeated measures latent class analyses were computed and determined that three latent classes provided optimal fit to the data. The three classes (1. *Unlikely* to report Thursday drinking; 2. *Irregular* Thursday drinking; and 3. *Regular* Thursday drinking) were first compared across year in school. Among the four groups (Freshmen, Sophomores, Juniors, Seniors), Seniors were least likely to be in the *Unlikely* group and neither juniors nor seniors were likely to belong to the *Irregular* group. The three latent classes differed across alcohol stage of change. In addition, the more positive feelings towards alcohol endorsed, the less likely the individual was in the *Unlikely* class compared to the *Regular* class. In contrast, the more costs of alcohol endorsed, the more likely the individual belonged to the *Unlikely* class, relative to the *Regular* class. Female students who regularly drink on Thursdays tend to be older and to experience more negative consequences. They are less likely to want to change their drinking behavior, endorse more of the benefits of drinking, and endorse more fewer of the costs of drinking. Female students whose "weekends" start early are high-risk drinkers and might be targeted for future intervention efforts using TTM variables.

0267

FURTHER EXAMINATION OF DELIBERATE INDUCTION OF ALCOHOL TOLERANCE : IS TRAINING FOR INCREASED TOLERANCE ASSOCIATED WITH NEGATIVE ALCOHOL OUTCOMES?

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Heavy alcohol consumption is common on college campuses. Consequences of heavy use include passing out, getting into fights, and legal difficulties. Despite these negative outcomes, college students continue to engage in risky patterns of alcohol use. Among reasons for continued use is reinforcement from peers, such as receiving praise for being able to "hold your liquor." Previous research has found that almost 10% of college students report deliberately training to increase tolerance in order to avoid passing out or to keep up with peers. In addition, these students reported more frequent binge drinking and drinking to intoxication. The current investigation was designed to replicate and extend previous findings by examining the association between tolerance training and alcohol-related problems. In addition, associations between tolerance training and the use of protective behavioral strategies was examined. A cross-sectional survey of 730 life-time drinkers was conducted at a large Midwestern university. Participants were excluded if they chose not to respond to the question assessing whether they had ever trained to improve tolerance for a future drinking occasion ($n = 19$). Of this sample, 5.6% ($n = 41$) reported training to increase their tolerance. Similar to prior studies, participants who endorsed having trained to increase tolerance reported significantly ($p < .001$) greater alcohol related problems than those who reported never training ($M = 12.08$, $SD = 7.96$; $M = 6.84$, $SD = 5.92$, respectively). Further, participants who endorsed tolerance training reported utilizing significantly ($p < .01$) fewer protective behavioral strategies when drinking than participants who had never trained on both the Manner of Drinking ($M = 14.08$, $SD = 5.30$; $M = 18.47$, $SD = 5.83$, respectively) and the Serious Harm Reduction ($M = 13.43$, $SD = 4.12$; $M = 15.55$, $SD = 3.44$, respectively) subscales of the Protective Behavioral Strategies Scale. Results of the current study support previous research and provide further evidence that deliberately training to increase tolerance is an indicator of hazardous drinking behavior. Prevention efforts might aim to challenge beliefs that increased tolerance reduces alcohol-related difficulties.

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0268

MOTIVATIONAL ORIENTATIONS, EFFORTFUL CONTROL AND ALCOHOL USE

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This study examined the relationships between two motivational orientations (i.e., autonomy and controlled orientations) and alcohol use among college students. Individuals higher on autonomy orientation regulate their behavior according to their own interests, goals, and values. Individuals higher on controlled orientation regulate their behavior on the basis of external rewards, directives, and approval. Additionally, the paper examined whether effortful control (the ability to voluntarily inhibit, activate, and change attention and behavior) mediate the relationship between these motivational orientations and alcohol use.

Study participants were 644 undergraduate students (67.2% female; 87.2% Caucasian; mean age=23.58, SD=6.86) who completed a series of online questionnaires as a part of a larger longitudinal study on sleep and substance use. Data were analyzed by structural equation model for zero-inflated count data (i.e., frequency and quantity of drinking) and categorical outcome (i.e., presence of alcohol related problems).

Students with a higher autonomy orientation were more likely than their counterparts to report that they did not drink in the last six months. In contrast, students with a higher controlled orientation were less likely to report that they did not drink. Among those who drank in the last six months, effortful control significantly mediated the effects of autonomy orientation and controlled orientation on frequency and quantity of drinking in the last six months. Autonomy orientation positively predicted effortful control, which was associated with a decrease in the expected frequency and quantity of drinking. In contrast, controlled orientation negatively predicted effortful control, which was associated with an increase in the expected frequency and quantity of drinking.

Intervention and prevention programs on college drinking could incorporate some form of education about strategies for self-control, including strategies for withstanding peer pressure and diverting one's attention to activities unrelated to substance use. Focusing on strategies of self-control may be a useful starting point for a more in-depth discussion about the motivations, values, and psychological needs satisfaction that are associated with drinking and other drug use.

0269

ALCOHOL USE BEHAVIOR MILESTONES AS A FUNCTION OF AGE IN CHILDREN AND ADOLESCENTS

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Progression in involvement with alcohol can be assessed through children's reports of various behavioral milestones. We examined the ages at which children transitioned from abstention into ever sipping/tasting alcohol, ever drinking more than few sips, ever having 3 or more drinks in a row, ever having 5 or more drinks in a row, ever having been drunk, and ever having experienced alcohol problems in two or more areas (family, friends, dates, school, police). Data derive from 14 waves of longitudinal data collected every 6 months as part of the Tween to Teen Project from a sample of 452 children aged 8 or 10 randomly sampled from Allegheny County (PA); 371 (82%) were still involved at Wave 14. Data were reorganized to reflect the child's status on each milestone at each age (in half years) from their baseline age to age 17.5 (or their Wave-14 age). Latent Class Analyses (LCA) were performed using Latent GOLD 4.0 at each of 19 separate ages (mean n = 334.6). Between ages 8.5 and 10.5, the LCA models were under-identified due to invariance on the more intensive statuses, but results suggested two classes, Abstainers and Sippers, with the percentage of Sippers increasing from 38% to 48%. From age 11.0 to age 12.5, 2-class LCA models were identified, again Abstainers and Sippers, and the percent of Sippers increased from 52% to 67%. From age 13.0 to age 17.5, 3 classes were identified consisting of Abstainers, Sippers, and Drinkers. With increasing age, the percent of Abstainers decreased to 20% at age 15.0 and 9% at age 17.5. The character of the Sipper and Drinker classes (as reflected in the conditional probabilities of the indicators) changed with increasing age. Within the Sipper class, the probability of also having had a drink increased from .09 at age 13.5 to .53 by age 17.5, suggesting the class reflects minimal alcohol experience (either sipping or a drink); and its prevalence decreased from 71% at age 13.5 to 62% at age 17.5. With increasing age, the Drinker class reflected more hazardous drinking experience: from age 13.5 to age 15.5, this consisted of 3-4 drinks per occasion and drunkenness (2% to 12% of sample); and from age 16.0 to 17.5, also included 5+ drinks per occasion (14% to 28% of the sample, respectively). These analyses illustrate the utility for describing alcohol progression of examining types of drinking experience at each age rather than reporting mean ages of initiation of various milestones. [Supported by Grant AA-012342.]

0270

ENERGY DRINK AND ALCOHOL USE: IT'S NOT WHAT YOU THINK

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Purpose: Over the past decade, there has been a dramatic increase in the use of caffeinated energy drinks by college students. These drinks are often used with alcohol, and their use has been associated with a host of problem behaviors including increased alcohol use, drug use, risky sexual behavior and other risk-taking behaviors. Like alcohol, perceptions about peer energy drink use may influence individuals' drinking behaviors. Overestimation of the amount of energy drinks used by their peers, may lead to increased use by the students themselves. The current study examined energy drink and alcohol use and perceptions about peer use in male and female college students.
Methods: N=176 students from an urban university were surveyed about their energy drink and alcohol use by using an IRB-approved, anonymous survey.
Results: Participants were young (mean age=22.4 yrs), primarily female (53%), and Caucasian (56%). Men were more likely than women to be energy drink users (38% vs 15%, $p<0.001$) and drank energy drinks more frequently than women (2.9 days/wk vs 2.6 days/wk, NS). Also, men reported drinking more alcohol in an average week than women (6.2 drinks vs 3.6 drinks, NS). Both men and women overestimated the amount of energy drink and alcohol use by their peers, estimating that 97% of women and all men were using energy drinks on a weekly basis, and that men and women were drinking 15.1 drinks/week and 10.0 drinks/week, respectively. A logistic regression analysis showed that gender, race, and perceptions of increased energy drink and alcohol use were independently associated with increased energy drink use.
Conclusions: Both male and female college students grossly overestimated the amount of energy drinks and alcohol that their peers consume. Further, there is a disturbing correlation between perceptions of other's use of energy drinks and alcohol and individual's own caffeinated energy drink use. The data from the current study suggest that interventions incorporating normative data regarding energy drink use, similar to that used in alcohol intervention programs, may be useful to address excessive energy drink use and prevent the associated adverse health behaviors including excessive alcohol use.

0271

ALCOHOL TRAJECTORY ESTIMATION IS SENSITIVE TO MEASUREMENT TIMING IN THE CONTEXT OF GROWTH MIXTURE MODELING

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Growth mixture modeling can be used to discern commonly occurring drinking patterns through the estimation of latent classes. Few studies have investigated the effects of measurement timing or interval on the shapes of the average alcohol trajectories for the latent classes. The timing and interval of the assessments may have important ramifications for the reliability of the latent classes. The current study presents preliminary work on how three variations of measurement timing affected the alcohol trajectories of the latent classes. Data were taken from the National Longitudinal Survey of Youth 1997 cohort. Participants were assessed approximately annually for a total of 12 assessments. Growth mixture modeling was conducted to compare the latent classes that were obtained using all 12 assessments, the first 6 assessments, and the last 6 assessments. In theory, results including the first 6 and last 6 assessments should mirror the results obtained using all 12. Participants for the current analyses were limited to those who were 15 and 16 years old at baseline (n = 2686). The outcome was a logged version of number of alcoholic drinks consumed per month. Models were estimated with an intercept factor, linear slope factor, and quadratic slope factor. When estimating latent classes using all 12 assessments, four latent classes were identified: two increasing classes with different initial levels (low versus moderate) and two decreasing classes with different initial levels (high versus very high). When using only the first 6 assessments, the four latent classes were similar to those found when including all 12 assessments, with the addition of a class that started low then sharply increased in use rather than a high-decreasing class. When using only the last 6 assessments, the four classes exhibited trajectories that were largely divergent from each other: low use, high use, increasing use, and decreasing use. In contrast, when using all 12 assessments, the trajectories of the four latent classes largely converged by the time of the last assessment. These preliminary findings illustrate that the shape of the alcohol trajectories for the latent classes can be substantially altered by the timing of the assessments. Caution should be used in the interpretation of the latent subgroups identified by growth mixture modeling. Additional work will further investigate how assessment interval and timing may affect class estimation. Supported by NIAAA F31AA020164.

0272

THE CLINICAL COURSE OF ALCOHOL USE DISORDERS: USING JOINPOINT ANLYSIS TO AID IN INTERPRETATION OF GROWTH MIXTURE MODELS

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A common method for identifying underlying classes of alcohol consumption over time is growth mixture modeling (GMM). GMM's output regarding trajectory describes it in its entirety for a given class. Joinpoint analyses (JPA) can complement such output by identifying discrete change points in the clinical course of AUD within a latent class.
This study consisted of secondary analysis of drinking outcomes for 558 AUD adults enrolled in a multisite study of AUD relapse (Allen et al., 1996). Alcohol use was measured bimonthly for one year following the initiation of treatment. JPA was used as a post-hoc analytic procedure following GMM analyses to identify latent classes of individuals' drinks per drinking day (DDD) and percent days abstinent (PDA), controlling for baseline drinking and gender. The best fitting GMM model for DDD had 4 latent classes: extremely heavy drinkers (EHD), improvers (Imp), stable heavy drinkers (SHD), stable light drinkers (SLD), and for PDA had 3 latent classes: stable occasional drinkers (SOD), slightly decreasing frequency drinkers (SDFD), greatly decreasing frequency drinkers (GDFD). The JPA provided the number of change points for each latent class as well as separate linear regression parameters for each segment of the total trajectory. For the DDD classes, EHD began drinking 13.13 DDD and increased to 46.02 DDD by month 3 (b = 15.85) then decreased to 24.77 DDD by month 12 (b = -2.38), Imp began drinking 32.61 DDD and decreased to 6.48 DDD by month 6 (b = -5.06) then increased to 11.46 DDD by month 12 (b = .70), the SHD began at 12.30 DDD and decreased to 9.22 DDD by month 12 (b = -.37), and the SLD began at .90 DDD, increased to 4.25 DDD by month 6 (b = .71), then decreased to 3.83 by month 12 (b = -.10). For the PDA classes, SOD began with 98.41 PDA, decreased to 90.63 PDA by month 3 (b = -4.02), continued to decrease more slowly to 86.50 PDA by month 6 (b = -1.38), and then decreased even more slowly to 85.16 PDA by month 12 (b = -.14), SDFD began with 59.98 PDA and increased steadily to 71.86 PDA by month 12 (b = 1.50), and GDFD began with 13.17 PDA, increased to 51.61 PDA by month 7 (b = 6.44), decreased to 39.49 PDA by month 10 (b = -3.78), and then increased to 50.41 PDA by month 12 (b = 5.42).
The results of this study show that the most common change points in this sample were 3 and 6 months post treatment. Future studies should address determinants of such change points and their implications for treatment.

0273

TEMPORAL TRENDS IN ECONOMIC INDICATORS, ALCOHOL SALES, AND DRINKING PATTERNS

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Purpose: To describe trends in economic indicators, alcohol sales, and survey-based measures of drinking, heavy drinking and alcohol problems for the US through 2010.
Methods: Unemployment data are from the Bureau of Labor Statistics. Housing price data are from the Federal Housing Finance Agency. Alcohol sales trends are based on data from the AEDS, Nielsen and industry trade groups. The National Alcohol Survey (NAS) includes 7 cross-sectional samples of the US conducted between 1979 and 2010 with reasonable similarity. Changes in alcohol volume, heavy drinking days and problems were evaluated across survey waves using adjusted Wald F-test statistics.
Results: The recent economic recession involved large declines in housing prices and increases in unemployment starting in 2008. For example, housing price declines began in early 2007 and continued through 2008 before stabilizing. In contrast to previous recessions, the number of long-term unemployed doubled in the last 7 months of 2008 and then doubled again in 2009. Long-term sales data show that US per capita alcohol consumption peaked around 1980, subsequently falling 25% by 1993 and then rising slowly each year thereafter through 2008. The most recent data from 2009 shows a small decrease. Recent trends differ by beverage type, with declining beer and increasing per capita consumption of wine and spirits. Data on alcohol expenditures indicate that quality downgrading occurred in 2009 for spirits and in both 2008 and 2009 for wine, illustrating that the recession also impacted wine and spirits purchasing. Focusing on the changes from 2005 to 2010 in the NAS, results for current drinkers indicate a significant overall increase in alcohol volume, heavy drinking days and alcohol-related consequences corresponding with measurements occurring before and after the recession. Age-group specific analyses show that these recent increases were driven primarily by respondents aged 26–40 in 2010. Long-term trends in the NAS indicate that the mean number of 8+ days among current drinkers in 2010 was similar to the mean in 1984 and significantly higher than the means in 1990, 1995 and 2005.
Conclusion: Aggregate data suggest that the recession has reduced beer sales and expenditures per drink. However wine and spirits sales have continued to increase. Examination of longer-term survey trends suggests that rates of heavy occasion drinking among drinkers may have returned to historic highs from the early 1980's.

0274

A PROSPECTIVE STUDY OF THE RELATIONSHIP AMONG SOCIAL NETWORK MEMBERS OF THEIR FREQUENCY OF ALCOHOL CONSUMPTION

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There is substantial debate over role of social networks in influencing alcohol consumption. There is clear evidence of differential affiliation among heavy drinkers. some studies report that specific network members may influence the level of alcohol consumption AMONG their members. In the current study, we longitudinal examine whether frequency of alcohol use among one network member predicted another network members use 18 months later. Alcohol use was categorized into quartiles. Participants were 325 dyads who were involved in an intervention study of HIV risk behaviors among impoverished inner-city women. 69% reported drinking alcohol in the prior 3 months. Of those who reported drinking alcohol, 32% reported that weekly they had at least 6 drinks per day and 15% reported that they drank 10 or more drinks per day. A three-level random effects proportional odds model examined the association over time among the drinking behaviors among network members. Frequency of alcohol use of partners, kin, and non-kin at baseline was a statistically significant predictor of frequency of use among individuals at the 18-month assessment (OR=1.424, 1.10–1.84). The results of this study suggest that there is significant correlation in drinking patters among network members regardless of their role relationship and suggested the potential utility of network focused interventions to address hazardous drinking.

0275

ECONOMIC LOSS AND ALCOHOL PROBLEMS DURING THE 2008-9 RECESSION: FINDINGS FROM THE NATIONAL ALCOHOL SURVEY

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Purpose: To assess overall associations between economic losses attributed to the recession and alcohol outcomes, and whether these associations vary by gender and age.
Methods: Data are from the 2009–10 National Alcohol Survey (*N*=5,382). Analyses examined various types of economic loss and hardship: loss of retirement savings, reduced work hours or pay, difficulty paying the rent or mortgage, loss of a job, and loss of housing. Outcomes included annual volume of alcohol consumption, monthly drunkenness, 2+ negative drinking consequences, and DSM-IV alcohol dependence symptoms. Multiple linear and logistic regressions were conducted, and interactions assessed. Multivariate models adjusted for demographics, as well as personal history of alcohol-related health problems prior to the recession, and parental history of alcoholism.
Results: More than half of the sample (52%) reported that their household was negatively affected by the recession. The most commonly reported loss was a reduction in working hours or pay (32%), followed by loss of retirement savings (24%), and loss of a job, and trouble paying the rent/mortgage (each reported by 16%). Loss of housing was reported by 3.5% of the sample. In multivariate models, loss of a job and loss of housing were most strongly associated with increased risk for alcohol problems (AORs ranged from 4.23 to 6.04 for housing, and from 2.35 to 2.44 for job loss). Trouble paying the rent or mortgage was also associated with alcohol problems, and reduced work hours/pay was marginally associated with alcohol dependence. Loss of retirement income was positively associated with annual volume but not problems. There were no significant interactions observed by gender or age.
Conclusion: Many Americans were affected by economic losses and hardship during the recession. These findings suggest that policies attempting to mitigate job loss and housing loss, two of the most severe economic impacts of the recession, might also help in the prevention of associated alcohol problems.

0276

ALCOHOL, DRUG USE DISORDERS, AND BORDERLINE PERSONALITY DISORDER IN NESARC: EVIDENCE FOR ENDOGENOUS OPIOID SYSTEM DYSREGULATION

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Borderline Personality Disorder (BPD) may involve a dysregulation of the Endogenous Opioid System (EOS) consisting of chronic low levels of endogenous opioids and hyperactive receptors. This may lead individuals with BPD to engage in behaviors that activate the EOS, such as opioid use. However, there are many ways to achieve EOS activation, including alcohol use. If BPD involves EOS dysregulation, it may be that when these individuals engage in one method of EOS activation they become less likely to engage in a second. Alcohol, due to its ubiquity and low cost, may be particularly likely to serve in this 'protective' role. Thus, it was hypothesized that individuals with BPD who are alcohol dependent would be less likely than those who are not to later develop an opioid use disorder. To test this, data from 29,876 participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) were analyzed using a Structural Equation Modeling (SEM) framework. A two latent-variable longitudinal model was fitted separately for individuals with and without BPD. Results indicated that having a use disorder at Wave 1 predicted a use disorder at Wave 2 for both groups. As predicted, however, individuals with BPD who were alcohol dependent at Wave 1 were less likely to have an opioid use disorder at Wave 2, while the opposite pattern was observed in individuals without BPD. These results provide support for a role for EOS dysregulation in BPD and suggest that individuals with BPD may use alcohol specifically because of its activating effects on the EOS.

0277

TOWARDS THE CHARACTERIZATION OF ALCOHOL USE DISORDER SUBTYPES: INTEGRATING CONSUMPTION AND SYMPTOM DATA

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There is evidence that measures of alcohol consumption, dependence, and abuse may be valid indicators of qualitatively different subtypes yet also seem to fall along a continuum of alcohol involvement. The present study attempts to resolve the extent to which alcohol involvement reflects a difference in kind versus a difference in degree by the use of factor mixture models (FMM), a new class of analytic models. FMMs are a hybrid of latent class analyses (LCA) and common factor analysis (FA). We tested and compared these models based on three indicators of alcohol involvement: alcohol dependence, alcohol abuse, and alcohol consumption. Data were drawn from the 2001–2002 National Epidemiologic Survey of Alcohol and Related Conditions (NESARC), a national, population-based interview of 43,093 non-institutionalized, U.S. citizens age 18 years and older (50.1% male, 72.5% White, non-Hispanic). Past-12 month alcohol abuse and dependence criteria were measured through a structured interview, the AUDADIS-IV. We also included five indicators of past-12 month alcohol consumption: drinking on a daily basis; on a weekly basis; on a monthly basis; heavy episodic drinking; ever intoxicated. The FMM had superior fit relative to the LCA and FA models, suggesting that unobserved population heterogeneity in alcohol involvement is captured simultaneously by continuous and categorical latent variables. Four classes of drinkers were identified: infrequent (47%); regular moderate (27%); moderate dependent (18%); high dependent (8%). Factor variances had relatively similar values for the three drinking classes but greater variability in the infrequent drinking class. The model was replicated using Wave 2 data, although the best-fitting model required setting factor variances to be equal across class. Class stability from Waves 1 to 2 was moderate (κ=.33; Cramer's V=.35). Within-class associations in the underlying latent factor revealed small-to-moderate agreement over time for regular moderate (r=.23) and high dependent (r=.28) classes but no agreement for infrequent (r=.05) and moderate dependent (r=.01) classes. Thus, there is evidence that alcohol involvement can be considered both categorical and continuous, with responses reduced to four types of patterns that quantitatively vary along a single dimension. Nosologists may consider hybrid approaches that consider groups that vary in pattern of consumption and dependence symptomatology as variation of severity within group.

0278

ALCOHOL USE DISORDERS AND ILLICIT DRUG USE IN THE US: EXAMINATION OF PATHWAYS USING STRUCTURAL EQUATION MODELING

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Alcohol and drug dependence often go hand in hand. Alcoholic often use multiple substances but little is known how illicit drug use affect alcohol use disorder. The purpose of this study was to examine the association of alcohol use disorder and illicit drug (such as cannabis and cocaine) use using Multiple Indicator Multiple Cause (MIMIC) model. This study used data from Wave2 of the NESARC, a large nationally representative sample of the United States adult population. To examine the dimensionality of alcohol use disorder, a confirmatory factor analysis (CFA) was performed. Finally a structural equation model (MIMIC) was estimated in which cocaine and cannabis use status were regressed on alcohol use disorder (AUD) to evaluate the association of cocaine and cannabis use disorders with alcohol use disorder. According to NESARC, about one-third of adult population in the United States met the criteria for a lifetime alcohol use disorder (AUD), whereas 8.9 percent met the criteria for lifetime cannabis use disorders and 3.1 percent met the criteria for lifetime cocaine use disorder. However, among those who had either cannabis or cocaine use disorders, more than 80 percent of them had alcohol use disorders. The structural equation model showed that lifetime cannabis and cocaine use had significant direct association with alcohol use disorder indicating that illicit drug users were much more likely to have alcohol use disorder than those who never used these illicit drugs or did not have disorders from these drugs (cannabis or cocaine). The MIMIC model provided a good fit of the data with TLI and CFI were more than 0.99 and RMSEA was 0.02.
This study suggests that people with co-occuring alcohol and illicit drug use disorders are more likely to have psychiatric disorders. So prevention and treatment of AUD will depend on the integration and refinement of alcohol and drug treatment services.

0279

COMORBID BINGE EATING AND ALCOHOL DEPENDENCE: CONTRIBUTIONS FROM PARENTAL ALCOHOL PROBLEMS, CHILD ABUSE HISTORY, AND EARLY MATURATION

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Binge eating and alcohol dependence (AD) often co-occur, and research has suggested that this comorbidity is due to shared risk factors, such as parental alcoholism, child abuse, and early pubertal development. Although these risk factors have each been shown to be associated with binge eating and alcohol use disorders separately, few studies have investigated their contributions to the risk for comorbid binge eating and alcoholism in young adult women. European-American young adult women participating in the Missouri Adolescent Female Twin Study (n = 3234; mean age = 21.63 ± 2.74) were interviewed using an adaption of the Semi-Structured Assessment for the Genetics of Alcoholism, which included diagnostic assessments of DSM-IV binge eating and AD, and questions regarding common childhood and adolescent risk factors for psychopathology and substance use disorders (e.g., parental separation, parental alcohol problems, childhood physical and sexual abuse, and early physical maturation). A multinomial logistic regression model was used to estimate relative risk ratios (RRR) for the associations between these risk factors and a four-level dependent variable (comorbid binge eating and AD, binge eating only, AD only, and neither [referent]). Overall, 46 women had both binge eating and AD, 190 had binge eating only, 218 had AD only, and 2755 had neither trait. Comorbid binge eating and AD was significantly associated with parental alcohol problems (RRR = 2.02 [1.05–3.86]), childhood sexual abuse (RRR = 3.36 [1.61–7.00]), and childhood physical abuse (RRR = 2.20 [1.10–4.39]). Binge eating only was significantly associated with childhood physical abuse (RRR = 2.09 [1.46–2.99]) and early physical maturation compared with peers (RRR = 1.73 [1.20–2.49]). AD only was significantly associated with parental alcohol problems (RRR = 1.65 [1.19–2.29]), childhood sexual abuse (RRR = 1.85 [1.24–2.74]), and early physical maturation (RRR = 1.57 [1.11–2.22]). Parental separation was not associated with any category of the outcome. No significant differences among the RRRs for a given variable for different levels of the dependent variable were found through post-hoc testing. Findings suggest that some childhood and early adolescent risk factors may not be specific to binge eating or AD in young adult women. Future analyses will focus on better understanding of factors contributing to the association between binge eating and AD in this and other demographic groups.

0280

ALCOHOL TREATMENT AND CORRELATES - THE FIRST BRAZILIAN NATIONAL SURVEY

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Background: Alcohol disorders account for an enormous burden in low and middle income countries. Despite the rise in substance misuse in Brazil, the access to public treatment services is still poor. This study aimed to estimate alcohol treatment prevalence and treatment options among participants with alcohol disorders.
Method: This is a cross-sectional study using data from the first Brazilian National Alcohol Survey. A multistage cluster sampling procedure was used to select 3007 individuals aged 14 years and older from the Brazilian household population. Prevalence of alcohol disorders and treatment factors were estimated. Mutually adjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated using the appropriate STATA survey commands to estimate the associations between socio-demographic characteristics and other possible correlates such as physical conditions caused by alcohol consumption, detriments caused by alcohol, problems caused by alcohol problems of another person, use of illegal substances and depression.
Results: Only 16.6% of the participants with alcohol abuse/dependence that reported willingness to stop drinking have ever treated their alcohol problem. Nearly half of the participants with alcohol problems are not willing to stop drinking. AA meetings and specialized surgeries were the most common treatment options mentioned. Illegal drug use was inversely associated with desire to stop drinking whilst alcohol's negative impacts, psychological problems and being advised to quit by a doctor were significantly associated with desire to stop drinking. The presence of physical and psychological problems as well as being advised to quit by a doctor were significantly associated with engaging treatment for alcohol problems.
Conclusions: This study found a disturbingly low proportion of treatment engagement among participants with alcohol disorders. There is an urgent need to improve access to alcohol treatment services and develop treatment strategies more in tune with patient's motivations to change.

0281

ALCOHOL INTOXICATION, CO-INGESTION AND WITHDRAWAL IN MEDICAL TOXICOLOGY CONSULTATIONS: A REVIEW OF THE TOXIC CASE REGISTRY

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Objective: Very few studies describe the type of patients seen by Medical Toxicology Consultation Services (MTCS). The Toxic Investigators Consortium (ToxIC) was developed by the American College of Medical Toxicology in January, 2010 to track patients seen by MTCS and to provide an infrastructure for research. In order to obtain information for further study, and for use in QA/QI projects involving ToxIC data, we reviewed registry data regarding alcohol intoxication, co-ingestion and alcohol-withdrawal syndrome (AWS).
Methods: The ToxIC registry was queried from its inception to 4/10/2011 using the search terms -Alcohols (ETOH) and -Withdrawal (WD) related to ETOH. Cases involving toxic alcohols (MeOH/EG) were also excluded. Descriptive statistics were used to compare and report data. Data were not reviewed for outcome information.
Results: Nearly 6,000 patients were registered in the ToxIC database from its initiation to 4/10/2011. Alcohol was involved in 574 consults, 10% of all consults registered. Alcohol-related consults were more common in men than woman (60%M/40%F) and occurred most frequently as part of polydrug overdoses (62%). EtOH as a sole intoxicant occurred only 4% of the time. Frequent co-ingestants included analgesics (14%), sedative-hypnotics (16%), antidepressants (12%), antipsychotics (6%), opioids (9%), and sympathomimetics (6%). 192 of the 574 consults (33%) involved AWS. AWS was separately reviewed. Most consults for AWS occurred in males (76%M/24%F). 91% of AWS consults occurred in patients age 19–65, 5% in age > 65 and 4% in ages 13–18. 24% of patients with AWS had contributing substances coded for, the most common being sedative-hypnotics (8%). Other common substances in patients with AWS included: opioids, antihistamines and antidepressants. AWS represented approximately 3% of consults performed by MTCS involved in ToxIC (192 out of nearly 6,000 cases) Less than 0.5% ToxIC cases (23) were for alcohol intoxication alone (24 out of nearly 6,000 cases).
Conclusion: Medical Toxicologists are rarely consulted for poisoning solely related to ethanol. Most alcohol-related consults occur in polydrug ingestions. AWS represents 33% of alcohol-related consults but only 3% of all consults performed by Medical Toxicologists. Although alcohol is reported to be involved in 20–70% of all poisonings admitted to hospitals it was less frequently (10%) involved in poisonings in the ToxIC Registry.

0282

INVESTIGATING OSTENSIBLE ONSETS OF ALCOHOL USE DISORDERS

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Individuals who do not meet criteria for a lifetime alcohol use disorder (AUD) at an initial assessment, but do so at a subsequent assessment, are typically thought of as onset cases of AUD. Considering previous research has documented the unreliability of lifetime measures, it is possible that lifetime reports at baseline may contradict subsequent lifetime assessments (e.g., based on subsequent assessments, cases that appear to be onsets may actually represent false negatives at the initial assessment). The goal of this study was to investigate ostensible onsets of lifetime AUDs using longitudinal data from the Alcohol, Health, and Behavior (AHB) study. Participants consisted of a prospective cohort of college students (baseline *N* = 489) from a large, public university who were at high and low risk for AUDs. Lifetime alcohol dependence (AD) and AUD diagnoses were assessed using DSM-IV criteria. Seventeen individuals (5% of 370) appeared to onset for DSM-IV lifetime AD between ages 29 and 35 (i.e., they did not meet criteria for lifetime AD at age 29 but did so at age 35). However, inconsistent with their age-29 lifetime AD assessment, at age 35, eleven (65% of the 17) of these individuals retrospectively reported experiencing three or more AD symptoms, clustering within the same 12-month period, before the age of 29. That is, a majority of participants who onset AD at their age-35 assessment also retrospectively reported three or more AD symptoms prior to their age-29 assessment. Similar results were found for DSM-IV lifetime AUD assessments. These findings further demonstrate the unreliability of retrospective reports of lifetime AUDs and call into question the validity of ''onset'' cases that rely on only two waves of assessment.
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0283

QUALITY OF LIFE MEASURES IN MEN AND WOMEN WITH COMORBID DEPRESSION AND ALCOHOL DEPENDENCE

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Quality of Life (QOL) has emerged as an important aspect of clinical care yet is understudied in Substance Use Disorders. Gender differences in QOL within the SUD population have been studied to an even lesser extent. We investigated differences in QOL measures between men and women with alcohol dependence and comorbid major depression in a sample of 78 subjects who participated in a pharmacotherapy clinical trial for the treatment of major depression with comorbid alcohol dependence. The QOL measures used were the Mezzich Cohn Quality of Life Index (MCQLI), WHO QOL assessment instrument (WHOQOL) and the Drinker Inventory of Consequences (DrInC). Groups were compared by T-test and Chi Square test. Results showed that males (n= 42 (54%) were similar to females (n=36 (46%) on age (40.5 vs 38.4 years), ethnicity, Addiction Severity Index score, HAM-D and HAM-A scores. While the men were slightly older than the women (by 2.1 years), more men were living with their spouses than women. Men had significantly more drug abuse than women (30.2% vs 8.1% p=0.0136) which mainly included marijuana and cocaine abuse. On the MCQLI, both M and F groups showed impairments in QOL, but women had lower overall QOL than men (4.7 vs 3.7, p=0.0233) and more interpersonal problems than men on the DrInC interpersonal problems score which approached significance but did not meet threshold criteria (10.0 vs 12.4, p=0.0871). Also approaching but not reaching significance, women scored higher on the DrInC impulse control problems measure than men (8.6 vs 10.5, p=0.1796). The combination of alcohol dependence and comorbid depression seems to affect women's QOL more severely than men. The differences in interpersonal problems and impulse control problems–though not reaching statistical significance–may have a bearing on lower QOL in women. The results of this study indicate potential gender differences in quality of life among patients with major depression and alcoholism despite having similar severity on depression and anxiety symptoms. Further studies are indicated to further elucidate the potential gender difference on quality of life among these comorbidity population.
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0284

HOUSING INSTABILITY AND MODERATORS OF RISK FOR ALCOHOL PROBLEMS

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Purpose: To assess the associations between housing instability and negative drinking consequences and DSM-IV alcohol dependence symptoms. Additionally, to identify factors that modify these associations.
Methods: Data are from the 2009–2010 National Alcohol Survey (N=5,382). Housing instability during the 2008–2009 recession was measured by classifying participants into three mutually exclusive categories: lost housing, unstable housing (trouble paying mortgage/rent), and stable housing (neither lost housing nor had trouble paying mortgage/rent). Outcomes included number of negative drinking consequences and number of DSM-IV alcohol dependence symptoms in the past 12 months. Multivariate negative binomial regressions were used and controlled for demographics, alcohol-related health problems prior to the recession, history of heavy drinking (past 10 years), parental history of alcohol problems, family support, and other recession-related hardships. Interactions between housing instability and family support, childhood economic difficulties, alcohol-related health problems, history of heavy drinking, and parental history of alcohol problems were assessed.
Results: Those who lost housing reported the most negative drinking consequences (mean: 0.99), followed by those with unstable housing (mean: 0.23), and those with stable housing (mean: 0.11, p<0.001). The mean number of dependence symptoms was significantly different between the 3 groups (p<0.001): 0.92, 0.36, and 0.23 respectively. Among participants with housing loss or instability, those with high family support reported fewer consequences and dependence symptoms compared to those with low family support. In multivariate models, a significant interaction between high family support and unstable housing was observed for the number of negative drinking consequences (beta = -1.41, p<0.05). A similar interaction between high family support and housing loss was observed for number of dependence symptoms (beta = -1.17, P<0.05).
Conclusion: Family support was associated with fewer alcohol-related consequences and dependence symptoms among those who experienced recession-related housing loss or instability. Findings point to potential buffering effects of family support during times of economic difficulty.

0285

THE RELATIONSHIP BETWEEN ALCOHOL USE DISORDERS AND SUICIDALITY: AN EXPLORATORY STUDY OF THE 2007 ADULT PSYCHIATRIC MORBIDITY SURVEY IN ENGLAND

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The aim of this study was to explore the relationship between alcohol use disorders and suicidality in a representative general population sample in England, and to examine the impact of confounding factors including socio-demographic and psychiatric factors in this relationship.
The Adult Psychiatric Morbidity Survey (2007) (n=7304) is representative of the population living in private UK residences. Standardised questionnaires and assessments were used to ascertain demographic information, psychiatric disorders, suicidality, and alcohol (AUD) and drug use disorders. The relationship between AUD and suicidality (suicidal thoughts and acts) was examined using univariate, partial correlational, and logistic regression analyses, the latter two taking account of potential confounding factors.
In univariate analyses suicidality was found to be strongly associated with psychiatric symptoms (CIS-R score), being female, younger, single, having lower household income, being in a lower socioeconomic group, and higher index of multiple deprivation, smoking, harmful alcohol consumption and alcohol dependence (AUDIT score >=16), lower IQ score and using other non-prescribed substances. Harmful consumption of alcohol was not found to be independently related to suicidality when controlling for other significant risk factors. CIS-R score – the most significant predictor of suicidality – was found to mediate the relationship between harmful alcohol use and suicide attempts. CIS-R score, marital status and misuse of other non-prescribed substances mediate the relationship between alcohol and suicidal thoughts in the past year.
This study contributes to international findings that suicidality is a product of a complex interaction of risk factors. Co-occurring psychiatric symptoms and harmful alcohol consumption and alcohol dependence can significantly increase the risk of suicidality. However the relationship between AUD and suicidality is more complex than suggested by previous research. An assessment of alcohol misuse should be incorporated into assessments in patients presenting with psychiatric symptoms in assessing the risk of suicidality.

0286

ACUTE ALCOHOL INTOXICATION AND SUICIDE MORTALITY

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Although it is well known that people with alcohol dependence are at markedly elevated risk for suicide, much less is known about the role of acute alcohol use in suicidal behaviors. The primary objective of this epidemiological study was to assess the prevalence of acute alcohol intoxication among 57,813 suicide decedents in 16 U.S. states. Restricted data from the National Violent Death Reporting System (2003–2009) for male and female suicide decedents aged 18 and older were analyzed by multiple logistic regression to compare decedents with and without acute alcohol intoxication (i.e., BAC ≥ .08 g/dl). Among suicide decedents tested for alcohol (76%), men (36%) were more likely than women (29%; c^2 = 187.1, p < .001) to have alcohol present at the time of death. Acute intoxication was found in 24% of men and 17% of women. Moreover, 21% and 9% of male suicide decedents had BACs ≥ 0.10 g/dl and ≥ 0.20 g/dl, respectively. Conversely, among women, 15% and 7% had BACs ≥ 0.10 g/dl and ≥ 0.20 g/dl, respectively. Among the male decedents, those who were younger (< 45 years), American Indian/Alaska Native (adjusted odd ratio [AOR]=1.77; 95% confidence interval [CI], 1.45–2.16), Hispanic (AOR=1.19; 95% CI, 1.06–1.35), veterans (AOR=1.12; 95% CI, 1.04–1.20), with less education (AOR=1.39; 95% CI, 1.28–1.53), rural area residents (AOR=1.02; 95% CI, 1.01–1.04), and those who completed suicide with firearms (AOR=1.76; 95% CI, 1.61–1.93) or hanging/suffocation (AOR=1.39; 95% CI, 1.25–1.53) were more likely to have had a BAC ≥ .08 g/dl at the time of death. Among women, the factors associated with a BAC ≥ .08 g/dl at time of death were younger age, being American Indian/Alaska Native (AOR=1.99; 95% CI, 1.36–2.90), and those who completed suicide with a firearm (AOR=1.69; 95% CI, 1.46–1.93), hanging/suffocation (AOR=1.48; 95% CI, 1.25–1.75), or drowning (AOR=1.61; 95% CI, 1.05–2.47). In both men and women alcohol intoxication was associated with violent methods of suicide (e.g., firearms) and declined markedly with age, suggesting that addressing risks associated with acute alcohol use may be of greatest aid in the prevention of violent suicides among young and middle age adults. The findings emphasize the need for the harmonization of alcohol control policy and suicide prevention strategies. This unique data set provides guidance for clinicians and policy-makers seeking to develop personalized strategies that can reduce suicides associated with acute alcohol use.

0287

TERRORISM, WAR, ONE-SIDED VIOLENCE AND GLOBAL BURDEN OF ALCOHOL USE DISORDERS

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Historically, terrorism, war and one-sided violence have not received the attention of alcohol researchers as have other causes of alcohol use disorders and political scientists have been more interested in the economic and political causes of terrorism, war and one-sided violence than on their impact on public health. This study was premised on the concept that terrorism, war and one-sided violence adversely affect public health long after fighting and bombings are over. This study integrates epidemiology, political science and economic perspectives to examine, for the first time, the impact of terrorism, war and one-sided violence in 1994-to-2000 on morbidity and mortality due to alcohol use disorders in 2002, measured by Disability-Adjusted Life Years (DALYs), in WHO member states. Regression analyses across sex and age subgroups of the population were adjusted for economic and political variables at baseline in 1994 including the number of refugees, number affected by natural disasters, health expenditures, ethnic heterogeneity, urban growth and life expectancy. Controlling for per capita alcohol consumption also provided for a measure of pre-existing vulnerability for alcohol use disorders at baseline. In 2002, alcohol use disorders were responsible for 20.3 million DALYs worldwide. Globally, per capita consumption in 1994 averaged 4.9 liters of pure alcohol. Deaths from terrorism and related violence were positively and significantly related to alcohol use disorder DALYs across the majority of sex and age subgroups of the population, even after controlling for economic and political factors and pre-existing alcohol use vulnerability at baseline. Overall, for each 1.0% increase in deaths due to terrorism, war and one-sided violence, there was a 0.10% increase in alcohol use disorder DALYs worldwide. The impact of terrorism, war and one-sided violence deaths on alcohol use disorder DALYs was pervasive across all sex and age subgroups of the total world populace, highlighting the devastating toll of death and disability that defines armed conflict and related violence. Unlike results from studies at the individual level of analysis, the prevalence of alcohol use was strongly related to alcohol use disorder DALYs across the majority of sex and age subgroups of the population. The results of this study can inform post-conflict interventions and ultimately influence decisions to use force.

0288

INCIDENCE OF DRUG AND ALCOHOL INVOLVEMENT IN COMPLETED SUICIDES: FLORIDA RESIDENTS 2008-2011

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Drug and alcohol involvement in suicide is common, however few studies include large population samples or detailed analysis of co-occurrence. The current study examined a de-identified database of suicide victims (n=10080) in the State of Florida from 2008–2011 (Florida Bureau of Vital Statistics). The intent of the study was to investigate substance use in completed suicides by examining (i) incidence of substance involvement, (ii) demographic differences, and (iii) specific drug classes. International Classification of Disease (ICD-10) codes distinguished decedents whose suicides involved drugs or alcohol (DA+). DA+ decedents constituted 16% of the total population (n=1599). Co-incidence of drug and alcohol involvement suggested an interesting relationship (χ^2=905.49, p<.0001); alcohol involvement occurred in the absence of drug use only rarely (>.5% decedents; n=41). Alcohol/drug co-involvement was more common (2%; n=208), although drug involvement without alcohol was most common (13%; n=1350). Demographic comparison indicated gender differences; the DA+ population included a disproportionate number (35%) of females (χ^2=747.89, p<.0001), relative to only 11% of males. Specific drug involvement in suicide was provided by ICD-10 codes describing different drug classes. The most common class included 'unspecified' agents (n=1059), followed by 'opioids' (n=539), 'anti-epileptic and sedative-hypnotic' agents (n=465), 'psychotropics' (n=292), 'non-opioid analgesics' (n=149), 'hematological agents' (n=96), and others (n's < 50). Classes were then further broken down into more specific compounds. These results suggest that consistent with other data, suicides among women were more likely to involve substances. Unexpectedly, alcohol involvement was low relative to estimates in other states (where alcohol appears involved in ~1/3 suicides). It is unknown whether this difference reflects an outcome unique to Florida, or an under-reporting of alcohol due to coding or other procedural issues in data collection. In contrast, drug involvement in suicide was similar to that reported at the national level. These analyses provide an initial description of this rich dataset, providing a foundation on which to base further analyzes of the complex relationships between substance use and other important demographic variables (e.g., race, marital status, occupation), potentially strengthening the understanding of suicidal behavior and improving preventative capacity.

0289

THE EFFECT OF ALCOHOL USE AND AGGRESSION ON SUICIDE ATTEMPTS IN AN ADOLESCENT CLINICAL SAMPLE

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Purpose: Both alcohol use and aggression influence suicidal behaviors in adolescents. The purpose of this study was to examine the relationship between alcohol use, aggression, and suicide attempts in adolescent inpatients. It was hypothesized that aggression would mediate the association between alcohol use and suicide attempts.
Methods: Participants included 186 psychiatrically hospitalized adolescents in the northeastern United States between the ages of 13 and 18. Adolescents were classified into groups of suicide attempters (N=98) and non-attempters (N=88) by their answer to the Kiddie-SADS-Present and Lifetime Version (K-SADS-PL) question if they had attempted suicide in their lifetime. The Substance Abuse Subtle Screening Inventory (SASSI) was used to measure amount of alcohol use in the past six months. The Aggression Questionnaire (AQ) was used to measure level of aggression. Linear and logistic regressions were used to test the hypothesis that aggression mediates the relationship between alcohol use and suicide attempts in adolescent inpatients.
Results: The MacKinnon z' test of mediation was used. Linear regression showed a significant relationship between alcohol use and aggression, such that greater alcohol use predicted higher aggression (B=1.67, SE=0.42, p<0.001). Logistic regression demonstrated a significant positive relationship between aggression and the odds of a suicide attempt (B=0.03, SE=0.01, p=0.02), and after accounting for the effects of alcohol use (B=0.03, SE=0.01, p=0.03). MacKinnon's test of mediation supported the hypothesis that aggression mediated the relationship between alcohol use and suicide attempt (Z=2.39, SE=0.02, p=0.02), such that alcohol use predicted greater aggression, which in turn predicted greater odds of a suicide attempt.
Conclusion: Alcohol use has a significant indirect effect on suicide attempts through aggression level in adolescent inpatients. Adolescents that exhibit both aggressive behaviors and frequent drinking may be at greatest risk for a suicide attempt. These findings suggest the need for integrated treatment protocols for adolescents with psychiatric disorders who demonstrate frequent alcohol use and aggressive behaviors. Such treatments should specifically address alcohol use as a risk factor for aggressive behaviors, which often include suicide attempts. One limitation of these findings is the use of cross-sectional data, and therefore should be replicated using a longitudinal design.

0290

ASSOCIATION OF HEAVY DRINKING AND DRUNKENNESS WITH INJURY MORTALITY FROM 11-22 YEAR FOLLOW-UP

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Objective: To examine the relationship between baseline alcohol consumption and follow-up mortality from injury using US nationally representative samples. We hypothesized heavy drinking episodes would be positively associated with deaths from injury, even after controlling for key confounding factors.
Methods: Baseline alcohol consumption (average volume, heavy drinking and frequency of drunkenness) from the 1984 and 1995 US National Alcohol Surveys (total N=10,146) were linked with mortality data from National Death Index through 2006 (11–22 years). Cox proportional hazard models were fitted to estimate the effects of baseline alcohol consumption on injury mortality, controlling for demographic, illicit drug use and risk-taking measures.
Results: Altogether 123 deaths with injury as either primary or non-primary causes were recorded. Neither average daily intake nor 5+ days significantly predicted injury mortality. Instead, a significant bivariate association was found between number of days having 8+ or getting drunk and the hazard of injury death. After controlling for the socio-demographic and risk-taking confounders, number of drunkenness days was the only significant drinking variable associated with subsequent injury mortality.
Conclusions: Findings suggest the commonly used heavy episodic drinking measure of 5+ days might be less predictive of injury mortality than frequency of drunkenness, which often implies higher intake. Consistent with earlier work showing the frequency of drunkenness as better predictor of alcohol dependence and alcohol-related harms, we highlight the value of this acute, subjective drinking measure for injury mortality risk. (Supported by grants P50 AA005595 and R01 AA016644 from NIAAA)

12. PHARMACOKINETICS AND METABOLISM 291–295/291–295

0291

PHARMACOKINETICS OF NICOTINE AND ITS METABOLITE COTININE IN THE BRAIN OF ALCOHOL-PREFERRING (P) RATS AFTER INTRAGASTRIC ADMINISTRATION

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Several tobacco companies are test marketing oral nicotine drinks, including some containing alcohol. The objective of the present study was to determine the time-course changes in the CNS levels of nicotine and its major metabolite, cotinine, following intragastric administration of nicotine and ethanol. The levels of nicotine and its metabolite cotinine were measured from 15 to 195 min after intragastric (gavage) administration of (-)-nicotine (0.35 and 0.70 mg/kg) in 15%(v/v) ethanol in alcohol-preferring (P) rats. Rats (n = 4/dose) were implanted with guide cannula aimed above the nucleus accumbens (NAC) shell and *in vivo* microdialysis was used to collect 15 min dialysate samples for nicotine and cotinine determination, using high performance liquid chromatography with ultraviolet detection. Following the 0.35 mg/kg dose, nicotine concentrations rose rapidly to 7 ng/ml at 15 min and remained between 5 and 8 ng/ml up to 75 min post injection. Thereafter, nicotine concentrations gradually declined to 5 ng/ml for the remainder of the 195 min sampling period. At the 0.35 mg/kg dose, cotinine concentrations gradually increased between 45 and 135 min post injection and remained elevated for the remainder of the sampling period with a maximal increase of 9 ng/ml at 195 min. The administration of 0.7 mg/kg nicotine resulted in a maximal nicotine concentration of 14 ng/ml at 45 min, nicotine concentrations gradually decreased between 75 and 135 min and stabilized at 3 to 7 ng/ml between 150 and 195 min. Following the 0.7 mg/kg nicotine dose, cotinine concentrations gradually escalated from 2 ng/ml at 45 min to 10 ng/ml at 90 min. Thereafter, cotinine concentrations remained elevated for the remainder of the sampling period with a maximal concentration of 12 ng/ml at 150 min. Overall, brain nicotine concentrations peaked sharply and declined slowly, whereas cotinine concentrations gradually increased and stabilized over the last 75 min of the sampling period. These findings indicate that intragastric administration of EtOH/nicotine solutions produces very rapid brain levels of nicotine and sustained brain levels of cotinine, which is pharmacologically active. (AA07611, AA019366)

0292

METABOLIC PRODUCTS OF [1-13C] ETHANOL IN THE AWAKE RAT BRAIN

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Introduction: Ethanol (EtOH) is metabolized to acetate (Ac) and consumed by the brain. Ac oxidation inhibits neuronal activity and may contribute to adaptation to EtOH. 13C-EtOH and 13C-Ac were administered to naïve and EtOH-treated rats by oral gavage [OR] or vapor chamber [V], and 13C labeling of cerebral amino acids determined by magnetic resonance spectroscopy (MRS).
Methods: Adult male Sprague-Dawley rats were studied: *OR:* 20 rats were treated with EtOH daily 10 days by gavage (1g/kg i.g., *OR-ET*), 20 were untreated (*OR-UN*), and 8 treated with gavage water (*OR-W*). For 13C MRS, rats received [2-13C]EtOH (1g/kg i.g.) and were decapitated to remove the brain after 15, 30, 60, and 240 minutes, or 4 rats/group were treated with [2-13C]Ac (0.5 g/kg ip).
V: 8 rats were treated with 23 g/L EtOH vapor for 8hr/day, 3 weeks, in Yale-built vapor chambers, and 9 rats were naïve. For 13C MRS, [2-13C]EtOH was infused via tail vein (method of Sean O'Connor, IUPUI) to reach 100 mg/dL plasma EtOH by 15 minutes, maintained 2 hours, when the brain was fixed by focused microwave and the brain removed. *OR&V*: Blood samples were obtained post-mortem from the inferior vena cava. Tissue and blood samples were prepared for MRS analysis. Brain 13C-Gln was normalized to Ac levels and enrichment.
Results: *[OR]* EtOH reached 70 mg/dL in *OR-ET* rats and 100 mg/dL in *OR-UN* rats. Ac peaked at 0.7–1.0 mM, with *OR-UN* rats increasing gradually but *OR-ET* rats peaking early and falling. Normalized Gln enrichments were 13.8% for *OR-UN*, 11.5% for *OR-ET*, and 12.9% for *OR-W*. When 13C-Ac was injected, normalized 13C-Gln was 4.9% for *OR-UN* and 11.5% for *OR-W*, less than seen with 13C-EtOH. *OR-ET* showed enhanced labeling from Ac, with 13.6%.The 13C consumption was high in *OR* rats, but different 13C-EtOH blood profiles could obscure effects. EtOH i.v. which was done in *V* rats, may facilitate more detailed analysis.
[V] 13C-EtOH plateaued at 100 mg/dL for both groups. Ac levels reached 2 mM for the controls, with treated rats at 1.6–1.8mM. normalized 13C-Gln was 12.6% for naïve rats and 13.7% with treatment (both p<0.001). Treated rats showed greater labeling from ethanol than untreated rats.
Discussion: OR and V yielded similar results. Chronic ethanol exposure appears to alter incorporation of hepatic-derived systemic Ac into brain Gln metabolism, a key neurotransmitter precursor linked to brain energy. Further work is needed to measure the potential role of brain EtOH oxidation.

0293

CHRONIC FREE-CHOICE DRINKING IN CROSSED HAP MICE LEADS TO METABOLIC TOLERANCE AND CYP2E1 ENZYME INDUCTION WITHOUT EVIDENCE OF LIVER DAMAGE

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Alcoholism is defined by excessive use of alcohol in the wake of adverse consequences. The crossed High Alcohol Preferring (cHAP) line, selected from a cross of HAP1xHAP2 replicate lines, demonstrates intakes and blood ethanol concentrations (BECs) that are reminiscent of those observed in alcohol-dependent humans (Matson and Grahame, 2011). This line therefore may provide an unprecedented opportunity to learn about the consequences of voluntary ethanol consumption with high daily BECs. The development of tolerance is thought to be an important factor in the development of alcohol dependence. Cytochrome p450 2E1 (CYP 2E1) induction plays a prominent role in driving metabolic tolerance and ethanol-induced liver injury. Given that cHAP intakes and BECs are similar to those observed in mice given an ethanol liquid diet, it is plausible that free-choice exposure will result in metabolic tolerance, hepatic enzyme induction, and hepatic steatosis, which we assessed. In Experiment 1 we injected 24 mice with ethanol following 3 weeks of access to 10% ethanol and water, or water alone, with repeated blood sampling to assess metabolic tolerance. In Experiment 2, 24 mice again had access to 10% ethanol and water or water alone for 4 weeks, followed by necropsy and hepatological assessment. Ethanol-exposed mice metabolized ethanol faster than ethanol-naïve mice, demonstrating metabolic tolerance. There was a main effect of Sex, with males metabolizing ethanol faster than females ($ps < .05$). In experiment 2, there were no significant alterations in hepatic histology between ethanol-exposed and ethanol-naïve mice. Nonetheless, expression of hepatic CYP2E1 was significantly increased in ethanol mice when compared to water controls ($p < .05$), consistent with the metabolic tolerance observed in Experiment 1. There were no significant changes in the levels of ADH and ALDH in cHAP mice following ethanol access compared to water controls. Future studies could compare liquid diet with free-choice ethanol access to understand if hepatic steatosis occurs following liquid-diet ethanol access in cHAP mice. These results demonstrate that excessive intake by cHAP mice results in the development of metabolic tolerance and evidence of CYP 2E1 induction, providing additional support for the cHAP mice as a highly translational rodent model of alcoholism. Supported by IUPUI SOS (NG), Alcohol Research Center Grant AA07611 (DC), and training grant AA07462 (LM).

0294

ROLE OF ADENOSINE A1 RECEPTORS IN EXACERBATION OF INFLAMMATION AND LIVER DAMAGE UNDER EXCESSIVE ALCOHOL CONSUMPTION

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Purpose: Acute alcohol-attributable deaths are as prevalent as for chronic. CDC recently estimated deaths from harmful effects of excessive alcohol at 75,766, of which 40,933 (54%) resulted from acute and 34,833 (46%) from chronic conditions. Moreover, individual morbidity is highly variable. Underlying mechanisms are still poorly understood and treatment is mainly symptomatic. Here, we investigate the role of adenosine, using a mouse model with alcohol-induced acute hepatitis.
Methods: For in vivo, adenosine A1 receptor knockout mice (A1R KO) with C57BL/6 background (8wk old, male, 25g), and wild-type from the same colonies were used. N6-cyclohexyladenosine (CHA) an A1 agonist, at 0.3 mg/kg, followed by ethanol (3.6 g/kg) after 30 min were intraperitoneally injected. Sera afterwards were assayed for alanine aminotransferase (ALT), a biomarker of liver injury, and TNF-alpha, an inflammation level indicator. For in vitro, HepG2 cell line, a model of hepatocytes, but lacking alcohol dehydrogenase, was co-cultured with ethanol at 100mM and (CHA) at 10(-5)M. TNF-alpha (1ng/ml) was employed as the positive control. The supernatants and cells were harvested at 45 hours to measure TNF-alpha.
Results: Following ethanol injection, serum TNF-alpha values were markedly high in the wildtype but only rose mildly, around one-sixth as much as wildtype, in the A1R KO. In wildtype, ALT values were markedly higher with ethanol and CHA, but almost in normal range with ethanol alone. In incubated HepG2 cells, co-stimulation of ethanol and CHA caused significantly higher expression of preform caspase 3, a marker of apoptosis even higher than the positive control with TNF-alpha stimulation, while ethanol stimulation alone caused only a slight increase in preform caspase 3. Activated caspase 3 was also induced by co-stimulation with ethanol and CHA while it wasn't with ethanol alone. Total protein from the ethanol + CHA group and ethanol + TNF-alpha group at 45 hours were below 65% of level in unstimulated cells.
Conclusion: These results suggest that A1R has proinflammatory effects and the stimulation of A1R aggravates inflammation and liver damage in acute hepatitis with excessive alcohol consumption. In vitro data show A1R stimulation in hepatocytes could induce apoptosis by direct interaction with ethanol, independent of TNF-alpha. This apoptosis could be a principal cause of alcohol-induced liver damage, and explain morbidity differences among individuals.

0295

COMPARING TRANSDERMAL AND BREATH ALCOHOL CONCENTRATION READINGS DURING PERIODS OF ALCOHOL CONSUMPTION FROM MODERATE DRINKING TO BINGE DRINKING

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Binge drinking is a public health concern due to its association with negative health outcomes as well as increased legal and social consequences. Previous studies have frequently used self-reported alcohol consumption to classify binge drinking episodes; however, these measures are often limited in both detail and accuracy. Some researchers have begun using additional measures such as blood (BAC) and breath (BrAC) alcohol concentrations to supplement self-report data. Transdermal alcohol testing, or the detection of alcohol expiration through the skin, offers advantages over BAC and BrAC measures by allowing for continuous and noninvasive monitoring of an individual's drinking behavior in real-time. Despite these advantages, this technology has not been widely used or studied outside of forensic applications. The present research compares transdermal alcohol concentration (TAC) and BrAC readings during the consumption of alcohol ranging from moderate drinking to binge drinking in 22 adult regular drinkers in order to investigate the sensitivity and specificity of the TAC monitors. Participants consumed 1-5 (4 for women) beers within a 2 hour time span in a simulated binge procedure over 1-5 days. BrAC and TAC readings were taken every 30 minutes until alcohol was no longer detected. We observed that BrAC and TAC measures were broadly consistent. Additionally, we were able to develop an equation that could predict BrAC results using TAC data, indicating TAC data would be an appropriate substitute in research and clinical contexts where BrAC readings are typically used. Finally, we were able to determine a cutoff point for peak TAC data that could reliably predict whether a participant had engaged in moderate or more than moderate drinking, suggesting TAC monitors could be used in settings where moderate or reduced drinking is the goal.

13. LIFESPAN / DEVELOPMENT

0296

RESPONSE PATTERNS ON THE ALCOHOL EXPECTANCY QUESTIONNAIRE FOR A SAMPLE OF 8-12 YEAR OLD CHILDREN OF ALCOHOLICS

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Children of alcoholics (COA) are at a higher risk for developing substance abuse disorders in adolescence and adulthood. Research has shown that both positive and negative expectancies can be learned vicariously during childhood from parents. Much of the research has focused on adolescents with little work on child alcohol outcome expectances or on the AEQ among pre-adolescents. This study looks at response patterns for the AEQ among a group of 8–12 year old COAs. Participants were 660 children who participated in a larger prevention trial of a parenting program. Of the 660, 53% were male; 6% were 8, 25% 9, 21% 10, 23% 11 and 25% 12. Data were from the baseline assessment of the child alcohol expectancies, with only 38 items, representing six of the original scales, included in the study. The response options for the children were "yes," "no," "don't know," or "refused." A total of 5% of the children refused to answer at least 1 of the 38 questions. In contrast, over 67% responded with "don't know" to at least 1 item. In addition, for 21 of the 38 items, more than 10% of the children indicated "don't know." There were no gender differences for valid, don't know, or refusal response rates. For age, there were no significant differences for don't know or refusal responses, while for the tension reduction subscale items, older individuals were more likely to respond true than younger individuals ($p < .001$). A confirmatory factor analysis (CFA) was attempted to determine, if the original factor structure would fit the data. However, because of low variability in a number of items, the CFA would not compute the model parameter estimates. Using exploratory factor analysis (EFA), a six factor solution fit the data, CHI-SQUARE = 532.60, df = 490, p = .0921; RMSEA = .011; CFI = .992; TLI = .988. The identified factors were similar in nature to the subscales from the original scale with some exceptions. The results of this study point to a need to gain a better awareness of how children understand questions related to substance use. While the results for the EFA suggest that the children seem to have a similar understanding to that of adults, the high rates of don't know responses for some of the items, suggests that in some areas, a lack of exposure may result in poor responding. Determining how to handle the "don't know" responses may help us build better predictive models. (Supported by NIAAA grant R01-AA11647).

0297

CHILDREN WITH A FAMILY HISTORY OF ALCOHOL AND OTHER DRUG USE DISORDERS SHOW INCREASED DISCOUNTING OF DELAYED MONETARY REWARDS

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Individuals with alcohol and other drug use disorders discount delayed reward more steeply than healthy controls, however it is unclear whether increased delay discounting contributes to or is a consequence of developing drug use disorders. Young adults with family histories of alcohol and other drug use disorders (FH+) show small to modest increases in delay discounting relative to those without such histories (FH-). Alternatively, young children with poor capacity to delay gratification are at increased risk for developing future substance use disorders and other psychopathologies. The purpose of the present study was to quantify delay discounting in a sample of at risk children that we are monitoring prospectively for the development of alcohol and other drug use disorders. We compared 210 FH+ and 53 FH- children ages 10 to 12 years old and who had not yet initiated regular alcohol or drug use at the time of testing. FH+ children discounted more than FH- children across small, medium, and large amounts of delayed hypothetical amounts of money with no magnitude by FH status interactions. All children discounted smaller amounts of delayed money more steeply than larger amounts, and there were no effects of gender on delay discounting. These results indicate that children at risk for developing future alcohol and other drug use disorder discount delayed rewards more prior to initiating any regular alcohol or drug use. In our ongoing study we will explore this relationship in additional participants and examine how delay discounting predicts development of alcohol and other drug use disorders.

0298

CORRELATES OF SELF-REPORTED AGGRESSION IN A SAMPLE OF CHILDREN AT RISK FOR DEVELOPING FUTURE ALCOHOL AND OTHER DRUG USE PROBLEMS

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Children with a family history of alcohol and other drug use disorders (FH+) are at increased risk for developing future alcohol and other drug use disorders relative those without this history (FH-). Previous research has found that FH+ children also show increased externalizing behaviors (e.g., aggression) that are associated with an increased risk for problem alcohol and other drug use (McGue et al., 2001; Tarter et al., 2003). The purpose of this study was to compare self-reported aggressive behaviors and factors associated with aggression among groups of FH+ (n=135) and FH- (n=36) children aged 10–12 years old. The FH+ group reported more aggressive behaviors, as well as more stressful life events and more affiliation with delinquent peers. Examining specific relationships between aggression and personality and environmental factors we found that, for the FH+ group, aggression was significantly predicted by self-reported sensation-seeking, impulsivity, and callous and unemotional traits. When environmental stressors and affiliation with delinquent peers were added to the model, both factors were significantly related to aggression and both sensation-seeking and callous and unemotional traits also remained significant predictors. These results suggest that personality traits and environmental influences may play a strong role in FH+-associated aggression. As part of our ongoing prospective research, we will examine how these relationships are associated with later problem alcohol and other drug use. Given that aggressive behavior in FH+ individuals is associated with a host of negative outcomes including future alcohol use disorders, these environmental factors may be an important target of intervention for FH+ children.

0299

HISPANIC CHILDREN AT RISK FOR DEVELOPING ALCOHOL AND DRUG USE DISORDERS HAVE INCREASED EXTERNALIZING BEHAVIORS

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Children with a family history of alcohol and other drug use disorders (FH+) are at increased risk for developing future alcohol and other drug use disorders relative to those without this history (FH-). Previous research as determined that externalizing behaviors are more common among FH+ children and adults and may moderate the relationship between family history and development of substance use problems. However, the majority of research testing these relationships has been conducted with Caucasian and African-American samples and less is understood about the relationship between externalizing behaviors and family history status in the development of alcohol and other drug use disorders among those of Hispanic ethnicity. To begin to address this, we examined dimensions of externalizing behaviors in a sample of 10 to 12 year old FH+ (n=150) and FH- (n=31) Hispanic children who had not yet initiated any regular drug or alcohol use. Externalizing behaviors were measured with the Child Behavior Checklist, the Connors 3rd Edition, the Inventory of Callous-Unemotional Traits, and the Peer Delinquency Scale. FH+ children had significantly increased externalizing behavior scores on all measures, including greater affiliation with delinquent peers. Similar findings were observed in smaller sample of comparable non-Hispanic FH+ and FH- children. This research suggests that the previously reported relationships between FH status and externalizing behaviors are also prevalent in Hispanic children. As part of our ongoing prospective research, we will examine how externalizing behaviors in this sample predict the onset and severity of future alcohol and other drug use problems.

0300

CHILDREN WITH FAMILY HISTORIES OF ALCOHOL AND OTHER DRUG USE DISORDERS EXPERIENCE INCREASED CHILDHOOD ADVERSITY

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Individuals with a family history of alcohol and other drug use disorders (FH+) are at increased risk for alcohol and other drug use disorders relative to those without this history (FH-), however it is not fully understood what role childhood adversity plays in contributing to this risk. As part of an ongoing prospective study on the development of adolescent substance use disorders, we compared histories of stressful life events in 137 FH+ and 37 FH- children ages 10-12, prior to the onset of any regular drug use. Stressful life events were quantified using the Stressful Life Events Schedule (SLES), a standardized, semi-structured interview that quantifies the number and severity of stressors across a variety of domains. FH+ adolescents reported more stressful life events and had a higher cumulative severity of stress than FH- children overall. The largest group differences in stress exposure were in domains of Crime (e.g. friend or family member had trouble with police), Housing (e.g. moved houses), and Education (e.g. changed schools). These results suggest family history of alcohol and substance use confers increased incidence of childhood adversity, which may be one mechanism by which substance use risk is transmitted within the family. In our ongoing studies we will examine how adversity contributes to the development of alcohol and drug use disorders in these individuals.

0301

ALCOHOL INITIATION CONTEXTS OF ADOLESCENT GIRLS

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Little is known about the contexts in which adolescent girls initiate alcohol use. Understanding the proximal factors associated with initiation may have important implications for the development of effective, diverse alcohol prevention programs. The current study used a mixed methods approach to examine the contexts in which adolescent girls begin to use alcohol, including motives for initiation.
Methods: Participants were young women, ages 18 – 19 years (N = 229). In addition to age and gender, to be eligible, participants had to consume alcohol at least monthly and have had sexual intercourse with a male at least once in their lifetime. Retrospective interviews included a semi-structured, event-based interview of alcohol initiation. Participants provided details about their first drinking experience, including the setting, type and quantity of alcoholic drink, presence of others, source of alcohol, motives for initiating drinking and consequences.
Results: On average, participants initiated alcohol use at age 14 years (*SD* = 2.04), consuming 3.26 (*SD* = 1.15) drinks. Initiation occurred in social contexts including sleep-overs, parties, family gatherings, and at bars. Participants most often initiated with friends or family members, including parents. Four themes related to motives for initiation emerged: (a) *Drinking is Exciting* – drinking was seen as novel or a solution for boredom; (b) *Elevation of Status* - there was a perception of being initiated into a more adultlike status, resulting in being accepted by older or more socially advanced peers or potential romantic partners; (c) *Familial Drinking Promotion* - parents or older siblings provided alcohol and encouraged drinking; (d) *Being in a 'Safe' Context* – some participants expressed an interest in trying alcohol, but were afraid of losing control or being taken advantage of while intoxicated. They sought out "safe" situations in which to initiate; that is, they believed that they were drinking with people (e.g., an older sibling) who were trustworthy and would keep them from harm while they were under the influence.
Conclusions: Adolescent girls initiate alcohol use in a variety of settings and may have positive expectations about drinking. It is not uncommon for families to be encouraging and supportive of adolescent drinking, making it unlikely that prevention efforts aimed solely at mitigating peer pressure or enhancing effective refusal skills will be universally effective.

0302

ASSOCIATIONS BETWEEN DIFFERENT DIMENSIONS OF IMPULSIVITY AND INCREASES IN ALCOHOL USE FREQUENCY AMONG EARLY ADOLESCENTS

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The purpose of this study was to examine associations between different dimensions of impulsitivity (i.e., dispositions to rash action) and growth in alcohol use among middle-school students over an 8-month period. Five dimensions of impulsivity were considered: lack of planning, negative urgency (the tendency to act rashly when in a negative mood), sensation-seeking, lack of perseverance, and positive urgency (the tendency to act rashly when in a positive mood). Secondarily, we examined whether the predictive power of these dimensions was significant above and beyond the effect of conduct disorder symptoms (a known risk factor for alcohol use). Participants were 144 low-income, minority youth (69% Hispanic, 32% African-American; mean age=11.9, range 10–14; 51% female); 85% of the original sample was followed-up 8 months later. The children's version of the UPPS-R (Zapolski et al., 2010, based on the UPPS-R, Whiteside & Lynam, 2001), was used to measure self-reported dispositions to rash action, and a 5-point scale (from "none" to "most days") was used to gather self-reports frequency of alcohol use in the previous 4 months. Five regression analyses were conducted, with each disposition to rash action used as an independent variable (while adjusting for age, gender, race, and alcohol use frequency at the first assessment) and alcohol use frequency 8 months later as the dependent variable. The results indicated that lack of planning, negative urgency, and positive urgency were associated with increases in the frequency of alcohol use over an 8-month period. Once the effect of conduct disorder symptoms was adjusted for, positive urgency remained a significant predictor of increases in alcohol use frequency. Therefore, emotion-based dispositions to rash action (negative and positive urgency), as well as a tendency not to think before acting (lack of planning), are associated with increases in the frequency of alcohol use among early adolescents over an 8-month period. In contrast to expectations, sensation-seeking did not predict increases in the frequency of alcohol use. Based on its significant effect above and beyond the effect of conduct disorder symptoms, positive urgency may be a particularly powerful predictor of increases in alcohol use and is therefore particularly deserving of research attention.

0303

INDIVIDUAL DIFFERENCES AND THE PREDICTION OF ADDICTIVE BEHAVIORS DURING THE TRANSITION FROM PREADOLESCENCE TO ADOLESCENCE

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We report that personality traits measured in elementary school predict involvement in addictive behaviors during the first year of middle school. This finding is important because involvement in addictive behaviors at the start of middle school/adolescence is highly predictive of subsequent diagnoses and life difficulties. Thus, past research has focused profitably on the phenomenon of addictive behavior during early middle school as a predictor of future problems. Due to the success of this research, there is now a clear need to understand the precursors to such early addictive behavior. It is important to determine whether characteristics of elementary school children predict addictive behaviors as this could prove highly useful for understanding etiology and for developing improved interventions. We tested such relationships using data from a longitudinal study of 1906 children transitioning from the 5th to 6th grade, i.e., from elementary school to middle school. We specifically looked at whether individual differences in urgency, conscientiousness, and sensation seeking measured in the spring of 5th grade were predictive of engagement in addictive behaviors, including drinking, smoking, and binge eating during the spring of 6th grade. We hypothesized that higher levels of urgency, or the tendency to behave rashly under intense mood states, would be positively associated with all three addictive behaviors, while low levels of conscientiousness and high levels of sensation seeking would be more behavior-specific. These hypotheses were supported. After controlling for sex, pubertal status, and prior engagement in addictive behaviors, we found that urgency at wave 1 was predictive of drinking ($p < .05$), smoking ($p < .05$), and binge eating ($p < .01$) at wave 2; low conscientiousness at wave 1 was predictive of drinking ($p < .05$), and smoking ($p < .01$) at wave 2; and sensation seeking at wave 1 was predictive of smoking ($p < .05$) at wave 2. These results highlight the importance of understanding the relationship between individual differences and addictive behaviors during the transition from elementary to middle school. Understanding differences in emotions-driven rash action (urgency levels) may be of particular interest. Risk for early onset drinking, and also risk for other addictive behaviors, is heightened in individuals to tend to act rashly when emotional. This research was supported by NIAAA.

0304

INTERACTIVE EFFECTS OF AGE AND EMOTION REGULATION FOR ADOLESCENT ALCOHOL USE

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The purpose of the present study was to understand age differences in the association between emotion regulation and adolescent alcohol use. We hypothesized that early adolescents' likelihood of alcohol use would be more strongly influenced by their interpersonal emotion regulation skills than older adolescents, given that peer influence and conformity spike in early adolescence, whereas intrapersonal emotion regulation and relationship interdependence are better developed in older adolescents.
Participants in the present study were 183 adolescents recruited from a psychiatric inpatient facility in the northeastern United States for a larger study of adolescent mood, behavioral, and alcohol use disorders. These adolescents were divided into two age-based groups: 66 adolescents aged 13–14 (younger group) and 117 adolescents aged 15–17 (older group). Adolescents completed the Bar-On Emotional Intelligence (EQ) questionnaire, Interpersonal EQ subscale (Bar-On, 2000), and the SASSI-A2 (Miller, 1990) report of alcohol use in the past 6 months. Past 6 months' alcohol use was translated into a dichotomous variable with 1 = any use in the past 6 months and 0 = no use in the past 6 months. Binary logistic regression was used to test the odds of past 6 months alcohol use. All analyses accounted for participant sex.
There was a significant age by Interpersonal EQ interaction effect, such that Interpersonal EQ predicted significant differences in the odds of alcohol use among younger adolescents, but not among older adolescents, *OR*=1.05, 95% CI: 1.01–1.10, *B*=.05, *SE*=.02, *Wald*=6.65, *df*=1, $p<.01$. At the post hoc analysis stage, younger adolescents on the high end of Interpersonal EQ showed a slight, but significant, reduction in odds of use compared to younger adolescents on the low end of Interpersonal EQ. Consistent with the literature, there was a main effect for age: younger adolescents showed significantly lower odds of alcohol use, *OR*=.28, 95% CI: .15-.58, *B*=-1.27, *SE*=.34, *Wald*=13.86, *df*=1, $p<.001$.
In clinical populations of adolescents, the emotion regulation skills associated with the presence of alcohol use may differ by age. These findings suggest the importance of tailoring emotion-regulation-based interventions for adolescent alcohol users to the appropriate developmental stages.

0305

ALCOHOL USE BEHAVIORS FROM ADOLESCENCE TO YOUNG ADULTHOOD: AN APPLICATION OF THE DEVIANCE PRONENESS MODEL

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Objective: To identify pathways from adolescent behaviors to young adulthood pathological alcohol involvement.
Methods: A three-wave prospective study was conducted in the Greater Hartford Connecticut Area. Participants (n = 338, 44% male) were recruited from high schools and youth organizations. Mean (SD) age at waves 1 to 3 were 16.5 (1.6), 21.2 (1.6), and 26.0 (1.7) years old, respectively. The follow-up retention rates were 83% at wave 2 and 72% at wave 3. Subjects completed SSAGA as well as a battery of other tests/instruments/self-reported questionnaires including AEQ, Epstein's CTI, FHAM, MAST, PASAT, Perceived Social Support–Friends, Porteus Maze Test, PANAS, Revised NEO Personality Inventory, WRAT, and Zuckerman's SSS Form. Structural equation model (SEM) was employed to evaluate a range of possible models under the deviance proneness/problem behavior framework.
Results: A number of pathways were identified. (1) Paternal substance dependence/antisocial personality disorder predicted adolescence sensation seeking behaviors, which predicted late-adolescence positive alcohol expectancy, which ultimately predicted young adulthood pathological alcohol involvement. (2) Adolescence sensation seeking behaviors were associated with more conduct disorder symptoms, which predicted poor peer relationships, which predicted early initiation of alcohol, tobacco and marijuana, which was associated with negatively perceived parent-child interactions, which ultimately predicted adulthood pathological alcohol involvement. (3) Adolescence cognitive function predicted constructive thinking, which was associated with positive affectivity, which in turn predicted delayed age of first substance use as well as negative alcohol expectancies.
Conclusions: There were various pathways to young adulthood pathological alcohol involvement. These pathways were influenced by family history, childhood/adolescence characteristics, peer-and-family environment as well as expectancy and early experience with substances.

0306

SHORT-TERM RECANTING OF LIFETIME ALCOHOL, TOBACCO, AND MARIJUANA USE IN A PROSPECTIVE ADOLESCENT SAMPLE

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Reports of substance use are most commonly based on retrospective self-reports of use. The goal of this study was to characterize rates of 'recanting,' the denial of previously asserted lifetime substance use in a follow-up among those previously admitting it. We also examined the degree to which recanting of alcohol, tobacco, and marijuana use varied as a function of gender, race, age (grade), and changes in alcohol expectancies and peer/sibling use. Consistency in self-reported lifetime substance use over a six-month interval was examined using three waves of data from an ongoing multiple-age cohort longitudinal study. Participants were 6^{th}-8^{th} graders (N=749; 53% female; 71% White) who completed an in-person computer baseline survey and two follow-up web surveys at 6-months and for a subsample (N=603) at 12-months. We examined recanting between Waves 1 and 2, between Waves 1 and 3, and between Waves 2 and 3, due to the different modalities and given evidence in the literature of greater recanting in the wave immediately following the wave of first disclosure. Data were examined for the following behaviors: sipping of alcohol, full drink of alcohol, puffing of a cigarette, smoking a full cigarette, and any use of marijuana. Overall, rates of ever recanting at any wave were extremely high, ranging from 57% for lifetime reports of sip of alcohol to 84% for lifetime reports of marijuana use. Wave 1-3 and Wave 2-3 recanting rates were lower than Wave 1-2 recanting for sip of alcohol and smoking a cigarette. Subgroup differences were evident for recanting sip of alcohol, with sixth graders most likely to recant and those with increases in positive expectancies, peer drinking, and sibling drinking over time being least likely to recant. Several reasons have been offered for recanting, including intentional recanting (e.g., initial exaggeration and response editing as a means for socially desirable behavior) and unintentional recanting (e.g., re-definition of what constitutes substance use, misunderstanding of time frame, a shifting of situational context from a school to a non-school setting, and careless consideration of responses among this young age group). Given the short follow-up interval, it is unlikely memory/recall bias is a major factor. The present study supports concerns that measurement error undermines survey research on substance use and has considerable implications for the validity of drug use reports derived from longitudinal research.

0307

ADOLESCENTS' MISUSE OF ALCOHOL AND CONTROLLED MEDICATIONS: ARE THE RISK FACTORS THE SAME?

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Purpose: There are similarities between alcohol and controlled medications, since both of these psycho-active substances can be used legally and thus, are readily available to adolescents. This study compared factors associated with adolescents' past-year alcohol use and nonmedical use of controlled medications. We hypothesized that risk factors for both alcohol use and nonmedical use of controlled medications would be similar among adolescents.
Methods. The sample consisted of 2,744 secondary school students residing in the Midwest from December 2009-April 2010. Respondents had a mean age of 14.8 years; 50.4% were female, 64.1% were Caucasian and 30.6% were African-American. Respondents were given the *Secondary Student Life Survey* (SSLS), a web-based survey that was administered during school hours.
Results. Strong parental monitoring was significantly associated with lower odds of using alcohol (OR=0.85, 95% CI=0.79,0.92, p<.05) but not lower odds for nonmedical use (OR=.97, 95% CI=0.87, 1.07, ns). Risk factors for alcohol use included: being female (OR=2.3, 95% CI=1.0, 3.0, p<.05) and in high school (OR=4.9, 95% CI=3.4, 7.0, p<.05); past-year use of tobacco (OR=5.9, 95% CI=3.8, 9.1, p<.05), marijuana (OR=5.0, 95% CI=3.3, 7.7, p<.05), and nonmedical use of controlled medications (OR=2.6, 95% CI=1.6, 4.3, p<.05). Notably, there were fewer risk factors for nonmedical use when compared to alcohol use. These risk factors included: past-year alcohol use (OR=2.4, 95% CI=1.6, 3.8, p<.01) and marijuana use (OR=2.0, 95% CI=1.2, 3.3, p<.01). Both alcohol use (OR=1.13, 95% CI=1.11, 1.16, p<.05) and nonmedical use of controlled medications (OR=1.05, CI=1.02–1.08, p<.01) were associated with externalizing behaviors.
Conclusion. Alcohol and nonmedical use of controlled medications are independently associated with externalizing behaviors; however, generally they do not share risk factors. Strong parental monitoring reduces the likelihood of alcohol use by adolescents but not their nonmedical use of controlled medications.
Support: This study was supported by research grants R01DA024678 and R01DA031160 from the National Institute on Drug Abuse, National Institutes of Health.

0308

CONTEXTUAL INFLUENCES ON ADOLESCENTS' CRAVING FOR ALCOHOL IN THEIR NATURAL ENVIRONMENTS: AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY

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A variety of methods find craving among both community-based and treatment-seeking adolescent drinkers. Furthermore, like adults, adolescents display increased levels of craving in response to alcohol cues in reactivity paradigms. Despite the importance of craving in treating alcohol use disorders, relatively little is known regarding the relationship between craving and drinking in adolescents. Also, due to a reliance on retrospective self-reports, even less is known regarding the types of contextual factors that influence craving for alcohol in adolescents. To investigate these factors, ecological momentary assessment (EMA) was used to measure craving and drinking throughout an adolescent's typical day in their natural environments. Momentary data were collected from non-treatment seeking adolescent drinkers (n = 29) ages 15 to 19 years (44% male, mean age = 18 years) for approximately 1 week (mean = 6.5 days; SD = 1.7). Youth were prompted to complete momentary assessments of craving on a handheld electronic diary at randomly selected times throughout each day. During these assessments contextual factors were also recorded (e.g., location, others present). Only assessments collected prior to the first drinking episode on a given day were included in analyses to eliminate the confounding effects of alcohol intoxication on the variables of interest. Generalized estimating equations (GEE) revealed that craving predicted the likelihood and quantity of subsequent drinking that day, such that higher levels of craving predicted greater drinking. An association was also found between certain contextual variables and craving. Specifically, teens reported higher craving when they were with people with whom they usually drink as well as when in a setting where alcohol was available or visible (either directly or indirectly through advertisements). Neither gender nor day of week influenced these effects. Findings from this study indicate that adolescents do experience craving for alcohol, and these levels of craving are predictive of subsequent drinking. Craving for alcohol in adolescents is modulated by a number of factors including the visibility and availability of alcohol, and the surrounding social context's association with alcohol consumption.

0309

AUTONOMY FROM ALCOHOL USE AND CHANGES IN PEER DRINKING AS PROMOTIVE FACTORS AGAINST EARLY ADOLESCENT DRINKING

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Purpose: Adolescent drinking is associated with negative outcomes including injury and diminished academic performance. While peer socialization effects are a known influence among early adolescents, not all adolescents conform to their peer's drinking behaviors. Autonomy from alcohol use and changes in self-reported peer drinking behaviors were examined as potential promotive factors against adolescent drinking.
Methods: Waves 2 and 4 of four waves of longitudinal data from 2,758 seventh grade students (mean age= 12.81, SD= .62) from 20 communities across the United States were examined. The data were collected as part of a social media intervention trial. Although the experimental conditions did not have a significant effect, experimental condition, age and gender were controlled for in all analyses. A subset of at-risk students (those who reported that they had not yet been drunk, but their friends had been drunk at wave 2 – end of 7^{th} grade) was selected for analyses (n= 545). Generalized estimating equations were used to examine the influence of a sense of autonomy from drinking on students' plans to try alcohol in the next two years (assessed at wave 2) and self-reported drinking (one year later; at wave 4 – end of 8^{th} grade). A change in peer drinking behaviors between waves 2 and 4 was also assessed in predicting students' drinking behaviors at wave 4.
Results: Within this at-risk group, autonomy from alcohol use was found to be a promotive factor against plans to drink at wave 2 (O.R. = .50, $p < .001$) and self-reported drinking at wave 4 (O.R. = .70, $p < .001$). A one-unit increase in autonomy was associated with a 49.9% decrease in the odds of a student's plans to try alcohol in the next two years and a 29.1% decrease in the odds of a student's reporting having been drunk at wave 4. A total of 111 students reported their peers were no longer getting drunk at wave two. Reporting this shift was associated with an 88.5% decrease in the odds of a student reporting having been drunk at wave 4 (O.R. = .16, $p < .001$).
Conclusions: Autonomy from alcohol use and changes in peer drinking behaviors may act as promotive factors against the influence of peer socialization effects. Intervention and prevention specialists might use this evidence to develop initiatives that foster autonomy from alcohol use and promote shifts in peer group affiliation or peer drinking behaviors among early adolescents.

0310

THE ASSOCIATION BETWEEN DISCRIMINATION AND ALCOHOL DEPENDENCE AND EXTERNALIZING BEHAVIORS AMONG MINORITY TEENS: THE MEDIATING ROLE OF ALIENATION

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There has been an increased focus on the deleterious effects of discrimination on a variety of dimensions of adolescent health. Discrimination has been consistently associated with both alcohol use and externalizing behaviors in particular. Although discrimination is linked to negative outcomes, the underlying mechanisms which explain this relationship are not well understood. This study was conducted with data culled from Alcohol Treatment Targeting Adolescents in Need (ATTAIN; PI: Wagner), a NIAAA-funded randomized clinical trial examining the efficacy of a brief motivational substance abuse intervention for racially/ethnically diverse (74% Hispanic; 14% African-American and 12% Other) adolescents with substance use problems in Miami, Florida. The sample included 508 adolescents with a mean age of 16.74 years old (SD 1.21). Youth were referred through the Miami-Dade County, Florida, juvenile justice system; most of the youth (66%) were not court mandated and voluntarily participated in treatment. Model fit indices indicated a good overall fitting model with no sources of ill fit. Examination of the statistically significant path coefficients revealed that for every one unit increase in perceived discrimination, alienation increased by .29 units, on average. Moreover, for every one unit increase in alienation the likelihood of having a diagnosis of alcohol dependence or externalizing behaviors increased by .004 and .034 respectively.Intervention efforts often target individual, peer and family level behaviors and neglect to explore system level factors such as how discrimination impacts behavior; this has important clinical implications. There is a paucity of research examining treatment related issues among racial/ethnic minority adolescents with substance use problems. Perceived racial/ethnic discrimination is a common and understudied phenomenon among African American and Hispanic/Latino teenagers. To better meet the treatment needs of racial/ethnic minority youth with substance use problems, it is critical to examine drivers of alcohol use unique to these subgroups.

0311

ADOLESCENT PERSONALITY TRAITS AS PREDICTORS OF ALCOHOL USE SEVERITY

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The goal of the current study was to examine the relations between sensation seeking, impulsivity, and alcohol outcomes in a sample of treatment-seeking adolescents. Personality traits such as impulsivity (Eysenck & Eysenck, 1977) and sensation seeking (Zuckerman, 1984) are related to involvement in risky behaviors.The purpose of these analyses is to present current data regarding these constructs and alcohol outcomes in an adolescent outpatient substance treatment program.
Population and Method. Thirty adolescents ages 12–17 (mean = 15.8), 80% male, 80% White. Participants completed a survey via online interface (Redcap).
Measures. The RAPI is an 18-item self-report screening tool for assessing adolescent problem drinking. RAPI measures the frequency with which an adolescent has experienced negative consequences of drinking alcohol. Eysenck Impulsivity Questionnaire, adolescent version, assessed the personality traits of impulsivity and venturesomeness (sensation seeking). The greatest number of drinks reportedly consumed in a 24-hour period during the previous 3-months measured alcohol use severity.
Results. Multiple regression analysis was used to test if personality traits were related to drinking outcomes. The results of the regression indicated that sensation seeking (venturesomeness), but not impulsivity, was significantly related to alcohol consumption (β=.68, p<.01), such that high levels of sensation seeking were related to a greater amount of drinks consumed. Impulsivity, but not sensation seeking, was significantly related to the frequency of alcohol consumption (β =.57, p<.05), such that higher levels of impulsivity were related to more frequent drinking. Impulsivity, but not sensation seeking, was significantly related to problem drinking over and above sensation seeking (β=.52, p<.05).
Conclusions. Impulsivity and sensation-seeking were associated with alcohol use and related problems. Sensation seeking was found to be related to the quantity of alcoholic beverages consumed, whereas impulsivity was found to be related to the frequency of alcohol use as well as alcohol-related problems. These analyses support that alcohol use frequency and negative consequences of alcohol use are best explained by impulsivity. Increased alcohol consumption during a 24-hour period is better explained by sensation seeking than impulsivity.

0312

ASSOCIATIONS BETWEEN MENTAL HEALTH PREDICTORS, DRINKING MOTIVES, AND ALCOHOL USE SEVERITY IN ADOLESCENTS

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The self-medication model of drinking has been studied extensively with mixed results. The goal of the current study was to examine the relations between depression, anxiety and drinking motives; as well as between drinking motives and alcohol outcomes.
Population and Method. Adolescents aged 12–17 (N=30, mean age =15.8; 80% male; 80% Caucasian), referred to a University-based outpatient addiction treatment program completed self-rated questionnaires during their intake appointment. The Child Depression Inventory and the Screen for Child Anxiety Related Emotional Disorders assessed depression and anxiety levels, respectively. The Drinking Motives Questionnaire assessed four motives (enhancement, social, coping, and conformity) for drinking. The number of drinks consumed in a 24-hour period during the previous 3-months measured alcohol quantity. The Rutgers Alcohol Problem Index assessed alcohol-related problems.
Results. Multiple regression was used to examine the relationship between depression, anxiety and the drinking motives. Anxiety (β = .57, p < .05), but not depression (β = .07, p = .75), was significantly related to conformity drinking motives. Furthermore, anxiety (β = .47, p = .05), but not depression (β = -.24, p = .31), was significantly related to coping drinking motives. As expected, neither depression nor anxiety was significantly related to enhancement or social drinking motives. Additional models were estimated to examine the relations between the four drinking motives and alcohol use severity. Enhancement motives (β = .62, p < .05), but not coping, social, or conformity motives were significantly related to the number of alcoholic drinks consumed in a 24-hour period. Furthermore, enhancement motives (β = .66, p < .05), but not coping, social, or conformity motives were significantly related to alcohol-related problems.
Conclusions. In the present study, anxiety was predictive of coping drinking motives, but coping motives did not predict alcohol use severity. In contrast, the adult literature suggests that coping drinking motives predict the most severe and problematic drinking severity. This discrepancy may suggest that the connection between coping motives and alcohol outcomes has not yet been established in teens and points to the importance of early alcohol use prevention, particularly with individuals who exhibit anxiety symptoms.

0313

ROLE OF PARENT AND CHILD PSYCHOPATHOLOGY IN SUICIDE ATTEMPTS AMONG CHILDREN OF ALCOHOLICS

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Purpose: Alcohol use disorders (AUD) confer risk for suicide attempts (SA) through the throes of chronic drinking and through comorbid conditions that may accompany AUD including depression and externalizing psychopathology (e.g., drug use disorder, conduct disorder). When such psychopathology is present in parents it is more likely to develop in children and to influence risk of SA in adolescence. We conducted a rare study of parental influences on SA during adolescence among children of alcoholics (COAs) and used a prospective study design and gathered detailed data from both parents and offspring.
Methods: The study is a CDC-funded, secondary analysis of Collaborative Study on the Genetics of Alcoholism (COGA) data. We examined a cohort of children who were on average age 9½ years at enrollment (Time 1, childhood) and who were reassessed approximately five years later, prior to reaching age 18 (Time 2, adolescence). Structural equation models (SEM) examined influences of parental psychopathology on youth psychopathology and youth SA. We ran separate SEM models to examine father-child (N=290), mother-child (N=394), and either/both parent-child (N=418) associations. There was a history of AUD in 221 (76.2%) fathers, 165 (41.9%) mothers, and 341 (81.6%) either parent. The primary outcome was SA over follow-up, assessed at Time 2.
Results: Nineteen adolescents reported SA during the 5 year follow up interval. We found evidence of ''transmission'' of risk factors for SA from parents to offspring, with parental antisocial personality disorder predicting conduct disorder symptoms in offspring both during childhood and adolescence (parent-child model, father-child model) and maternal AUD predicting conduct disorder symptoms during childhood (mother-child model). We did not find evidence to support transmission of depression from parents to offspring either during childhood or adolescence. Interestingly, none of the paternal, maternal or parental variables showed a statistically significant association with SA during adolescence but offspring own psychopathology was associated.
Conclusion: The study was novel because it examined parental influences on SA and risk factors for SA among COA's during the transition from childhood to adolescence. Results provided mixed support for hypothesized parent-child associations. The low number of suicide attempts during adolescence limited statistical power, potentially explaining nonsignificant findings.

0314

EFFECTS OF NALTREXONE ON ADOLESCENT DRINKING

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Alcohol dependence (AD) is a major reason for substance abuse treatment admissions among teenagers. Despite clinical demand for effective interventions for youth, less than one-third of treated youth experience sustained benefit from existing treatments. While medication development research has advanced treatment for adults, double-blind pharmacotherapy research with adolescents is virtually nonexistent. Our major objective was to test the effects of naltrexone (NTX) – one of the most efficacious medications for treating adults with AD – on drinking, craving, and subjective responses to alcohol intoxication among adolescents. To this end we captured the real-time occurrence of adolescents' subjective responses to alcohol in their natural environments using ecological momentary assessment (EMA) methods. Non-treatment seeking adolescent drinkers (n = 29; ages 15–19 years) were enrolled in a double-blind, placebo-controlled, crossover study (55% female, 69% Caucasian, and 83% non-Hispanic; 72% met criteria for an alcohol use disorder). Participants completed two 10-day medication periods in which they received NTX (50 mg/day) or matched placebo in randomized and counterbalanced order; the two arms of the study were separated by at least a 4-day washout period. During each condition, youth completed momentary assessments of mood and craving immediately before and after the first three drinks of a drinking episode using a handheld electronic diary. Medication and EMA compliance was high across the trial. Generalized estimating equations (GEE) showed that teens consumed fewer drinks per day and were less likely to drink heavily while taking NTX compared to placebo ($p < .05$). In addition, youth reported less craving and tension and more sedation after drinking while taking NTX as compared to placebo (p values < .05). Notably, decreases in craving were associated with reductions in subsequent drinking that day. Findings of this initial study show that NTX decreased drinking and altered subjective responses to alcohol among teens and support the need for larger-scale clinical trials with longer-term follow-ups. The clinical utility of NTX in this population may be especially high given that adolescents and young adults are more likely to engage in controlled drinking, as opposed to adhering to an abstinence-only model of treatment.

0315

SOLITARY ALCOHOL AND DRUG USE AMONG ADOLESCENTS INVOLVED IN THE CHILD WELFARE SYSTEM

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Background: While alcohol and drug use during adolescence is often motivated by social reasons, solitary substance use is not uncommon. Studies indicate that 29% of high school students (Beck et al., 1999) and 17% of 8th graders have ever drank alone (Tucker et al. 2006). Given that a sizable minority of adolescents appear to have a history of solitary alcohol or drug use, surprisingly little research has focused on understanding this potentially vulnerable group. The purpose of the current study is to examine the prevalence of solitary alcohol and drug use among a high-risk sample of adolescents. Specifically, we investigate the demographic profile of solitary substance users and how this group might differ from other teens in key psychosocial and behavioral domains (e.g. family and peer relations, psychological well-being and other alcohol and drug related behaviors).
Methods: This study utilizes data from the National Survey of Child and Adolescent Wellbeing-II (NSCAW-II), a large nationally representative study of youth who have had contact with the child welfare system. The subset of participants (ages 15 to 18 years old) all reported a lifetime history of alcohol or drug use (n=472). Logistic regression analyses was used to test associations between solitary alcohol and drug use, demographic characteristics (e.g. age, race, gender) and psychosocial/behavioral domains. Analyses were weighted to adjust for sample design and nonresponse.
Results: A quarter of the youth (24%) reported a history of solitary alcohol or drug use. Results of logistic regresssion indicate solitary substance use was not significantly associated with age, race/ethnicity, gender, heavy-episodic drinking, PTSD, relationship with parents, or the adolescents' number of friends ($p>0.05$). Solitary alcohol and drug use was, however, significantly associated with depression, using alcohol or drugs to gain acceptance, the amount of free-time spent with friends and other illicit drug use (e.g. cocaine, heroin) ($p < 0.05$). There were also significant interaction effects between race/ethnicity and depression.
Discussion: Results of this study provide insight on the characteristics of adolescents who engage in solitary alcohol and drug use and highlight the clustering of problem behaviors during adolescence. These findings may be useful in shaping intervention efforts to reduce solitary alcohol and drug use and coping motivations for substance use among adolescents.

0316

RESILIENCE IN CHILDREN OF ALCOHOLICS AND CONTROLS: INDIVIDUAL CHARACTERISTICS AND PARENT-CHILD INTERACTION

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Children of alcoholics (COAs) are at higher risk for developing alcohol and drug related problems and substance use disorder than controls. This study examined factors in early adolescence (age 12–14) that predicted resilience in COAs in late adolescence and young adulthood (age 18–20). Resilience is successful adaptation in spite of adversity (Masten, 2001; Luthar et al., 2000). In this study, resilience was operationalized as an absence of substance use disorder, alcohol related problems and drug related problems among COAs. Participants were 397 boys and 155 girls participated in the Michigan Longitudinal Study (Zucker et al., 2000). Based on previous research, we selected eight factors in early adolescence that were hypothesized to predict resilience in subsequent developmental periods. They include individual characteristics (i.e., internalizing problems, externalizing problems, self-esteem, peer functioning, and sleep problem) and parent-child interaction variables (i.e., parental monitoring, parental bad mood and sadness as reported in the parental daily report).
Data were collected by instruments that have established reliability and validity – Youth Self Report (behavioral problems), Harter Perceived Competence Scale (peer functioning, self-esteem), Parental Monitoring Form for Youth (parental monitoring), Parental Daily Report (parental bad mood and sadness) and the Diagnostic Interview Schedule (substance use disorder diagnoses).
Logistic regression models were used to analyze the relationship between early adolescence predictors and three indicators of resilience – substance use disorders, alcohol related problems (e.g., binge drinking) and drug related problems (e.g., miss school or work). Externalizing problems at age 12–14 predicted the presence of substance use disorders at age 18–20. In contrast, IQ scores and parental bad mood at age 12–14 negatively predicted the presence of substance use disorders. Moreover, externalizing problems and parental sadness predicted the presence of alcohol-related problems. Lastly, having trouble sleeping predicted the presence of drug-related problems. Further analyses showed that these factors have similar effects for both COAs and controls. To summarize, externalizing problems, sleep trouble, as well as parental bad mood and sadness were predictive of resilience in COAs and adaptive functioning among controls. (Supported by NIAAA Grants AA00304 and AA07065).

0317

PAIN AND ALCOHOL USE AMONG OLDER ADULTS: PROSPECTIVE EVIDENCE FROM THE HEALTH AND RETIREMENT STUDY

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This prospective study addressed whether late-middle-aged adults' baseline pain affects their use of alcohol over a subsequent 8-year interval. At baseline in 1996, then 2, 4, 6, and 8 years later, a national sample of Health and Retirement Study participants (*N*=5,446; *M*=60 years) provided information about their pain (number of painful medical conditions, pain severity, pain interference) and their use of alcohol (drinking problems; frequency and amount of alcohol consumption). Logistic regression and two-part latent growth modeling were used to determine concurrent and prospective associations between participants' baseline pain characteristics and their use of alcohol. At baseline, 57% of participants reported having painful medical conditions; among participants with pain, average pain severity was moderate and likely to interfere with usual activities. At baseline, about half of participants reported recently consuming alcohol; on average, drinkers consumed 1-2 drinks per drinking occasion and drank 3 times per week. About 23% of participants had drinking problems. Participants with more numerous painful medical conditions, and with more severe and debilitating pain, were more likely to have drinking problems. Having more painful medical conditions at baseline predicted lowered likelihood of consuming alcohol over the next 8 years, but this did not influence the rate of change in likelihood of consuming alcohol over 8 years. Among participants who drank, each of the baseline pain predictors was associated with lower frequency of drinking and a faster rate of decline in frequency of alcohol consumption over the next 8 years. Some of these associations were moderated by African American background; for example, non-African Americans with baseline pain interference declined in drinker prevalence from 43% to 36% from 1996 to 2004; African Americans with baseline pain interference stayed about the same (27%) in drinker prevalence during the same interval. In sum, having more numerous, severe, and debilitating painful conditions at entry to later life predicts lower likelihood of drinking, lower quantity and frequency of drinking, and faster rate of decline in frequency of drinking over the subsequent course of later life. However, some of these associations are moderated by African American background, and having more pain is associated with having more drinking problems in late-middle-age.

0318

DIFFERENTIAL EFFECTS OF MODERATE ALCOHOL CONSUMPTION ON PERFORMANCE AMONG OLDER AND YOUNGER ADULTS

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Overview: Studies exploring differential effects of acute alcohol consumption on younger and older adults are lacking within the field of alcohol research, especially those using moderate doses. Previous studies addressing this question have tended to use complex behavioral tasks which are too broad to isolate specific neurocognitive processes affected by both alcohol and aging. Compromises in cognitive efficiency (i.e. the ability to respond both quickly and accurately) have previously been identified in both elderly and acutely intoxicated individuals.
Method: The present study employed a visual-spatial, two-choice reaction time task to evaluate the interactive effects of aging and alcohol on cognitive efficiency. Our primary outcome measure was an efficiency ratio derived from each participant's response accuracy (ACC) and mean reaction time (RT) (%correct/RT). Younger (25 – 35) and older (55 – 74) participants were randomly assigned to receive either a placebo or moderate alcohol dose intended to produce a peak BrAC of 0.04%. Participants performed the task at peak alcohol levels.
Results: A significant interaction between age group and dose assignment was observed ($F_{3,55}$=4.86, p=.03). Younger participants who received alcohol performed significantly better than their older counterparts (p=.003) despite no differences in performance between the two groups at placebo (p>.9). Additional correlational analyses between ACC and RT suggested that older adults increased response time to improve accuracy and maintain efficiency when they received alcohol (r=.46, p=.03). This pattern was not observed in any other experimental group.
Conclusion: These data suggest that individuals may experience a change in the effects of even low to moderate alcohol doses on their performance as they transition to older age. Unfortunately, due to the presumed safety of moderate alcohol doses and a lack of studies investigating the interactive effects of acute alcohol consumption and aging, most individuals are unlikely to expect such a change or adjust their behavior to account for this outcome. These data may be of particular importance to the operation of motor vehicles if older adults who have consumed alcohol increase their reaction times (slow down) to enhance the accuracy of their performance.

0319

THE IMPACT OF RETIREMENT AND SOCIAL SUPPORT ON DRINKING AMONG MIDDLE-AGED AND OLDER ALCOHOLICS

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Aggregate evidence suggests that retirement has a negative impact on middle-aged and older adult drinking, increasing it slightly. The context of retirement and changes in social milieu that occur with retirement are stronger predictors of drinking frequency, quantity or problems than retirement itself. Little research has examined the effects of both retirement and social support on alcoholics using longitudinal methods that include clearly defined measures of drinking.
Purpose: This study aimed to examine the relationships between social support, retirement, and drinking (and its consequences) among alcoholics 50 and older.
Method: Secondary data analysis was performed using data from the Life Transitions Study (LTS). LTS was a longitudinal panel study of 364 treated and untreated alcoholics who were followed for 36 months. Data were collected every 6 months on retirement status, social support, and drinking. In this analysis, only those aged 50 and older were included (N=133). Generalized estimating equations were used to determine the independent, long-term effects of retirement and social support on drinking over time, specifically percent days abstinent (PDA), heavy drinking days (HDD), drinks per drinking days (DDD), and drinking consequences (Short Inventory of Problems, SIP). Retirement's effect on social support was also explored.
Results: Retirement was a dynamic state, as 39.3% of the sample reported being retired during at least one time point, but not all remained retired. Although being retired predicted fewer HDD (p<.05), this relationship was not significant when controlling for time. A trend relationship emerged for retirement predicting negative social support (p<.06). Controlling for time, negative social support was found to be a significant positive predictor (p< .02) of SIP scores. Positive social support was found to be a significant negative predictor of DDD. All other relationships were at the trend level and insignificant when controlling for time.
Conclusion: Contrary to predictions, results show a weak direct effect of retirement on drinking outcomes among older alcoholics, decreasing drinking intensity. Social support was a consistent significant predictor of drinking outcomes; negative social support led to increased alcohol problems and positive social support led to decreased drinking intensity. This suggests the importance of retirees cultivating positive social support to prevent alcohol problems.

0320

UNDERSTANDING AND RESPONDING TO ALCOHOL/SUBSTANCE ABUSE IN ELDERS BY ADULT PROTECTIVE SERVICES

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Purpose: The purpose of this exploratory study is to identify how Adult Protective Services (APS) professionals understand and respond to the problem of alcohol and/or substance abuse among older adults reported for self-neglect. APS is an agency that investigates reports of older adults in crisis. Alcohol/substance use or abuse often contribute to the problems endured by the client. Alcohol/substances used in moderate amounts by older adults can contribute to problems due to age-related physical changes in metabolism, medical conditions, or adverse medication interactions.
Methods: 25 semi-structured expert interviews (a convenience sample gathered through referral) were conducted by telephone with experts in the field of APS. The interview elicited a description of a typical self-neglect case investigation process, followed by questions concerning alcohol use, substances, and capacity assessment of the older adults they investigate for self-neglect. The interviews were audio-taped, transcribed, and analyzed by theme and content using ATLAS.ti.
Results: The interviews reveal that alcohol and substance abuse is understood by APS professionals as a problem for many older adults reported for self-neglect. However, these problems are apparent only when they are extreme, characterized by near constant drinking or other visible use patterns. For clients whose alcohol or substance use is not visible, yet still consequential for the subject, the contributing factor of alcohol or other substance use may go unrecognized. Capacity assessment is often fraught by the presence of alcohol or other substances, and use patterns may conceal underlying health or other problems that could be remediated. APS workers feel that they are limited in their intervention when alcohol or other substances are in use by the subject undergoing investigation.
Conclusions: APS workers need better tools and increased awareness of the ways alcohol and substances contribute to the problems they investigate. Further research is needed to 1) develop training programs for APS workers that address alcohol/other substance use among elders and its impacts; 2) identify obstacles to intervention with older adults who use alcohol/other substances and may be self-neglectful; 3) establish new tools and strategies for APS workers to employ in these complex social and behavioral situations.

0321

AGE INDEPENDENT EFFECTS OF ACUTE MODERATE ALCOHOL CONSUMPTION ON EARLY INDICES OF ATTENTIONAL PROCESSING

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Introduction. Despite the purported benefits of a moderate drinking lifestyle for older adults, little systematic research addressing acute effects of moderate drinking episodes in older drinkers is reported (Nixon, 2009). The current study utilizes a remember/ignore task, allowing us to examine potentially differential effects of alcohol and/or aging on top-down attentional control; i.e, 'enhancement' of attention to relevant stimuli vs. 'suppression' to irrelevant stimuli (Gazzeley et al., 2008). Based on existing data, we predicted older drinkers would perform more poorly than young drinkers on neurophysiological indicators of suppression while indicators of enhancement would be less affected. We asked whether low dose alcohol and age would interact such that older adults receiving alcohol would show greater neurophysiological alteration than younger adults on either measure.
Methods. 30 younger (25–35 years old; 12 women) and 17 older (55–70 years old; 9 women) community-dwelling participants were screened to retain healthy moderate drinkers. Subjects were administered either placebo or a dose of alcohol targeted to a BAC of 40 mg/dl or 65 mg/dl (Watson et al., 1981). Following absorption, subjects completed testing. P1 amplitude and N1 latency in averaged epochs for each condition (enhance/suppress/passive viewing) within each subject were determined by consensus of two research assistants. For this preliminary report, active doses were collapsed.
Results. Mixed models ANOVA (repeated measure: task condition) revealed no main or interactive effects of age (F's<1); however, an interaction of task condition and dose for N1 latency was detected ($F_{2,86}$=3.88, p=0.03) with the active alcohol dose disrupting enhancement (i.e., increased N1 latency relative to placebo; t_{45}=2.41, p=0.02) but not suppression (t_{45}=0.56, p>0.57). No main effects or interactions were noted for P1 amplitude (F's<0.70).
Discussion. These preliminary results suggest that administration of low-to-moderate alcohol doses disrupts top-down enhancement of attention to relevant stimuli independent of age group. Contrary to expectations, suppression was not affected by age or alcohol. While provocative, these preliminary findings demand further study focusing on a) potential dose-dependent alcohol effects and b) comparisons using a no treatment group, given previous work showing differential sensitivity to the placebo effect between younger and older drinkers (Gilbertson et al., 2010).

0322

ALCOHOL REGULATES EXPRESSION OF GLIAL-DERIVED NEUROIMMUNE FACTORS IN AN AGE-DEPENDENT MANNER

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Alcohol use occurs across the lifespan beginning in adolescence through adulthood and extending into senescence. Ethanol-induced pathology varies with age and includes changes in neurogenesis, neurodegeneration, and glial cell activation. Ethanol-induced changes in glia have the potential to contribute to neuronal survival and function as well as to neuronal loss and dysfunction. Recent studies indicate an emerging role of glial- derived neuroimmune molecules in alcohol abuse and addiction. In this study, we compared the effects of ethanol on chemokine and cytokine expression in the hippocampus and cerebellum of adolescent (P35-45), adult (P84), and aged (P385-432) C57BL/6 mice. Mice were treated via gavage with 6 g/kg ethanol (15% w/v as a split dose) for 10 days and tissue was harvested one day post-treatment. Control animals received an equal volume of water by gavage. Ethanol increased mRNA levels of the chemokine MCP-1 in both the hippocampus and cerebellum relative to control animals. It more strongly induced MCP-1 levels in adult and aged animals compared to adolescents. The cytokine IL-6 was selectively increased by ethanol in the adult cerebellum but not the hippocampus. The induction of IL-6 was not observed in the cerebellum of adolescent and aged animals. In contrast, mRNA levels of the cytokine IL-1β were decreased in adolescent but not adult or aged hippocampus. In this paradigm, ethanol did not affect mRNA levels of the cytokine TNF-α at any of the ages investigated. It will be important to evaluate the significance of these changes in the context of astrocytic and microglial cell activation in these regions. Collectively these data indicate an age- and region-specific susceptibility to ethanol regulation of neuroinflammatory and addiction-related molecules. These studies could have important implications concerning alcohol-induced neuropathology and alcohol addiction across the human lifespan. Funded by NIH awards AA18834, AA18839, and AA19108.

MONDAY – Posters 1–321/ Abstracts 323–643
1. GENETICS
a. Lab Animal – behavioral 1–17/323–339

0323

IDENTIFYING GENES THAT INFLUENCE ACUTE ETHANOL RESPONSIVE BEHAVIORS IN CAENORHABDITIS ELEGANS

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Alcohol abuse has a poorly understood etiology with both genetic and environmental influences. One factor influencing drinking behavior and subsequent liability for dependence is variation in genes encoding ethanol metabolism machinery, alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH). We directly tested the effects of altering the function of these enzymes on ethanol responsive behaviors in worms. We tested two ADH enzymes encoded by the genes *sodh-1* and *H24K24.3*. Animals carrying a deletion of *sodh-1* are acutely hypersensitive to ethanol's depression of locomotion, but animals with knockdown by RNA interference (RNAi) of *H24K24.3* are not. We found that tissue ethanol concentration is increased in *sodh-1* deletion animals, but not in *H24K24.3* knockdown strains. Importantly, we found that both strains develop robust acute functional tolerance (AFT) to ethanol, indicating that these enzymes are dispensable for this process. The nematode genome encodes ALDH enzymes that are highly conserved compared with human ALDHs. Knockdown by RNAi of *alh-6* and *alh-13* resulted in hypersensitivity of ethanol's depression of locomotion. Interestingly, internal tissue ethanol concentrations in these two strains are higher than wild type, suggesting that the lack of ALDH function causes a buildup of acetaldehyde, which can be converted by ADH into ethanol. Collectively, these data suggest that altered ethanol metabolism in worms results in a mild but detectable effect on ethanol response behaviors. A second risk factor for alcohol dependence in humans is an individual's naive level of response to ethanol. The progression from initial and acute ethanol responses to dependence is not well understood, but many studies have shown that acute ethanol administration induces changes in gene expression, which may contribute to later dependence behaviors. Our major goal is to identify genes and molecular pathways that are important in mediating ethanol responsive behaviors. We will identify ethanol responsive genes by performing a series of microarray experiments at different times and doses of ethanol exposure. Candidate genes from this analysis will be tested for their functional relevance in ethanol responses. We will test several ethanol-responsive behaviors including those measuring initial sensitivity and the development of AFT, two components of the phenotype in humans that is described as initial level of response.

0324

COMPARATIVE GENETICS OF THE TARGETS OF TWO CNS DEPRESSANTS: IDENTIFICATION OF ETHANOL- AND TOLUENE-RESISTANT *C. ELEGANS* MUTANTS

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Toluene is an abused inhalant that, like ethanol, fits the pharmacological profile of a classic central nervous system depressant. The goal of this work is to better understand the action of ethanol and toluene on specific targets in the brain. We have taken the approach of screening for novel *Caenorhabditis elegans* mutants that are resistant to the effects of ethanol or toluene on locomotion behaviors. The rationale for this approach is that mutants that are resistant to the effects of a drug may have a mutation specifically affecting a gene encoding a pharmacological target of the drug. The conservation of the nervous system of *C. elegans* and humans at the molecular level means that targets identified in worms are likely to also be present in humans.
Both ethanol and toluene generate concentration-dependent decreases in the speed of locomotion of wild-type *C. elegans*, however, the pattern of locomotion that is displayed by ethanol-intoxicated worms is distinct from that shown by toluene-intoxicated worms, suggesting that the drugs are likely to have at least some non-overlapping effects. This conclusion is further supported by the observation that loss-of-function mutants of *slo-1* (KCNMA1) and *rab-3* (Rab3A), which are significantly resistant to ethanol effects, show a wild-type sensitivity to toluene.
Using random mutagenesis of a wild-type strain, we have screened for and isolated six new mutants that are resistant to ethanol and two mutants that are resistant to toluene. Importantly, most of these ethanol- or toluene-resistant mutants do not display resistance to the other drug, with one exception. Together, these mutants suggest that there are overlapping and non-overlapping mechanisms by which these drugs affect neurons. The genes affected by mutations in these mutants are being identified using genetic mapping and whole-genome sequencing methods. Once identified, the genes and the products they encode will provide significant insight into the effects of these drugs on the nervous system, including the shared and distinct mechanisms of action of the two drugs.
Supported by NIAAA Grant AA016842 (AGD) and NIDA Grant DA020553 (KLS).

0325

MEMBRANE LIPID ENVIRONMENT MODULATES THE DEVELOPMENT OF ACUTE FUNCTIONAL TOLERANCE TO ETHANOL IN CAENORHABDITIS ELEGANS

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Variation in an individual's initial level of response to ethanol is strongly correlated with the propensity to develop alcohol abuse disorders, and genetics strongly impacts that level of response. Our laboratory studies the genes influencing the two major components of level of response, initial sensitivity and the development of acute functional tolerance (AFT). We use the model organism *Caenorhabditis elegans*, a nematode worm with a simple and well-characterized nervous system that is highly conserved with the mammalian brain, because of the ease of genetic manipulation and behavioral testing in this animal. We performed a forward genetic screen for mutants that were unable to develop AFT. From this screen, we recovered mutations in the genes *ctbp-1* and *pag-3*; these genes encode transcription factors that repress transcription of many genes (Nicholas, H. *et al.*, J Mol Biol 375:1–11). Among the targets of these genes is the triacylglycerol (TAG) lipase-encoding *lips-7* gene; in a *ctbp-1* mutant, *lips-7* is overexpressed, which results in a decrease in TAG levels (Chen, S. *et al.*, PNAS 106(5): 1496–501). We found that while an increase in *lips-7* expression resulted in a decrease in the ability of animals to develop AFT, a loss of *lips-7* function resulted in a faster development of AFT, and a decrease in initial sensitivity to ethanol. This was not a result of a general change in stored fat levels, as changes in fat levels caused by a variety of mutations did not correlate with ethanol response. In contrast, changing membrane composition did profoundly impact ethanol response; animals that were depleted of cholesterol were both hypersensitive to ethanol initially and also unable to develop AFT. Altering *lips-7* levels was able to suppress gain-of-function mutations of the transmembrane ethanol target BK channel SLO-1, further supporting the hypothesis that membrane architecture is important in the development of AFT. Together, these data suggest a model in which modulation of protein function underlies the development of AFT and requires membrane microarchitecture that is influenced by TAG and cholesterol levels.

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0326

CHLORIDE INTRACELLULAR CHANNELS (CLICS) MODULATE ACUTE ETHANOL BEHAVIORS IN DROSOPHILA, C. ELEGANS AND MICE

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Identifying genes that influence behavioral responses to alcohol is critical for understanding the molecular basis of alcoholism and ultimately developing therapeutic interventions for the disease. Using an integrated approach that combined the power of the *Drosophila*, *C. elegans* and mouse model systems with bioinformatics analyses, we established a novel, conserved role for Chloride Intracellular Channels (CLICs) in alcohol-related behavior. CLIC proteins might have several biochemical functions including intracellular chloride channel activity, modulation of TGF-β signaling, and regulation of ryanodine receptors and A-kinase anchoring proteins. We initially identified vertebrate *Clic4* as a candidate ethanol-responsive gene via bioinformatic analysis of data from published microarray studies of mouse and human ethanol-related genes. We confirmed that *Clic4* expression was increased by ethanol treatment in mouse prefrontal cortex and also uncovered a correlation between basal expression of *Clic4* in prefrontal cortex and the locomotor activating and sedating properties of ethanol across the BXD mouse genetic reference panel. Furthermore, we found that disruption of the sole *Clic Drosophila* orthologue significantly blunted sensitivity to alcohol sedation in flies, that mutations in two *C. elegans Clic* orthologues, *exc-4* and *exl-1*, altered behavioral responses to acute ethanol in worms, and that viral-mediated overexpression of *Clic4* in mouse brain decreased the sedating properties of ethanol. Together, our studies demonstrate key roles for *Clic* genes in behavioral responses to acute alcohol in *Drosophila*, *C. elegans* and mice. Ongoing studies are exploring the possibility that *Clic4/Clic* influences ethanol sensitivity by functioning within the TGF-β and other signaling pathways.

0327

USING A MUTAGENIC AND TRANSGENIC SCREEN TO UNCOVER THE MOLECULAR BASIS FOR THE ACTION OF ETHANOL ON THE BK CHANNEL

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A highly conserved target protein that is emerging as a key mediator for behavioral intoxication and tolerance is the big conductance potassium (BK) channel. The BK channel is activated by low levels of alcohol ($\sim$20 mM) across many species including *C. elegans*, rodent and human, which is equivalent to the legal level of intoxication. In mice, this channel contributes to both behavioral intoxication and tolerance. A gain-of function mutation in the BK channel results in hypersensitivity to alcohol in humans. In addition, a genetic screen performed in the model organism *C. elegans* discovered that null mutations in the worm ortholog of the BK channel, SLO-1, produced an extreme level of resistance to behavioral intoxication. In order to elucidate the interaction of ethanol and the BK channel at the molecular level, we are using two genetic approaches with *C. elegans* to uncover novel non-null mutations in the worm and human BK channel gene that result in resistance to behavioral intoxication. We will be able to study the human BK channel in the worm because we have "humanized" the worm by rescuing ethanol sensitivity in a *slo-1*(null) *C. elegans* with the human BK channel. First, we will perform a specialized genetic screen to isolate novel non-null mutations in the worm version of BK channel that result in behavioral resistance to intoxication. Second, we will carry out targeted random mutagenesis on the human BK channel gene, and transform the mutated gene into *slo-1*(null) *C. elegans*. Transformed *C. elegans* will be tested for behavioral resistance to intoxication. For both approaches, non-null candidate mutations will identify key portion(s) of the gene that are critical for behavioral intoxication. We will distinguish null from non-null mutations by analysis of locomotory posture and subsequent DNA sequencing. So far, one of the 22 mutants obtained from the first approach has been identified as a candidate non-null mutant. After non-null mutants are identified, we will perform *in vivo* patch-clamp recordings to assess how the mutation alters basal BK channel function and response to alcohol at the level of single-channel activity. This study will provide knowledge on what residues are critical for ethanol modulation of the BK channel that results in behavioral intoxication across species, and a better understanding of how ethanol interacts with ion channels at the molecular level.

0328

ETHANOL-INDUCED BEHAVIORAL DISINHIBITION

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Behavioral disinhibition such as increased impulsivity and aggression is typically observed in inebriated humans and alcoholics. Moreover, trait behavioral disinhibition has strong correlation with alcohol abuse and addiction, suggesting that disinhibition and alcohol abuse/addiction have overlapping genetic or neural components. Despite the clinical significance, the neurobiological basis of alcohol-associated behavioral disinhibition is poorly understood. To address this, we employed the powerful genetic model system Drosophila. Drosophila males were subjected to ethanol administration once a day for 6 days and their behaviors were recorded with a camcorder and scored. Wild-type males exhibited disinhibited inter-male courtship, a type of impulsivity, under the influence of ethanol upon recurring ethanol administration, and dopamine neuronal activity was crucial for this phenomenon. To explore the key cellular and neural components crucial for this activity, we examined the flies defective in D1 or D2 dopamine receptors. The dumb males defective in D1 receptor displayed enhanced inter-male courtship while the D2 receptor mutant flies exhibited defective behavioral sensitization to the ethanol's effect on disinhibition. Furthermore, the flies lacking dopamine transporter displayed anomalous inter-male courtship under the influence of ethanol and this activity was suppressed by D1 receptor mutation. These findings are novel and provide a unique system to unravel the cellular and neural mechanisms underlying ethanol-induced behavioral disinhibition. Supported by the ABMRF/The Foundation for Alcohol Research and NIH/RCMI 5G12RR008124 grants.

0329

CREBA AND THE ACQUISITION OF TOLERANCE TO ALCOHOL IN DROSOPHILA

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We use Drosophila to study the mechanisms that underlie the acquisition of tolerance to drugs of abuse. Drug tolerance is defined as to a reduced response to a drug caused by previous drug exposure, and is a core component of addiction. We are attempting to understand the molecular processes that lead to acute functional tolerance. Our lab has previously shown that the BK channel gene *slowpoke* is necessary for the acquisition of tolerance and that artificial induction is sufficient to mimic the tolerant state. We have also shown that the Drosophila CREB homolog *Creb2* plays a role in the acquisition of tolerance to organic solvent anesthetics and regulation of *slowpoke* following sedation. We also found that the other Drosophila CREB gene *CrebA* is induced following sedation, but its role was not investigated further. In this study we seek to establish *CrebA*'s role in the acquisition of tolerance to ethanol.

In this study we use a two day behavioral assay to test for the ability to acquire tolerance to the sedative effects of ethanol. Animals are divided into two groups, and on the first day one group is sedated with ethanol vapor while the other group receives a mock treatment. 24 hours later both groups are exposed to ethanol vapor while movement and climbing are recorded. Wild type flies receiving their second dose of ethanol take longer to sedate than naïve flies.

We show that three alleles that disrupt the *CrebA* locus interfere with the acquisition of tolerance to ethanol. Two of the alleles are P-element insertions that disrupt the *CrebA* locus and the third is a 65Kb chromosomal deletion that spans *CrebA*. All of these alleles are recessive lethal and the stocks are tested as heterozygotes. Each of these independently generated alleles diminishes the animal's ability to acquire tolerance. These results show that *CrebA* is involved in the acquisition of tolerance to ethanol. We are currently investigating whether *CrebA* regulates *slowpoke* following sedation in order to induce the tolerant state.

0330

PASSIVE ETHANOL EXPOSURE INCREASES INTRAGASTRIC ALCOHOL CONSUMPTION (IGAC) IN WSP-1 AND WSR-1 MICE

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Intermittent passive ethanol (EtOH) exposure has been shown to produce later increases in IGAC in several mouse genotypes, an effect attributed to alleviation of withdrawal (i.e., negative reinforcement) and/or tolerance to aversive post-absorptive EtOH effects (Fidler et al., 2011). DBA/2J (D2) mice display greater withdrawal severity as measured by Handling Induced Convulsions (HICs) and greater sensitivity to manipulations of passive EtOH exposure than do C57BL/6J mice (Fidler et al., 2012). In this experiment, we investigated whether the same pattern would be observed in the first replicate of mice selectively bred to be Withdrawal Seizure Prone (WSP-1) or Withdrawal Seizure Resistant (WSR-1). Adult male mice from each line were implanted with IG catheters, allowed to recover and assigned to groups that received 0, 3, 5 or 10 consecutive days of passive EtOH infusions; the 0 group received water infusions. Mice then had access (23 h/day) to one or two Kool-Aid solutions in drinking tubes without EtOH. During the first 2 days, only one flavor was available (No-Choice) and licks produced IG EtOH infusions (20% v/v). During the next 5 days (Choice), a second flavor was also available and licks on this flavor were paired with infusions of water. As expected, WSP mice showed significantly more HICs than WSR mice. Choice EtOH intake was generally low (< 2.1 g/kg/d) in non-dependent (0 group) mice, with no line difference. Intake was positively related to duration of passive exposure in both lines, with the 5- and 10-day WSR groups showing significantly higher choice intakes (13.9 ± 1.4 and 14.9 ± 1.5) than the corresponding WSP groups (8.7 ± 1.2 and 6.3 ± 0.7). This negative genetic correlation between withdrawal sensitivity and choice EtOH intake supports the conclusion that common genes influence these phenotypes in ethanol dependent mice. Interestingly, like D2 mice, WSP mice showed a significant positive phenotypic correlation [$r(32) = +0.51$, $p < .005$] between the mean HIC score measured on passive EtOH days and mean choice EtOH intake while WSR mice did not [$p > 0.6$], suggesting dissociation between the mechanisms underlying genetic and phenotypic correlations in this model of dependence-induced EtOH intake. Supported by PARC AA010760.

0331

GENE-EARLY ENVIRONMENT INTERACTIONS DETERMINE ALCOHOL REWARD IN ADULT MICE

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Alcoholism is mediated by a complex phenotype resulting from gene-environment interactions. Prenatal stress (PNS) is an early environmental insult which can alter neurodevelopment in a variety of ways, producing long-lasting changes in behavior patterns, including increased reactivity to stressors, learning and memory impairments, and altered responses to and consumption of alcohol and other drugs of abuse. Here, we examine the impact of PNS on alcohol conditioned place preference in male and female mice of the C57Bl/6J and DBA/2J inbred strains. Dams of these two strains were timed-mated to males of their same strain and subjected to repeated restraint stress (3 x 1 h/day) from E14 until birth (PNS) or left undisturbed (control). The offspring were undisturbed from birth until weaning, after which they were maintained in same-sex groups with ad libitum access to food and water throughout testing, which began at 8–10 weeks of age. Place conditioning occurred in an unbiased two-chambered apparatus with distinctive visual elements and textured flooring in each chamber. Measurements of pre-conditioning time in both chambers of the apparatus were taken, and then subjects received 8 pairings of alcohol (2 g/kg) in one of the two distinctive chambers and 8 pairings of saline in the other on alternate days. In the post-conditioning test, mice were again allowed access to the whole apparatus and the time spent in each chamber was recorded. DBA/2J male and female mice in both the PNS and control conditions showed a place preference for the alcohol-paired side of the apparatus. In contrast, C57Bl/6J mice showed a significant interaction of sex and PNS such that PNS males showed a conditioned place preference for the alcohol-paired side, while females and control males did not. The same patterned emerged between the sexes and strains when conditioning score was calculated. The results of the present study indicate that genetic background interacts with PNS to determine alcohol-seeking behavior in adult mice, thus, PNS and recombinant inbred mouse strains derived from the progenitor strains C57Bl/6J and DBA/2J offer an avenue to elucidate the details of the impact of gene-early environment interactions on alcohol seeking and, potentially, elements of alcoholism. Supported by NIDA 1DA027115-01 and National Alliance for Research on Schizophrenia and Affective Disorders.

0332

DETERMINING THE HERITABILITY OF LOCOMOTOR SENSITIZATION TO ETHANOL AND ITS RELATIONSHIP TO ETHANOL'S POSITIVE MOTIVATIONAL EFFECTS IN MICE

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Sensitization to the locomotor stimulant effects of alcohol (ethanol) is thought to be a heritable risk factor for the development of alcoholism that reflects progressive increases in the positive motivational effects of this substance. However, very little is known about the genetic influences involved in this phenomenon or the extent to which ethanol's positive motivational effects are altered in parallel to its development. The first goal of this work was to determine the heritability of ethanol-induced locomotor sensitization using short-term behavioral selection. C57BL/6J (B6) x DBA/2J (D2) F2 mice were generated from B6D2F1 progenitors, phenotyped for the expression of locomotor sensitization, and bred for high (HLS) and low (LLS) expression of this behavior. A secondary goal was to characterize possible line differences in ethanols positive motivational effects using conditioned place preference and limited access voluntary ethanol consumption assays. Animals from the fourth generation of selection (S4) were assayed for conditioned place preference (CPP) or given daily access to ethanol or water using Drinking-in-the-Dark (DID) procedures. There were large and significant differences in locomotor sensitization between HLS and LLS lines by the fourth generation. Twenty-two percent of the difference between lines was due to genetic differences (h^2=.22). However, whereas there were no significant differences in conditioned place preference between lines, there were marginal differences (p=.06) in voluntary ethanol consumption (albeit in females only) with LLS animals generally consuming more ethanol than HLS animals. The results of this work have several implications. First, that *changes* in ethanol sensitivity following repeated exposures are in part genetically regulated highlights the relevance of studies aimed at determining how genes regulate susceptibility to ethanol-induced behavioral and neural adaptations. Additionally, line differences in ethanol intake but not in ethanol-induced CPP suggest that the utility of locomotor sensitization as a model of alterations in ethanol's positive motivational is still unclear. Together these studies provide evidence that genes are capable of regulating alterations in ethanol-induced locomotor behavior but provide little support for ethanol-induced locomotor sensitization as a model for increases in ethanol's positive subjective effects.

0333

BI-DIRECTIONAL SELECTIVE BREEDING FOR SEVERE ETHANOL WITHDRAWAL COUPLED WITH LOW ETHANOL DRINKING VERSUS MILD WITHDRAWAL COUPLED WITH HIGH DRINKING

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It has been well-established that naïve animals that are genetically susceptible to severe withdrawal from ethanol will choose water over ethanol if given a choice. Likewise, naïve animals that are genetically liable to drink ethanol preferentially over water experience mild ethanol withdrawal when rendered physically dependent. These findings in mouse and rat models suggest that at least some genes affecting each trait independently have pleiotropic effects on both traits. In order to identify genes involved in this relationship, we first examined whether order of testing affected either trait. Separate groups of F2 intercross progeny derived from the inbred strains C57BL/6J (B6) X DBA/2J (D2), which are known to differ for both traits, were first tested for 24 hr two-bottle choice and then a week later for acute ethanol withdrawal, or vice-versa. To assess acute withdrawal, we scored handling-induced withdrawal convulsions following a single injection of a hypnotic dose of ethanol (4 g/kg, ip). Drinking preference was measured as ethanol intake (g/kg) of 10% v/v ethanol during 4 days of 24 hr two-bottle choice. Results showed that ethanol intake was greater if withdrawal was tested first, while withdrawal severity did not show an effect of test order. Selective breeding is a powerful genetic tool that enables identification of common genetic control over multiple traits and has been successfully used to assist gene mapping efforts. We next selectively bred lines of mice to display either low-withdrawal-*and*-high-drinking or low-drinking-*and*-high-withdrawal. Starting from a separate population of B6D2F2 intercross progeny, mice were tested for drinking and then withdrawal in the same manner as described above. Breeders of the SOT line were chosen for their high ethanol intake and mild ethanol withdrawal severity. Breeders of the NOT line were selected for their low ethanol intake and intense ethanol withdrawal severity. By generation S3, SOT mice consumed nearly 3 times more ethanol (4.8 ± 0.4 g/kg) than NOT mice (1.7 ± 0.3 g/kg) and withdrawal scores were correspondingly about 3-fold more severe in NOT mice compared with SOT mice. These data indicate that some genes affect both traits. Results of genotyping using a genome-wide single nucleotide polymorphism panel nominate specific genes associated with the SOT and NOT phenotypes. Supported by: P60 AA010760, U01 AA013519, R01 AA006243, R01 AA011114, and the Department of Veterans Affairs.

0334

VOLUNTARY ETHANOL CONSUMPTION IN THREE *PEROMYSCUS* SPECIES THAT DIFFER IN SOCIAL STRUCTURE

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The question of the relationship of social interactions and bonding to ethanol consumption has received recent attention and some research suggests that there is social facilitation of ethanol intake in a species with strong social bonds, namely the prairie vole (Anacker et al., 2011). The purpose of the present study was to examine the relationship of social structure to voluntary ethanol consumption in the genus *Peromyscus* or deer mice. This rodent genus diverged from *Rattus Norvegicus* and *Mus domesticus* over 25 million years ago and has not been used to examine voluntary ethanol intake. Two species of deer mice and their hybrid were examined. *Peromyscus polionotus* (PO) shows partner preference with the conspecific with which they have been bred. In contrast, *Peromyscus maniculatus* (BW) fails to show partner preference, exhibiting a promiscuous pattern of sexual behavior more typical of rodents. First generation genetic hybrids (PO x BW F1), whose partner preference is unknown, were also tested for their ethanol intake. Males of all species were pair housed (n=6 pairs per species) and allowed access to a 6% ethanol solution for 16 hours during the night cycle for five days per week for six weeks. Animals were not deprived of food or water at any point and water intake and ethanol intake were measured each day. A mixed-design ANOVA, with day as the repeated measure, and species as the between-subjects factor, was performed. The results demonstrated that *Peromyscus polionotus* (PO) consumed significantly more ethanol (expressed at % of total fluid consumption) than *Peromyscus maniculatus* (BW). F1 hybrids showed a pattern of ethanol consumption consistent with *Permomyscus polionotus*, consuming significantly more ethanol than *Peromyscus maniculatus*. This study suggests that strong social bonding in the social structure may predict increased ethanol consumption in rodents. The reason for the increased ethanol consumption in the POs compared to the BWs remains to be determined and detailed behavioral studies describing the phenotype of these animals followed by a genetic analysis of the phenotype are planned. The current findings suggest that *Peromyscus* may be a novel model system to examine the mechanisms underlying ethanol consumption.Support by NIAAA 11566 to SJK

0335

SELECTIVE BREEDING FOR ETHANOL RESPONSE ALTERS CIRCADIAN PHENOTYPE

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Recent studies have identified bidirectional interactions between alcohol intake and the circadian timing system at both the physiological and molecular-genetic levels. For example, selective breeding for high and low ethanol preference results in co-selection for circadian phenotype in both mice (Hofstetter et al. 2003) and rats (Rosenwasser et al. 2005). The animals employed in these studies were selectively bred for 2-bottle preference drinking, a condition that does not generally lead to intoxication or signs of dependence, even in high-preferring lines. In contrast, the present studies characterized light-entrained and free-running circadian activity rhythms in mice selectively bred for other ethanol-related phenotypes that might be more closely associated with excessive ethanol intake. Thus, Experiment 1 employed a newly developed mouse line selected for high binge-like drinking to intoxication in the ‘‘drinking in the dark’’ test (HDID-1 mice) and their genetically heterogeneous HS/Npt controls, while Experiment 2 compared lines of mice selectively bred for high (withdrawal seizure-prone, WSP-2) and low (withdrawal seizure resistant, WSR-2) sensitivity to handling-induced convulsions after withdrawal from chronic ethanol vapor inhalation. Under a normal light-dark cycle, high ethanol-responsive HDID-1 and WSP-2 mice both displayed relatively less activity in the early night and relatively more activity in the late night compared to their low-responsive counterparts. Under free-running conditions, WSP-2 mice showed significantly longer free-running periods than WSR-2 mice, while in constant light, HDID-1 mice showed significantly shorter free-running periods in than HS/Npt mice. Taken together with previous studies, these results show that selective breeding for diverse responses to ethanol results in co-selection for circadian phenotype, and strengthen the evidence for genetic linkages between circadian clock function and ethanol responsiveness. These genetic linkages could reflect the overlapping regulation of circadian rhythms and ethanol responses by several neurotransmitter systems (e.g., GABA, glutamate, serotonin). Nevertheless, further work will be required to identify the specific physiological mechanisms mediating these relationships.

0336

VOLUNTARY EXERCISE IN ADOLESCENCE OR ADULTHOOD IN ALCOHOL-PREFERRING (P) AND HIGH-ALCOHOL DRINKING (HAD-1) RATS, AND EFFECT ON LATER ALCOHOL INTAKE

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Research in high E drinking rats has indicated that adolescent E consumption enhances the acquisition of free-choice and oral operant E self-administration, inhibits extinction of operant responding for E, augments operant E-seeking behaviors, and increases relative reward value of E during adulthood. The current research was conducted to determine whether voluntary exercise, a natural reward, made available during adolescence could have a priming effect on E self-administration in adulthood. Female HAD-1 and P rats were separated into 3 groups per age (∼PND 30 or 90 start, n = 10/age/group): run, wheel lock, and homecage. Run groups received 2 hr access to running wheel chambers (Lafayette Instruments), 5 days a week, for 4 weeks. Wheel lock groups received access to identical chambers with locked wheels. Homecage groups remained naive. After this period, all groups received 2 hr bank access to 15% E and water (food ad lib) 5 days a week, for 3 weeks (∼PND60 or 120 start). Week 1, there was no significant difference between distance average across lines or ages. Weeks 2, 3, and 4, adolescent P rats ran significantly farther than adult P rats (week 4 average, 3787 m +-284 vs. 1801 m +-127). In HAD-1 subjects, this finding was reversed; weeks 2, 3, and 4, adult HAD-1 rats ran significantly farther than adolescent HAD-1 rats (week 4 average, 3170 m +-114 vs. 2147 m +-154). All groups voluntarily consumed 15% E; group intake average was 2.5 g/kg or greater (in 2 hr) by week 3. There was no significant difference in 15% E consumption between any P groups, adult or adolescent. Adolescent HAD-1 running wheel subjects acquired E drinking behavior faster than wheel lock or homecage groups, and consumed greater levels than the homecage group through the end of week 3. Also, adult HAD-1 running wheel and wheel lock subjects acquired E drinking behavior faster than the homecage group. Overall, the results indicate that adolescent exercise exposure facilitated acquisition of early adult E intake in HAD-1, but not P, rats. Furthermore, distance run was higher in adolescent P compared to adult P rats, but lower in adolescent HAD-1 compared to adult HAD-1 rats. These differential effects indicate that exercise-related neural pathways may be involved in E intake behavior in both adolescent and adult HAD-1 rats, as evidenced by priming of EtOH intake behavior compared to controls. AA07611, AA013522, AA010256

0337

UNCOVERING GENETIC DETERMINANTS OF ALCOHOL PREFERENCE IN THE SELECTIVELY BRED ALCOHOL-PREFERRING AND NON-PREFERRING RATS

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The selectively bred alcohol-preferring (P) and –non-preferring (NP) rat lines provide great access to the genetic elements influencing alcohol-related phenotypes. We conducted a whole genome-based sequencing analysis to uncover sequence variants that segregate between the two rat lines and profile gene expression difference resulted from the genetic variations and responsible for their differences in alcohol preference and consumption. Using strand-specific mRNA sequencing of hippocampal transcripts coupled with methyl-CpG binding protein precipitation-targeted genomic sequencing, we detected a total of 132,067 SNPs among the 16 sequenced P and NP rats with an average SNP distance of 20,561 base pair. There were a total of 19,129 SNPs that showed allelic segregation between the two rat lines, among which 52.4% mapped within 10 kb of annotated genes. We constructed a genome map which highlighted the genetic differences across all of the chromosomes between the P and NP rat lines. We also identified 1342 SNPs with allelic segregation in the untranslated regions (UTR) and 837 in the coding sequences of the genes, including missense and stop-codon variants. Among the missense variants, several were identified to adversely affect the protein functions by both Polyphen and SIFT, bioinformatic tools that predict the impact of amino acid substitution on the protein functions. We also examined the effects of the stop-codon and missense variants on alcohol preference and consumption by quantitative trait locus (QTL) analysis. The hippocampal gene expression differences revealed by transcriptome profiling were also convergent with the genetic variations between the P and NP rats. There was significant enrichment of the differentially expressed genes (FDR < 0.05) among the genes that carry segregated SNPs in the promoters, UTR, and coding sequences. These findings in the selectively bred P and NP rat lines provide new insights to the genetic factors that play critical roles in determining alcohol preference and dependence.

0338

ENT1 REGULATES ETHANOL DRINKING AND GOAL-ORIENTED BEHAVIOR THROUGH A2A RECEPTOR SIGNALING IN THE DORSOMEDIAL STRIATUM

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Striatal adenosine signaling has been implicated in the pathophysiology of psychiatric disorders including alcoholism. In the nucleus accumbens, deficiency of ethanol-sensitive adenosine transporter, ENT1 (*slc29a1*), resulting in the reduction of extracellular adenosine levels ultimately leads to diminished NMDA glutamate receptor (NMDAR)-mediated signaling and increases ethanol intake. However, the molecular consequences of hypo-adenosine levels on the regulation of ethanol drinking in the caudate-putamen remained unknown. In this study, we identified that decreased A2AR signaling in the dorsomedial striatum (DMS) of ENT1 null ($ENT1^{-/-}$) mice decreased PKA-driven NMDAR activity. A2AR antagonist (ZM241385) dampened PKA activity and NMDAR-mediated signaling cascades in the DMS and promoted excessive ethanol drinking of ENT1 wild-type littermates, which were similar to those of $ENT1^{-/-}$ mice. Furthermore, $ENT^{-/-}$ mice showed a higher rate of initial acquisition and vulnerability to transition to habitual behavior in operant conditioning tests, which might be regulated by reduced A2AR signaling. Taken together, our studies suggest that decreased A2AR-mediated NDMAR signaling in the DMS contributes to goal-oriented action, habitual behavior development and excessive ethanol drinking.

0339

INTERMITTENT (EVERY-OTHER-DAY) ACCESS TO BEER PROMOTES GREATER BEER DRINKING AND PREFERENCE IN ADOLESCENT RELATIVE TO ADULT C57BL/6J MICE

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A number of rodent studies have shown that the schedule by which ethanol is offered proves to be an essential factor in promoting ethanol escalation. Using C57BL/6J (B6) mice we previously showed that weekly (i.e., intermittent) 24 h access to 15% ethanol leads to gradual escalation of ethanol intake and preference compared with continuously exposed mice (Melendez et al., 2006). A limitation of this procedure, however, is that it requires many weeks of testing, which makes it difficult to study the acquisition of escalated drinking during the adolescent (i.e., 2-week) period. This is important considering the prevalence of excessive drinking among human adolescents. In this respect, we employed the intermittent every-other-day (EOD) access procedure initially described by Wise (1973). Our findings revealed that EOD access to 15% ethanol was sufficient to induce rapid escalation of ethanol intake and preference in both adolescent and adult mice (Melendez, 2011). However, the average levels of EOD drinking were significantly greater in adolescents (15.3 ± 0.4) compared to adults (11.4 ± 0.8 g/kg). Given that beer is the most common alcoholic beverage in the world (WHO, 2004), we recently tested the hypothesis that EOD access to 5% (v/v) Medalla, a beer commonly used among human adolescents in Puerto Rico, will promote greater beer drinking in adolescent compared to adult B6 mice. Our findings revealed that EOD access to beer resulted in significant escalation of beer intake and preference in both adolescent and adult mice. Nevertheless, the average escalated levels of beer intake were significantly greater in adolescents (12.6 ± 0.5) relative to adults (9.3 ± 0.6 g/kg), which resulted in greater blood ethanol concentrations in the adolescent group. Interestingly, beer preference scores were nearly 0.95 and 0.80 during the initial drinking session in adolescent and adult mice, respectively, and remained significantly elevated in adolescents (0.97 ± .01) compared to adults (0.91 ± .02). Collectively, these findings indicate that the EOD access model can induce rapid and impressive levels of beer and ethanol drinking and preference in B6 mice. Thus, the EOD access procedure appears to be suitable for studying the acquisition of various ethanol drinking solutions and the transition to excessive ethanol intake during adolescence. (Funded in part by R21AA015953 and UPR-SOM Institutional Funds).

2. PHARMACOLOGY C.N.S.

0340

CHRONIC ALCOHOL DRINKING REDUCES GLUTAMATE CLEARANCE AND ENHANCES BASAL EXTRACELLULAR GLUTAMATE LEVELS WITHIN THE MESOLIMBIC SYSTEM

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The objective of the present study was to determine the effects of chronic alcohol drinking on basal extracellular levels of glutamate in the nucleus accumbens shell (NACsh) and posterior ventral tegmental area (pVTA), and tested the hypothesis that chronic ethanol drinking would increase basal glutamate neurotransmission within the mesolimbic system. Alcohol preferring (P) rats were given access to either ethanol under a two-bottle choice (water vs 15% ethanol) paradigm or water for 8 weeks. After the last episode of alcohol drinking, quantitative no-net-flux microdialysis experiments were conducted to determine basal extracellular concentrations and clearances of glutamate in the NACsh and pVTA. At the end of the drinking session, P rats consumed approximately 5.0 ± 1.0 g/kg/day of ethanol. Chronic alcohol drinking by P rats significantly increased basal extracellular glutamate concentrations in both the pVTA (6.9 ± 0.4 vs 4.4 ± 0.4 μM, $p < 0.05$) and NACsh (6.1± 0.5 vs 2.7 ± 0.4 μM, $p < 0.05$) compared to water drinking. In addition, the extraction fractions of glutamate, an index for glutamate clearance, were significantly reduced in ethanol-drinking rats in both regions (pVTA: 22 ± 2% vs 31 ± 1%, $p < 0.05$; NACsh: 12 ± 2% vs 20 ± 2%, $p < 0.05$). Brain tissues from separate groups of rats were harvested for measurements of protein levels of glutamate transporters (EAAT1 & 2) and glutamate-cystine exchanger (xCT) utilizing Western blot technique. The results indicated that chronic ethanol drinking, compared to water drinking, reduced EAAT1 protein levels by approximately 40 – 45% (p values < 0.05) in both the pVTA and NACsh. No significant changes in protein levels of EAAT2 or xCT were observed in either region. Overall, these results suggest that chronic ethanol drinking impaired glutamate reuptake function, thus contributing to the enhanced basal extracellular glutamate concentrations. The study also suggests that hyperglutamatergic neurotransmission within the mesolimbic system may contribute to the maintenance of alcohol drinking. (AA07611, AA012262, AA010721)

0341

THE UNIQUE ACTION OF ETOH AND NICOTINE ON GLUTAMATE IN THE MEDIAL PREFRONTAL CORTEX: A POSSIBLE MECHANISM UNDERLYING THE CO-ABUSE OF ETOH AND NICOTINE

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There is an exceedingly high rate of co-morbidity between alcohol (EtOH) consumption and tobacco use with 75% of alcoholics also reporting tobacco addiction. Pre-clinical data from our laboratory suggests that EtOH and nicotine (NIC) act in a synergistic manner as sub-threshold doses of EtOH and NIC exhibit reinforcing properties when the two drugs are presented in combination. Glutamate (GLU) transmission in the medial prefrontal cortex (mPFC) has been extensively linked to the development and maintenance of both EtOH and NIC addiction. Therefore, the current research examined the effects of oral operant self-administration of EtOH, saccharin (SAC), EtOH and NIC combined (EtOH + NIC), or SAC and NIC combined (SAC + NIC) on basal GLU levels and GLU clearance in the mPFC in alcohol preferring (P) rats. During operant training and testing P rats were allowed to concurrently self-administer 10, 20, and 30% EtOH alone or in combination with .14 mg/ml nicotine or .025 SAC alone or in combination with .14 mg/ml NIC. Nine days after the final operant session all P rats were implanted with guide cannula aimed at the mPFC and provided one week recovery time prior to the start of quantitative microdialysis. Probes were inserted approximately 24 hrs prior to the start of microdialysis testing. Samples were collected every 10 minutes as the probes were first perfused of artificial cerebral spinal fluid (aCSF) followed by aCSF containing three GLU concentrations (1 μM, 5 μM, and 10 μM; presented in randomized order across rats). Samples were analyzed using high pressure liquid chromatography and the no-net flux technique was utilized to calculate the slope (extraction fraction; a measure of in vivo recovery of GLU) and the x intercept (basal level of GLU). Multiple linear regression revealed a significantly higher level of GLU clearance in the SAC + NIC (70%) group than all other groups. Further, analysis of the x intercepts revealed that basal GLU levels were significantly higher in the mPFC of P rats that had self-administered EtOH + NIC (8.1 μM) compared to all other groups. Thus, the data suggest that the consumption of EtOH in combination with NIC may act to attenuate the compensatory increase in GLU clearance, as seen in the SAC + NIC group, thereby resulting in an enduring increase in basal GLU levels within the mPFC. The current findings may represent an underlying mechanism contributing to the high co-morbidity of EtOH and NIC.

0342

ADOLESCENT ETHANOL EXPOSURE REDUCES ADULTHOOD COMT LEVELS IN THE MEDIAL PREFRONTAL CORTEX

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During adolescence, the prefrontal cortex (PFC) undergoes a critical period of cortical development and refinement of neuronal circuits that occurs in conjunction with the maturation of complex cognitive behaviors. Although accumulating evidence suggests that binge-like alcohol consumption during adolescence adversely affects the development of the PFC, little is known about the long-term consequences of this on PFC-dependent behaviors in adulthood. Efficient information processing of glutamatergic networks in the mPFC depends upon an optimal extracellular concentration of dopamine (DA), and enzymatic breakdown of DA by catechol-O-methyltransferase (COMT) plays a primary role in determining the extracellular concentration of DA in the PFC where the expression of DA transporters is very low. The aim of this study was to determine the effects of adolescent binge-like alcohol exposure on the expression of proteins associated with DAergic, glutamatergic and GABAergic neurotransmission in the mPFC of adult rats. Long-Evans rats were exposed to repeated cycles of binge-like intermittent ethanol exposure by vapor inhalation during post-natal days (PD) 28 to 42 (AIE). Following AIE exposure, rats were grown to adulthood (PD90) prior to preparation of mPFC tissue for Western blot analysis. We isolated PSD (synaptic) and soluble (or extrasynaptic) fractions, and examined AIE-induced prolonged neuroadaptations in glutamatergic and DAergic systems. We did not observe significant changes in synaptic expression levels of subunits of the AMPA (GluR1) or NMDA (GluN1, GluN2A, and GluN2B) receptors. Also, AIE did not alter extrasynaptic GluR1 subunit expression levels. However, AIE exposure significantly down-regulated COMT levels in adulthood (control, 96.9 ± 13.3; AIE, 60.4 ± 13.4; $p < .05$). These data suggest that while AIE exposure does not appear to produce persistent neuroadaptations in synaptic glutamate receptors in the mPFC, AIE may affect adulthood extracellular DA concentrations through a reduction in COMT. These data are consistent with the suggestion that AIE exposure may disrupt DA modulation of optimal PFC performance in adulthood, leading to degradation of PFC-dependent control of complex cognitive behaviors.

0343

AC/cAMP/PKA PATHWAY IN MOUSE CEREBELLAR CORTEX MEDIATES HETROLOGOUS CROSS-TOLERANCE BETWEEN Δ^9-TETRAHYDROCANNABINOL (Δ^9-THC) AND ETHANOL

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Ataxia is one of the earliest and consistent behavioral effects of acute ethanol and Δ^9-THC in humans and laboratory animals. We have previously reported development of cross- tolerance between ethanol and Δ^9-THC following chronic intracerebellar (ICB) infusion of Δ^9-THC and acute ethanol (ip) injection and vice versa. We have also demonstrated cerebellar adenosinergic A_1 and GABA-A receptor potentiation of ethanol-, Δ^9-THC-, and ethanol + Δ^9-THC-induced ataxia. In the present study, we investigated the possibility of the AC-cAMP-PKA pathway mediating cross-tolerance between the two psychoactive substances. Ataxia was evaluated by Rotorod test using male CD-1 mice. All drugs in the present study (Δ^9-THC 10–20μg; cpt-cAMP 2pmol; AC inhibitor, miconazole 0.1pmol; PKA activator, Sp-cAMP 22pmol; PKA inhibitor, Rp-cAMP 22pmol; adenosine A_1 agonist, N^6-cyclohexyladenosine [CHA] 23pmol; and GABA-A agonist, muscimol 126pmol) were given ICB via stereotaxically implanted stainless steel guide cannulas except ethanol (2g/kg; ip). The drug doses and routes of administration were selected based on our previous work. In acute studies, pretreatment with cpt-cAMP and miconazole attenuated and accentuated, respectively, ethanol + Δ^9-THC-induced ataxia suggesting involvement of AC-cAMP. Also, ICB Sp-cAMP and Rp-cAMP markedly attenuated and accentuated, respectively, ethanol + Δ^9-THC-induced ataxia indicating role of cAMP-dependent PKA. The data support mediation of functional interaction of Δ^9-THC and ethanol by AC-cAMP-PKA pathway. In chronic studies, when infusion of acute Δ^9-THC was preceded by either miconazole or Rp-cAMP (16 h after the last ethanol dose given once daily for 3 days), the Δ^9-THC-induced ataxia was totally abolished indicating that miconazole and Rp-cAMP pretreatment has blocked the development of cross-tolerance. Similar results were observed with either miconazole or Rp-cAMP pretreatment when acute treatment of Δ^9-THC was replaced by ethanol and chronic administration of ethanol was replaced by Δ^9-THC. Finally, in chronic studies, miconazole and Rp-cAMP pretreatment also markedly antagonized the CHA- and muscimol-induced potentiation of ethanol + Δ^9-THC-induced ataxia. These results support participation of AC-cAMP-PKA pathway in the functional interaction and development of cross-tolerance between Δ^9-THC and ethanol. The results also support the pathway modulates potentiation of Δ^9-THC+ ethanol-induced ataxia by CHA and muscimol.

0344

MICROINJECTIONS OF SULPIRIDE INTO THE MEDIAL PREFRONTAL CORTEX REDUCES ETHANOL DRINKING IN ALCOHOL-PREFERRING (P) RATS

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The medial prefrontal cortex (MPF) integrates input from limbic, motor, and cortical brain regions and is thought to serve an executive function in processing information associated with drug stimuli, and initiating responses to acquire drugs of abuse. The MPF is part of the mesocorticolimbic dopamine (DA) system and DA neurotransmission in the MPF is thought to play a role in ethanol (EtOH) drinking behavior. The objectives of the current study were to assess the effects of microinjections of a DA D2 (sulpiride) or D1 (SCH23390) receptor antagonist into the MPF on EtOH drinking behavior. Adult female P rats were given access to EtOH (15%, v/v) in a one-hour scheduled access paradigm for a minimum of 4 weeks until basal intakes were established. One week prior to the experiment, unilateral guide cannulae were implanted 1.0 mm above the MPF and scheduled daily ethanol access continued for the following five days; the rats were acclimated to the microinjection procedure during this period. On the seventh day post-surgery, a microinjector was inserted into the guide cannula. Then 0.5 ul of either vehicle (artificial cerebrospinal fluid; aCSF), or 1.0, 2.0, or 4.0 ug/ul of the DA D2 receptor antagonist sulpiride, or the D1 antagonist SCH23390, was injected into the MPF over 30 sec, and the injector remained in place for an additional 30 sec. Each rat was then returned to its home cage and its daily one hour scheduled access to EtOH was initiated and EtOH intake was recorded. The average baseline EtOH intake for the 3 one hr scheduled access sessions prior to the experiment was 1.3 ± 0.1 g/kg and did not differ between groups. Sulpiride microinjection dose-dependently reduced scheduled EtOH drinking 15 ± 8; 20 ± 9; 46 ± 13; and 46 ± 9% baseline following injections of 0, 1.0, 2.0 and 4.0 ug/ul, respectively. EtOH intake in the 4.0 ug/ul dose group was significantly reduced compared with the vehicle group ($p < 0.05$, t-test). SCH23390 microinjections had no effect on EtOH intake at any dose tested. These data are consistent with the hypothesis that DA neurotransmission in the MPF plays a role in mediating EtOH drinking behavior and implicates DA D2 receptors in scheduled EtOH consumption. *Supported by:AA10717, AA07611*

0345

NMDA RECEPTOR SUBUNIT COMPOSITION AND FUNCTION ARE ALTERED IN THE DENTATE GYRUS OF ADULT MICE THAT WERE EXPOSED TO ALCOHOL THROUGHOUT GESTATION

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Adult offspring of female mice that consume moderate levels of alcohol throughout gestation display deficits in hippocampal-dependent learning and memory (Brady et al. 2011). In the present studies, we assessed the effects of prenatal alcohol exposure (PAE) on the levels and subcellular distribution of the *N*-methyl-D-aspartate receptor (NMDAR) subunits and on NMDAR-dependent long-term potentiation (LTP) in the adult (2–5 months of age) mouse dentate gyrus. Using a limited access, PAE drinking paradigm (Brady, et al. 2011), dams were offered 10% (w/v) ethanol sweetened with 0.066% (w/v) saccharin for 4 hours a day during pregnancy, reaching BACs of 90.5 ±11.61 mg/dL (n = 11); controls consumed 0.066% (w/v) saccharin (SAC). NMDAR subunit levels present in characterized synaptic and extrasynaptic (non-synaptic) subcellular fractions were measured by semi-quantitative immunoblotting. We found that, compared to SAC control mice, in PAE mice, the levels of GluN1 and GluN3A were increased (GluN1 – SAC 1.00 ± 0.03, PAE 1.87 ± 0.19, $p < 0.05$, n = 5; GluN3A – SAC 1.00 ± 0.07, PAE 1.54 ± 0.19, $p < 0.05$, n = 8) in the synaptic fraction, while levels of GluN2B were decreased (SAC 1.00 ± 0.12, PAE 0.65 ± 0.06, $p < 0.05$, n = 7), with no changes in subunit levels in the non-synaptic fraction. We also prepared coronal brain slices and used field recordings to determine whether the observed deficit in synaptic GluN2B-containing receptors resulted in changes in synaptic transmission. Although we found no difference in NMDAR-dependent I/O curves, we did find that ifenprodil, a GluN2B subunit specific antagonist, blocked a reduced percentage of the NMDAR-dependent field potential in PAE animals compared to controls (SAC 11.19 ± 2.51%, PAE 3.01 ± 2.47%, $p < 0.05$, n = 7), indicating that fewer functional GluN2B subunits were present in PAE animals. Furthermore, using an LTP protocol that was both NMDAR-dependent and GluN2B-dependent, we found that LTP in the dentate gyrus was impaired in PAE animals [at 45 min SAC – 178.6 ± 35.61%, PAE 108.9 ± 25.71%; repeated measure ANOVA found a significant effect of time ($F[36, 432] = 4.655$, $p = 0.0001$), treatment ($F[1, 12] = 5.365$, $p < 0.05$), and an interaction ($F[36, 432] = 2.754$, $p = 0.0001$)]. These data indicate the alterations in NMDAR subunit levels, particularly a decrease in GluN2B levels in the synaptic fraction, in PAE animals result in LTP deficits, and may underlie, at least partially, the learning and memory deficits observed in these animals.

0346

MODULATION OF OPERANT SELF-ADMINISTRATION OF ETHANOL BY MU AND DELTA OPIOID RECEPTORS IN TWO-WEEK OLD RATS

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Opioid control of operant behavior for ethanol reinforcement was tested in 2-week old rats. Although mu opioid receptors are increasingly prevalent during the rat's first postnatal days, delta opioid receptors are barely noticeable until the second postnatal week. Both have been implicated in ethanol reinforcement in adult rats. Preweanling (infant) rats were trained in an operant learning task to obtain ethanol [5.0%, 7.5%, 10.0% or 15.0%]. Daily training sessions (15 min each) were given on postnatal days (PD) 14–17. All experimental pups rapidly acquired the operant response to gain access to the drug. Significantly more operant responses and greater ethanol intake occurred for 7.5% and 10% than for 5% or 15%. A second experiment analyzed blood ethanol levels (BELs) of animals infused with 7.5 and 10.0% ethanol. Trunk blood samples were obtained immediately after sessions of PDs 15, 16 and 17. BELs achieved when pups were reinforced with 10% ethanol were higher than the ones observed with 7.5% ethanol. BELs were increasing across each daily operant session. In a third experiment, the involvement of mu and delta opioid receptors in ethanol-related operant behavior for 10% ethanol was examined. The protocol was similar to that employed in Experiment 1. In addition, a 15-min extinction session was given on PD18. On PD 16–18, 30-min before operant task, pups were injected ip with CTOP (mu antagonist, 0.1 or 1.0 mg/kg), Naltrindole (delta antagonist, 1.0 or 5.0 mg/kg) or saline. Results indicated that all experimental pups learned the operant response for 10% ethanol on PDs 14–15. During PDs 16–17, experimental pups treated with 5.0 mg/Kg Naltrindole or 0.1 mg/Kg CTOP had significantly less operant responses than controls. These differences persisted throughout extinction session. Results from this study indicate that delta as well as mu opioid receptors are involved in mechanisms of ethanol reinforcement at this early stage of development.

0347

INTERACTIONS BETWEEN PKC EPSILON AND PI3K WITHIN THE CENTRAL NUCLEUS OF THE AMYGALA REGULATE BINGE ALCOHOL DRINKING

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Binge alcohol drinking elevates PI3K and PKCe activity within the central nucleus of the amygdala (CeA) and both kinases within the CeA regulate binge alcohol drinking by mice under Drinking-in-the-Dark (DID) procedures. PI3K can be activated by Group1 metabotropic glutamate receptor (mGluR) stimulation and this can lead to the activation of PKCe. To determine the roles for Group1 mGluRs and PI3K in mediating the ''anti-binge'' property of PKCe inhibition, we employed neuropharmacological strategies to target PKCe, along with mGluR5, mGluR1 and PI3K within the CeA of C57BL/6J mice and then assayed the intake of 20% alcohol from a 50 ml bottle under DID procedures (2 hrs, bottle presentation at 3 hrs into the circadian dark). As reported previously, intra-CeA microinjection with a TAT-eV1-2 inhibitor reduced alcohol intake as did pretreatment with the mGluR5 antagonist MTEP and the mGluR1 antagonist JNJ16259685. While the local infusion of the PI3K antagonist wortmannin also significantly reduced alcohol drinking, infusion of an IC50 dose of another antagonist, LY294002, did not. However, when co-infused with the PKCe inhibitor, LY294002 (0.17 ng) prevented the ''anti-binge'' effects of TAT-eV1-2, while the effects of mGluR antagonist co-infusion with TAT-eV1-2 appeared to be additive. These data suggest that PI3K activity is somehow involved in the ''anti-binge'' properties of PKCe inhibition, while that of mGluR1 and mGluR5 are not. Such observations suggest that mGluR-independent activation of PI3K/PKC epsilon signaling within the CeA is a molecular pathway regulating the continued propensity to consume high amounts of alcohol in a binge-like pattern.

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0348

INCREASED ALCOHOL SELF-ADMINISTRATION FOLLOWING POSITIVE MODULATION OF AMPA RECEPTORS IN THE AMYGDALA

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Previous findings have shown that chronic alcohol consumption results in strengthened excitatory neurotransmission and increased AMPA receptor (AMPAR) signaling within limbic brain regions that regulate reward. However, it remains unclear how enhanced activity at AMPARs could influence alcohol-reinforcement processes. The purpose of this study was to characterize the functional role of enhanced glutamate activity at AMPARs in modulating alcohol reinforcement. Thus, the effects of the AMPAR positive modulator, aniracetam, were assessed in alcohol-preferring rats (P-rats) trained to self-administer alcohol (15%v/v) vs. water using operant self-administration techniques via systemic administration (IP). Aniracetam pretreatment (5 mg/kg; IP) resulted in a significant increase in alcohol-reinforced responses vs. vehicle treatment. However, aniracetam (0–30 mg/kg; IP) did not alter sucrose-reinforced lever responses in sucrose-trained P-rats, suggesting that positive modulation of AMPARs is selective in modulating the reinforcing effects of alcohol but not a non-drug reward. Given that glutamate signaling in the amygdala and nucleus accumbens plays a critical role in drug-induced neuronal plasticity and drug-taking behavior we tested the effects of aniracetam via site-specific microinjections within these regions prior to self-administration sessions. Localized infusion of aniracetam (1 μg) in the amygdala significantly increased alcohol-reinforced lever responding in P-rats vs. vehicle treatment. In contrast, intra-accumbens infusion of aniracetam (0–6 μg) did not alter alcohol self-administration, suggesting a region-specific role for AMPARs of the amygdala in modulating increased alcohol self-administration. To confirm that increases in self-administration were not due to non-specific changes in behavior, we assessed the effects of systemic and intra-amygdala aniracetam on locomotor behavior in an open field. Neither IP administration (5mg/kg) nor intra-amygdala aniracetam (1ug) altered locomotor behavior vs. vehicle-treatment, suggesting that increased lever responding during alcohol self-administration sessions was not likely due to aniracetam-induced hyperactivity. Collectively, these data present a novel role for AMPARs in selectively modulating increased alcohol self-administration and suggest that amygdala AMPARs play a key role in facilitating alcohol reinforcement. Supported by NIAAA: AA021063(RC), AA014983(CWH), AA016629(CWH), AA011605(CWH)

0349

TOLERANCE TO ETHANOL'S AVERSIVE EFFECTS IN ETHANOL DEPENDENCE: THE ROLE OF NMDA RECEPTOR SIGNALING IN THE BASOLATERAL AMYGDALA

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Repeated cycles of chronic intermittent ethanol exposure (CIE) results in tolerance to ethanol's aversive effects using a Conditioned Taste Aversion (CTA) procedure. This study examined the role of NMDA receptor signaling in the basolateral amygdala (BLA) in mediating ethanol tolerance in ethanol dependent mice. Adult male C57BL/6J mice were implanted with bilateral guide cannulae positioned above the BLA. After 7 days of recovery, mice were exposed to ethanol vapor (EtOH group) or air (CTL group) in inhalation chambers (16 hr/d for 4d), followed by a week of home cage rest. This pattern was repeated for 3 more cycles. At 72hr after CIE, EtOH and CTL mice were tested in the CTA paradigm. Thirty minutes of access to a saccharin solution after the 3rd cycle (1% w/v) or kool-aid (1% w/v) after the 4th cycle served as the conditioned stimulus (CS). Mice were microinjected with test drugs at the end of the CS access period followed immediately by an IP injection of ethanol (1 or 2 g/kg), which served as the unconditioned stimulus (US). Intake of the CS was evaluated 24 hr after conditioning, with data expressed as a percent of CS intake from the conditioning session. Microinjection of vehicle (PBS) coupled with 2 g/kg ethanol revealed significant ethanol-induced CTA in CTL mice (67±8% reduced CS intake) while only moderate aversion in EtOH mice (31±15% reduced CS intake), consistent with tolerance. Separate mice microinjected with AP-5 (5 ng/side) followed by 2 g/kg ethanol showed this NMDA receptor antagonist partially blocked the ethanol-induced CTA in CTL mice (39±10% reduced CS intake) but did not alter aversion in EtOH mice (32±13% reduced CS intake). Finally, another group of mice were microinjected with NMDA (0.3 nmol/side) to enhance CTA with 1 g/kg ethanol, a dose that does not produce aversion. NMDA enhanced ethanol-induced CTA in CTL mice (27±7% reduced CS intake) as expected, but this was not found in the EtOH mice. Taken together, these data clearly implicate NMDA receptor signaling in the BLA as critical for the development of aversion to ethanol. Further, our data suggest that there are adaptations in NMDA receptor signaling in ethanol dependent mice that may underlie tolerance to the aversive effects of ethanol. Ongoing studies are continuing to examine NMDA related mechanisms of tolerance to ethanol's aversive effects. Supported by NIAAA grant AA018036 and VA Medical Research.

0350

ROLE OF GLUTAMATERGIC NEUROTRANSMISSION IN THE NUCLEUS ACCUMBENS IN ETHANOL DRINKING IN ETHANOL DEPENDENT AND NON-DEPENDENT MICE

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We have shown that chronic intermittent ethanol (CIE) exposure significantly increases ethanol consumption in C57BL/6J mice and, using in vivo microdialysis procedures, that CIE exposure also increases extracellular glutamate (GLU_{EX}) levels in the nucleus accumbens (NAc). In the present study, we pharmacologically manipulated glutamatergic tone in the NAc to test the hypothesis that increased GLU_{EX} in the NAc may drive escalation of drinking in this CIE model. After implanting bilateral guide cannula positioned above the NAc, mice were trained to drink ethanol (15% v/v) in a 2-bottle choice, limited access paradigm (water as the alternate fluid). After establishing stable baseline ethanol intake, mice received 4 weekly cycles of chronic intermittent exposure (16 hr/d for 4d) to ethanol vapor (EtOH group) or air (CTL group) in inhalation chambers, with each exposure cycle alternating with a week of limited access drinking test sessions. As expected, ethanol drinking increased in EtOH compared to CTL mice (3 ± 0.1 vs 2.5 ± 0.1 g/kg). During the 4th drinking test period, mice were microinjected with either vehicle (PBS), the non-selective GLU reuptake inhibitor DL-threo-beta-Benzyloxyaspartic acid (TBOA; 0, 250 or 500 μM/side), or the mGluR2/3 agonist LY379268 (0.5, 1 and 5 nmol/side) into the NAc 30 min prior to their usual access to ethanol. Therefore, TBOA increased GLU_{EX} while activating mGluR2/3 receptors with LY379268 reduced presynaptic glutamate release. After vehicle injection, EtOH mice continued to drink more ethanol than CTL mice ($p<0.05$) while TBOA dose-dependently increased ethanol drinking in both groups ($p<0.05$). Conversely, LY379268 dose-dependently reduced drinking ($p<0.05$) and EtOH mice were more sensitive to this effect at lower doses than CTL mice. Taken together, these data are consistent with the idea that a hyperglutamatergic state in the NAc that results from CIE exposure underlies increased ethanol consumption in dependent (EtOH) mice. Additionally, the apparent greater sensitivity of EtOH mice to the intake reducing effects of LY379268 suggests that the increased GLU_{EX} is derived from neuronal rather than glial sources. Supported by NIAAA grant P50 AA10761 and VA Medical Research.

0351

GLUTAMATE NMDAR EXCITABILITY AND AGGRESSION DURING WITHDRAWAL FROM ESCALATED ETHANOL CONSUMPTION IN OUTBRED AND C57BL/6J MICE

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Glutamate excitability and an upregulation of NMDA receptors have been observed in the brains of mice in withdrawal from ethanol consumption. This study examined the effects of the uncompetitive NMDA receptor antagonist memantine on aggression during withdrawal from ethanol. Outbred CFW and inbred C57BL/6J (B6) male mice were given intermittent access to 20% w/v ethanol and water for eight weeks. CFW males voluntarily consumed ethanol, ranging from 5–20 grams/kilogram (g/kg) bodyweight in 24 hours while B6 males consumed greater than 20 g/kg/24h consistently over the 8 weeks of intermittent access. Alcohol withdrawal severity was assessed by handling-induced convulsion scores every two hours after ethanol was withdrawn. Mice showed the most moderate seizures (scores at or above 2 on 0–4 scale) at 6–8 hours into ethanol withdrawal, with B6 mice showing greater convulsion scores during this time period than CFW mice. In the same individuals, aggression during withdrawal was probed with a memantine challenge to assess glutamate excitability. Resident CFW mice were injected with memantine (0, 3, 5, 10, or 30 mg/kg, i.p.) and tested for aggression against an intruder at eight hours into withdrawal. Since B6 mice displayed heightened sensitivity to the compound, they were administered lower memantine doses (0, 1, 3, 5, 10 mg/kg, i.p.). Memantine significantly increased aggression in CFW mice during the withdrawal period, maximally at the 5 mg/kg dose. However, memantine dose-dependently reduced aggression in B6 mice, with 10 mg/kg being completely suppressive. These findings suggest that the uncompetitive NMDA receptor antagonist biphasically increases withdrawal-related aggression in outbred CFW mice, but dose-dependently reduces aggression in high ethanol drinking B6 mice. Ongoing experiments contrast the effects of the noncompetitive NMDA antagonist ketamine on aggression with those of memantine. Also, microinjection studies in the DRN and VTA will help determine specific subpopulations of glutamatergic receptors that are necessary for aggression during alcohol withdrawal.

0352

UNCOMPETITIVE NMDA RECEPTOR ANTAGONISM AND ESCALATED AGGRESSIVE BEHAVIOR IN ALCOHOL-DRINKING MICE

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Memantine is a clinically well-tolerated NMDAR channel blocker, recently suggested as a treatment option for patients suffering from alcoholism. The present study demonstrates that memantine-like compounds interact with a low dose of ethanol to heighten aggressive behavior in mice. Initially, male CFW residents were conditioned to self-administer 1 g/kg of 6% EtOH (w/v) or the equivalent volume of water. Following acquisition of this task, the resident males confronted non-aggressive, group-housed intruders. Subjects that displayed stable aggressive behavior were administered doses of memantine, neramexane or ketamine. For comparison, other animals received doses of either the $mGluR_5$ antagonist, MTEP, or the $mGluR_{2/3}$ agonist, LY379268. Following fluid self-administration and drug treatment, aggression was quantified using the resident-intruder protocol. Low doses of memantine, neramexane and MTEP interacted with ethanol to heighten aggressive behavior while ketamine did not. The $mGluR_{2/3}$ agonist, LY379268, dose-dependently reduced aggressive behavior. While memantine-like compounds have low receptor affinities, ketamine has a high receptor affinity and a slow off-rate. The binding characteristics of memantine and neramexane allow for 'partial trapping' by which some NMDARs are unblocked between depolarizations. This feature may contribute to the differential aggression-heightening interactions between these compounds and ethanol. MTEP also interacted with ethanol to escalate aggression, possibly through inhibition of $mGluR_5$ modulation of NMDARs. Ongoing investigations examine the interaction between acute ethanol consumption and systemically administered or microinjected NMDAR antagonists. Additional research focuses on the effects of memantine-like compounds on aggressive behavior during ethanol withdrawal. These studies will provide necessary information pertaining to the clinical uses of memantine.

0353

GLUTAMATE TRANSPORTER EXPRESSION IN NUCLEUS ACCUMBENS AND DORSAL STRIATUM AFTER CHRONIC INTERMITTENT ETHANOL EXPOSURE

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Using an established model of ethanol dependence and relapse drinking, previous studies have demonstrated increased glutamate levels in the nucleus accumbens (NAc) and dorsolateral striatum (DLS) of mice that have experienced repeated cycles of chronic intermittent ethanol (CIE) exposure. This increase in basal striatal glutamate tone has been demonstrated at least 1 week following final CIE exposure, and may mediate increased ethanol drinking in dependent mice. However, the source of this elevation in extracellular glutamate levels is as yet unclear. One potential cause is altered excitatory amino acid transporter (EAAT) expression in the dorsal and ventral striatum. Removal of glutamate from the extracellular space in these brain regions occurs predominately through EAAT2_and EAAT3. This study tested the hypothesis that reduced EAAT2 and/or EAAT3 expression contributes to elevated glutamate levels in the NAc and DLS in ethanol dependent mice. Adult male C57BL/6J mice received repeated cycles of CIE exposure in inhalation chambers (16 hr/day, 4 days/week to achieve BECs at 175 – 225 mg/dL) alternated with weekly limited access two-bottle choice ethanol (15%) consumption (2 hr/day, 5 days/week, water as the other available fluid). CIE exposed mice showed significant escalation of voluntary ethanol consumption compared to air-exposed controls over 4 weekly test cycles (3.7 ± 0.7 vs. 2.2 ± 0.3 g/kg for CIE and control groups, respectively). Following the 4th test drinking period, Western blot analysis was used to measure total, surface, and intracellular EAAT2 and EAAT3 expression in the NAc and DLS. Mice were sacrificed 7 days post-chamber, 18–22 hours following their last 2-hr drinking session. Results showed that when comparing ethanol dependent and non-dependent mice, no difference was found in total, surface and intracellular EAAT2 and EAAT3 expression in the NAc or DLS brain regions. These data suggest that differences in glutamate release mechanisms (e.g., via system Xc) rather than altered uptake mechanisms may be responsible for the elevated extracellular glutamate levels observed in CIE mice. Ongoing studies will address the role of system Xc in the CIE model as well as the possibility that neuronal hyperexcitability may contribute to increased extracellular glutamate levels in the NAc and DLS which, in turn, may mediate increased ethanol consumption associated with ethanol dependence. Supported by grants T32 AA007474 and P50 AA010761.

0354

ACTIVATION OF GLUTAMATE TRANSPORTER 1 IN CENTRAL REWARD BRAIN REGIONS RESULTS IN REDUCTION OF ETHANOL INTAKE IN ALCOHOL-PREFERRING RATS

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Alcohol-drinking behavior is promoted by increased glutamate transmission in key regions of the mesocorticolimbic motive circuit. We hypothesized that because glutamate transporter 1 (GLT1) is responsible for the removal of most extracellular glutamate, up-regulation of this transporter would attenuate ethanol consumption. We have previously reported that administration of ceftriaxone, a β-lactam antibiotic known to elevate GLT1 expression, has a long-lasting effect in reduction of ethanol consumption in alcohol-preferring (P) rats (Sari et al., 2011). In this study, we investigated whether rats exposed to alcohol show deficit in GLT1 levels as compared to naïve rats exposed to water only, and whether ceftriaxone administration can attenuate this deficit. P rats were given 24-hour concurrent access to 15% and 30% ethanol, water, and food for five weeks. On Week 6, P rats received 50 or 100 mg/kg ceftriaxone (i.p.) or a saline vehicle for five consecutive days. Ethanol consumption was measured daily for 8 days starting on Day 1 of injections. Additional control group was exposed only to water and food. Statistical analyses revealed a significant reduction in daily ethanol consumption for 7 consecutive days, starting on Day 3 of injections, for both ceftriaxone dose groups as compared to saline-treated group. There were also significant increases in water intake in ceftriaxone-treated groups as compared to saline. There was no significant difference in body weight among all groups. Examination of GLT1 levels in all groups showed downregulation of GLT1 expression in nucleus accumbens core (NAcc) and shell (NAcs) separately, but not in the prefrontal cortex (PFC) or hippocampus. Importantly, ceftriaxone administration upregulates GLT1 level only at a dose of 100 mg/kg (i.p.) as compared to saline-treated ethanol-exposed group in NAcc, NAcs, and PFC, but not in the hippocampus. Although the reduction in alcohol intake was not correlated with changes in GLT1 expression in central reward brain regions at 50 mg/kg (i.p.) of ceftriaxone, we suggest here that the drug may have an effect that involves the activation of GLT1 or other unknown mechanisms of action that will be further investigated. These findings provide ample information about the potential uses of ceftriaxone for the treatment of alcohol dependence.

0355

TRANSMEMBRANE SITES OF ALCOHOL ACTION IN GLYCINE RECEPTORS

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Glycine receptors (GlyRs) have become a target of investigations into the sites of action for alcohol in the nervous system and mediate inhibitory neurotransmission in the brainstem and spinal cord as well as higher brain regions including the hippocampus. The transmembrane (TM) domains of GlyR subunits are composed of four alpha-helical segments (TM1-4), and although amino acid residues involved with alcohol action have been previously identified in TM1-3 (I229, S267, and A288) and more recently in TM4 (Y406, W407, I409, and Y410), the specific orientation of these residues with regard to a putative alcohol binding cavity remains controversial. Using cysteine mutagenesis and cross-linking agents, we have previously shown that residues Y406, W407, I409, and Y410 in TM4 are able to form cross-links with A288 in TM3, and the formation of a cross-link between residue 288 in TM3 and these residues in TM4 reduces the ability of alcohol to bind and produce its effect. Similarly, we have previously demonstrated the ability of A288 in TM3 to form cross-links with I229 in TM1, which also appears to reduce the ability of butanol to bind and produce its effect. However in the absence of a GlyR crystal structure, it remains uncertain whether these cross-links are formed between residues within the same subunit or between subunits. In an effort to address these possibilities, we first used homology modeling to examine plausible explanations and potential hypotheses to test. Interestingly, we found that C290 was oriented to cross-link with I229 or its near neighbors. Therefore, the I229C/A288C/C290S was tested in addition to the single mutants. While the I229C/C290S displayed no evidence of cross-linking, the I229C/A288C/C290S mutant showed almost identical evidence of cross-linking to that of the I229C/A288C mutant, suggesting that the endogenous C290 does not play a role. Moreover, the effects of butanol are significantly diminished on the I229C/A288C/C290S triple mutant following application of the cross-linking agent, which also corresponds to the I229C/A288C double mutant. In conclusion, while the additional mutagenesis experiments involving position C290 provide further insight into the participation of residues involved in alcohol action, the orientation of a putative alcohol binding cavity remains controversial. We plan to pursue biochemical procedures such as immunoblotting and mass spectrometry in order to confirm intra-subunit vs. inter-subunit cross-linking.

0356

MUTATION OF A ZINC BINDING SITE (D80) ON THE α1 GLYCINE RECEPTOR CHANGES ETHANOL SENSITIVITY IN VITRO AND ALCOHOL CONSUMPTION AND PREFERENCE IN VIVO

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Ethanol is among the most widely used drugs, yet the molecular targets to which it binds to produce its physiological effects are not completely understood. Among the strongly-supported protein targets of ethanol in the central nervous system are glycine receptors (GlyRs), which in addition to being modulated by alcohols, are also modulated by endogenous zinc. Recent evidence from *in vitro* investigations of recombinant GlyRs suggests that zinc also modulates ethanol action at GlyRs. In the present study, we sought to investigate whether the high-affinity zinc binding position, D80, on the α1 GlyR subunit is important for the enhancing effects of zinc on ethanol modulation of GlyR function. We first conducted *in vitro* experiments using two-electrode voltage clamp electrophysiology to test the effects of ethanol and zinc on mutant α1D80A GlyRs expressed in *Xenopus* oocytes. Data from these experiments revealed that mutant D80A GlyRs showed reduced sensitivity to 50 mM and 200 mM ethanol compared to wild type (WT) GlyRs. In addition, unlike WT α1 GlyRs in which chelating contaminating zinc decreases the effects of ethanol and adding physiological nanomolar zinc increases ethanol enhancement, manipulating the concentrations of zinc in which ethanol was tested on mutant α1D80A GlyRs did not change the magnitude of ethanol's effect. Next, using heterozygous *Glra1*D80A knock-in (KI) mice as an animal model, we evaluated the effects of a zinc-insensitive GlyR mutation on alcohol consumption and other related behavioral tests in mice. *Glra1*D80A KI mice showed decreased alcohol consumption and preference compared to WT littermates, however, this effect was only observed in female mice. There were no differenes detected in ethanol induced loss of righting reflex between KI and WT mice. In addition, D80A KI mice had increased startle responses compared to their WT littermates. Ethanol (0.5 and 1.0 g/kg i.p.) had no effect on startle responses of mutant KI mice. However, both ethanol doses increased startle responses in male WT mice, whereas only 0.5 g/kg increased startle responses in female WT mice. Other behavioral tests were also conducted including tests of ethanol motor incoordination (rotarod) and strychnine induced convulsions, but there were no significant differences detected between KI and WT mice in these assays. Supported by R01AA06399 (RAH) and F31AA019852 (LMM).

0357

POSITIVE ALLOSTERIC MODULATORS DIFFERENTIALLY AFFECT FULL VS. PARTIAL AGONIST ACTIVATION OF THE GLYCINE RECEPTOR

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Taurine acts as a partial agonist at the glycine receptor (GlyR) in some brain regions such as the hippocampus, striatum and nucleus accumbens. Ethanol, volatile anesthetics, and inhaled drugs of abuse are all known positive allosteric modulators of GlyRs, but their effects on taurine-activated GlyRs remain poorly understood, especially their effects on the high concentrations of taurine likely to be found after synaptic release. Two-electrode voltage-clamp electrophysiology in *Xenopus* oocytes was used to compare the enhancing effects of ethanol, anesthetics, and inhalants on human homomeric a1 GlyR activated by saturating concentrations of glycine vs. taurine. Allosteric modulators had negligible effects on glycine-activated GlyR while potentiating taurine-activated currents. In addition, inhaled anesthetics markedly enhanced desensitization rates of taurine- but not glycine-activated receptors. Our findings suggest that ethanol, volatile anesthetics and inhalants differentially affect the time courses of synaptic events at GlyR, depending on whether the receptor is activated by a full agonist or a partial agonist.

0358

MANIPULATION OF PHARMACOLOGICALLY RELEVANT FREE-CHOICE DRINKING IN HAP1 MICE USING THE TRIPLE MONOAMINE RE-UPTAKE INHIBITOR AMITIFADINE (DOV 21,947)

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It is increasingly clear that alcohol acts on many neurotransmitter systems, and therefore research on pharmacological treatments for alcohol dependence has become focused on developing treatment regimens that modulate multiple neurotransmitter systems. Recently, we established that with food and water freely available, HAP1 mice consistently drink to intoxicating levels (~250 mg/dl BAC) during the active (dark) portion of the light-dark cycle. Their consistent behavior allows us to predict intakes during pharmacologically relevant drinking across the active period. In addition, we can explore how differences in timing drug administration affect drinking behavior. In this study, we assessed whether the triple reuptake inhibitor (5-HT, DA, and NE) amitifadine (formerly EB-1010/DOV 21,947) is effective in decreasing ethanol intake during a known period of high ethanol intake. Subjects were HAP1 mice of both sexes (N=36). Mice were single housed in reverse-cycle and had *ad libitum* access to water and food throughout the experiment. After 3 weeks of free choice access to 10% alcohol, injections of 0, 8, 14, or 25 mg/kg of amitifadine were given on 4 days with 5–7 days of wash out between injections, and readings were taken bi-hourly from 8 am to 8 pm. During the first 2 days, injections occurred 30 minutes prior to drinking onset (lights off). During the successive days, injections were performed during a period of high intake (2 h after lights off). For the first two injection days, there was a main effect of Dose, such that all doses of the drug significantly decreased ethanol intake ($ps < .05$). Corresponding increases in water intake were observed for the 14 and 25 mg/kg dose groups ($ps < .05$). When drug was administered 2 h into the drinking period, an effect of Dose was also observed, although only the 14 and 25 mg/kg doses reduced ethanol intake ($ps < .05$). There was also an increase in water intake at these 2 doses ($ps < .05$). Although tolerance to the drug may have developed, it is possible that amitifadine may be more effective at decreasing intake before ethanol is on board than after drinking is initiated. These results also suggest that enhancing monoaminergic neurotransmission with amitifadine may be a promising pharmacological target, as it decreased ethanol intake, but did not affect normal fluid intake as shown by compensatory increases in water intake. IUPUI School of Science to NJG, NIAAA training grant AA07462 support to LMM.

0359

TRIPLE REUPTAKE INHIBITORS REDUCE IMPULSIVITY IN HIGH ALCOHOL PREFERRING MICE AS MEASURED BY THE DELAY DISCOUNTING TASK

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High levels of impulsivity, defined as the tendency to choose a small immediate reward over a larger delayed reward, have been shown to be characteristic of alcoholics, and children of alcoholics tend to be more impulsive than children of non-alcoholics. Therefore, impulsivity may be an endophenotype of alcoholism. Consistent with this theory, mice selectively bred to volitionally consume high amounts of ethanol and reaching high blood ethanol levels during free-choice access (High-Alcohol Preferring, or HAP mice) have been shown to be more impulsive than lines with low alcohol consumption, as measured by the Delay Discounting (DD) task. HAP mice, therefore, are good candidates in which to search for medications that might decrease both impulsivity and alcohol intake.
HAP2 mice (ns = 9–12) were run in an adjusting amount DD task, in which the delay to the large reward was 10 s. This delay has previously shown sensitivity to drugs, such as amphetamine, that reduce impulsivity (Oberlin et al., 2010). All drugs were given prior to a 1-hr DD test session for 2–5 consecutive days. Three putative pharmacotherapies were tested. Firstly, we tested tolcapone (3, 10, 30, and 50 mg/kg), a COMT inhibitor previously shown to preferentially increase DA neurotransmission in the prefrontal cortex. Then we tested two putative antidepressant compounds that inhibit monoamine uptake transporters, amitifadine (formerly DOV 21,947; 4, 8, or 12 mg/kg) and DOV 102,677 (10, 20, 30, or 40 mg/kg). Amitifadine is an unbalanced reuptake inhibitor, with preferential inhibition of the serotonin transporter (Skolnick et al, 2003), while DOV 102,677 shows more balanced inhibition of the DA, 5-HT, and NE transporters (Popik et al., 2006).
Results demonstrated that the impulsivity of this cohort of mice at baseline was consistent with prior studies using HAP mice. Tolcapone failed to decrease impulsivity, while each DOV compound did decrease impulsive choice. Amitifadine showed significant efficacy only at 8 mg/kg dose, a dose effective in the forced swim test, but that does not produce locomotor hyperactivity. DOV 102,677 showed dose-dependent decreases in impulsive responding. These findings suggest the utility of these uptake blockers in attenuating impulsive choice. Future studies will assess whether they also decrease alcohol consumption. IUPUI School of Science to NJG and AA07611 to David Crabb.

0360

A NOVELSEROTONIN 5HT2C AGONIST/5HT2A-2B ANTAGONIST SELECTIVELY DECREASES ETHANOL SELF ADMINISTRATION AND INHIBITS THE ALCOHOL DEPRIVATION EFFECT

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Serotonin receptor subtypes 5HT2A and 5HT2C modulate limbic circuitry and addictive behaviors in opposite ways, such that 5HT2A receptor activation increases ethanol reinforcement while 5HT2C receptor activation decreases ethanol reinforcement. We recently reported a first-in-class serotonin 5HT2C agonist/5HT2A-2B antagonist, (1*R*,3*S*)-(−)-*trans*-1-phenyl-3-aminotetralin, (PAT). The hypothesis tested here is that 5HT2C agonist activity together with 5HT2A inverse agonism in a single drug specifically decreases responding for ethanol reward. Female Sprague-Dawley rats were trained to self-administer plain or 10% ethanol gel using operant schedules. Average ethanol consumption during 30-min FR5 sessions was 1.2 ± 0.05 g ethanol/kg body weight. Drugs were injected i.p. 20 min prior to the start of the operant session. (-)-*Trans*-PAT produced a dose-related inhibition of ethanol gel operant responding with a maximal inhibition of 50% at 10 mg/kg i.p ($p<0.05$, N=10). (-)-*Trans*-PAT did not affect operant responding for plain gel. In contrast, 10 mg/kg (1*RS*,3*R*)-(+)-*trans*-PAT, a weak partial agonist at 5HT2A/2C receptors, nonspecifically decreased responding for ethanol and plain gel. Using PR10 schedules, 10 mg/kg (-)-*trans*-PAT decreased consumption 25% (0.178±0.04 to 0.137±0.04) and breakpoints were also decreased 22% (38±8 to 30±10; N=5). Also, the effect of (-)-*trans*-PAT in rats experiencing the alcohol deprivation effect were measured. Rats responded on an FR5 schedule for ethanol gel reinforcement either continuously or were deprived of ethanol for 21 days (i.e. received only plain gel reinforcement). Rats were further subdivided into (-)-*trans*-PAT (5 mg/kg, i.p.) and saline groups prior to the first day of ethanol gel re-access (N=6). Deprived rats exhibited a 70% increase in ethanol consumption during the first three days of re-access to ethanol gel. (-)-*Trans*-PAT (but not saline) abolished the difference between deprived and non-deprived rats on the first day of re-access and also decreased ethanol consumed on the second and third day of ethanol re-access. These results indicate PAT-type 5HT2C agonist/5HT2A-2B antagonist drugs could translate to effective pharmacotherapy of alcoholism. This work was funded by NIH RO1 DA023928.

0361

THE DOPAMINE STABILIZER (-)-OSU6162 ATTENUATES VOLUNTARY ETHANOL INTAKE AND ETHANOL-INDUCED DOPAMINE OUTPUT IN THE NUCLEUS ACCUMBENS

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New medications for alcohol use disorder (AUD) are needed. ''Dopamine stabilizers'' is a class of dopamine D2 receptor antagonists characterized by a balanced action on different populations of dopamine receptors and capable of dampening high, while stimulating low dopamine-dependent behavioral activity levels of experimental animals. Thus, they may be hypothesized to normalize dysregulated dopamine activity induced by, for example, long-term alcohol consumption. Here we evaluated the effects of the dopamine stabilizer (-)-OSU6162 (OSU6162) on ethanol-mediated behaviors in rats voluntarily consuming ethanol for at least three months before treatment. We found that OSU6162-treatment selectively decreased voluntary ethanol consumption and preference without decreasing intake of water or a salty solution. The effect on ethanol intake was more pronounced in rats voluntarily consuming high compared to moderate amounts of ethanol. There was no tolerance development to OSU6162's ability to decrease ethanol intake during repeated OSU6162 treatment and no rebound increase in ethanol intake after the treatment was terminated. Furthermore, we studied the interaction of OSU6162 with ethanol on dopamine release and metabolism in awake rats, using microdialysis. We found that pretreatment with OSU6162 blunted the ethanol-induced dopamine output in the nucleus accumbens. These results highlight OSU6162's ability to stabilize the dopamine activity depending on the prevailing dopaminergic tone and indicate that OSU6162 might decrease ethanol intake by attenuating the acute rewarding properties of ethanol. The present study is to our knowledge the first to show that OSU6162 may serve as a novel treatment of AUD.

0362

BIASED AGONISTS OF DELTA OPIOID RECEPTORS FOR THE TREATMENT OF ALCOHOLISM AND ANXIETY DISORDERS

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The delta opioid receptor (DOR) is a promising target to treat multiple neurological diseases, including depression, anxiety and alcohol disorders. Recently, we found that DOR1 and DOR2 subtype selective agonists modulate ethanol consumption and anxiety-like behavior in a distinctly different manner. More specifically, the DOR1 agonist TAN-67 reduces ethanol consumption and does not reduce anxiety-like behavior, whereas the DOR2 agonist SNC80 has anxiolytic-like effects, but increases ethanol consumption. This would suggest that a DOR2 agonist may not be an optimal drug to treat anxiety disorders (AD), as it would lead to alcohol use. We have begun to examine what mechanisms could be responsible for the subtype selective effects of these DOR ligands. It has been known that G protein-coupled receptors, such as the DOR, are able to signal both via a G-protein dependent way and a G-protein independent/beta-arrestin dependent manner. Therefore, we investigated the beta-arrestin dependence of DOR-subtype selective agonists effects *in vitro* and *in vivo*. We find differences in the downstream signal proteins, commonly associated with beta arrestin mediated signaling, that are activated after TAN-67 and SNC80 binding to DORs *in vitro*. Moreover, we find that the effects on ethanol consumption of the DOR2 agonist SNC80 but not those of the DOR1 agonist TAN-67 are dependent on beta-arrestin. However, neither the anxiolytic-like nor the locomotor effects of SNC80 are dependent on beta arrestin. Our results show clear biased agonism for DOR-subtype selective drugs and suggest that it may be possible to develop a DOR2-selective agonist that decreases anxiety without increasing alcohol consumption. Similarly, it may be possible to develop a DOR2 antagonist that solely modulates beta-arrestin mediated signaling pathways and would thus reduce ethanol consumption, without increasing anxiety.

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0363

STRESS AND CRAVING: PREDICTING ALCOHOL TREATMENT OUTCOMES USING A HUMAN LABORATORY PARADIGM OF INTERPERSONAL STRESS INDUCTION

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Background: Alcohol dependence is associated with high rates of relapse. Alcohol abuse is associated with alterations in the brain stress and reward system that may contribute to increased relapse vulnerability. Although there is substantial epidemiological and anecdotal support for stress-induced relapse, empirical support that stress causes relapse poses both methodological and ethical challenges, and results are equivocal. Methodological designs that more closely model interpersonal stress may provide an effective and ethical approach. The aim of the present study was to develop and validate a standardized paradigm of stress-induction based on an individualized, interpersonal stressful event and its effects on alcohol craving and drinking in treatment seeking, alcohol dependent (AD) subjects.
Method: A stress-script development session occurred in which subjects were asked to identify a recent, highly stressful event. A semi-structured interview was developed to ascertain specific details, visceral, and muscular responses surrounding the stressor. An individualized, 250-word script depicting the event was created using a standardized template. The script was then audio-recorded for later playback during a laboratory session and validated with objective (salivary cortisol) and subjective measures of distress. Moreover, *in vivo* craving for alcohol was assessed pre- and post- stress induction and subsequent measures of drinking and craving were obtained for the remaining 10-wks of outpatient treatment.
Results: Subjects were 70 (42=male, 28=female) AD outpatients that participated in a laboratory paradigm of stress-induction at Week 2 of a 12-wk treatment study. Stress script exposure was associated with significant increases in distress and alcohol craving and a blunted cortisol response (p's<.05). Moreover, stress-induced craving in the lab significantly predicted latency to relapse, mean drinks per week, days abstinent, and rates of treatment failure.
Conclusions: The findings support the use of craving in response to an acute, interpersonal, psychosocial stressor as a predictor of alcohol relapse propensity. Presented with stressful stimuli of equal severity, alcoholics respond with varying degrees of craving and hormonal response. Those with increased craving and blunted cortisol had the poorest outcome. Furthermore, treatments targeting high stress levels and the associated high levels of alcohol craving are likely to improve treatment outcomes.

0364

ASSESSMENT OF PREGNENOLONE EFFECTS ON ALCOHOL INTAKE IN MALE ALCOHOL PREFERRING RATS

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Neuroactive steroids modulate neurobehavioral function in rats. Among other actions, these steroids produce anxiolytic effects when given to rodents. The goal of this study was to assess the effects of acute and chronic administration of the neurosteroid pregnenolone, a precursor of GABAergic neuroactive steroids, on alcohol intake in alcohol preferring P rats. Following the standard procedure rats were given a free choice of alcohol and water. After establishment of a stable baseline, rats were injected IP with the vehicle or one of the three dose of pregnenolone (25, 50 or 75 mg/kg) or orally (vehicle or 75 mg/kg) following repeated measures counterbalanced order and their alcohol and water intake were recorded at 2, 4, 6 and 24 hr. Also, the chronic (10 days) effects of 50 mg/kg pregnenolone on alcohol intake were determined. In another experiment, rats were withdrawn from alcohol for 3 consecutive days while had free access to food and water. Then, 15 min before re-exposure to alcohol, they were given a dose of 75 mg/kg pregnenolone or vehicle and their alcohol intake were measured at 2, 4, 6 and 24 hr.
Results: our results show that the main effect of IP injection of pregnenolone in reducing alcohol intake was significant ($p<0.025$). Compared with the vehicle, pregnenolone only at 75 mg/kg significantly ($p<0.01$) reduced alcohol intake. The main effect of pregnenolone on alcohol preference was also significant ($p<0.05$). Compared with the vehicle pregnenolone both at 50 mg/kg ($p<0.025$) and at 75 mg/kg ($p<0.025$) significantly reduced alcohol preference. However, oral administration of 75 mg/kg did not have a significant effect on alcohol intake. Pregnenolone at these doses did not exert a significant effect on water intake or total fluid intake. In chronic experiments, tolerance to the suppressant effects of pregnenolone developed on the second day. In the post-deprivation study, when the urge for drinking is enhance, injection of of 75 mg/kg pregnenolone failed to exert a significant effect on alcohol intake or alcohol preference.
Conclusions: These results show that pregnenolone given IP, but not orally, reduces alcohol intake in P rats. However, the fact that tolerance developed quickly to its suppressant effect and it also failed to significantly reduce post-deprivation alcohol intake diminishes its promise.

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0365

THE CRF-R1 ANTAGONIST, CP376395, DECREASES 20% ETHANOL CONSUMPTION IN LONG-EVANS RATS TRAINED TO DRINK ON AN INTERMITENT, BUT NOT CONTINUOUS, SCHEDULE

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Rationale: Stress has long been postulated to play a role in mediating pathological ethanol intake in both humans and laboratory animals. Corticotrophin releasing factor (CRF) is a critical mediator of the stress response and has been shown to be a key modulator of ethanol-mediated behaviors. In the present study, we examined the effects of the CRF receptor 1 (CRF-R1) antagonist, CP-376395, on two-bottle choice ethanol consumption and on CRF binding in the brain.
Methods: Two groups of Long-Evans rats were trained to consume 20% ethanol; one group on a continuous schedule (seven 24 hour sessions per week) and another on an intermittent schedule (three 24 hour sessions per week; Monday, Wednesday, Friday). Following nine weeks of ethanol exposure, CP-376395 (0, 5, 10 mg/kg, i.p.) was administered in a Latin-square design 30 min prior to the onset of the drinking session. At the completion of the treatment regimen, brains were collected and microdissected for [35S]GTPγS binding studies.
Results: CP-376395 (10 mg/kg) reduced 20% ethanol consumption in animals trained on the intermittent, but not the continuous, schedule. [35S]GTPγS binding assays revealed significant CRF stimulation in the hypothalamus, which was attenuated by CP-376395.
Conclusions: The data provides further support for the use of CRF-R1 antagonists for the treatment of alcohol use disorders and suggests that ethanol consumption alters CRF function in the hypothalamus.
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Keywords: CRF; CP-376395; intermittent-access; ethanol; hypothalamus

0366

LEVETIRACETAM AND INTERMITTENT ALCOHOL DRINKING IN C57BL/6J MICE

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Rationale: Excessive glutamatergic activity is thought to contribute to the consequences of repeated alcohol exposure. Levetiracetam (LEV) is an anti-epileptic drug that reduces glutamatergic activity by inhibiting the glutamate synaptic vesicle 2A transporter. In C57BL/6J (C57) mice, acute administration of LEV reduces the effects of alcohol on sensitized locomotor activity in an open field and brain stimulation reward (BSR) in the intracranial self-stimulation (ICSS) procedure. This suggests that LEV may attenuate the effect of alcohol on mesocorticolimbic activity and modify alcohol drinking.
Objective: The objective was to determine the effects of acute LEV on alcohol intake by C57 mice using two models of intermittent alcohol drinking.
Methods: In the first experiment, separate groups of male C57 mice consumed either a 20% alcohol or a 0.5% sucrose solution presented in one bottle in their home cage for four hours, every other day. In the second experiment, separate groups of male C57 mice were presented with two bottles, one containing water (H2O) and the other containing either 20% alcohol or 0.5% sucrose for 24 hours, every other day (after Hwa et al. 2011). Levetiracetam (0.3 – 100 mg/kg, i.p.) was administered 30 minutes before the start of the drinking session.
Results: In experiment one, the mice consumed an average of 4.4 g/kg and had blood alcohol levels of 75 mg/dl in the second hour of the drinking session. Acute LEV dose-dependently increased alcohol, but not sucrose drinking. The 3mg/kg dose was the most effective dose, increasing alcohol intake by ca. 25%; the 100 mg/kg dose was less effective, increasing alcohol intake by ca. 10%. In experiment two, the mice consumed an average of 21 g/kg in 24 hours, 5.4 g/kg during the first 4 hours of the drinking session. The results of experiment two will determine if LEV affects alcohol drinking that is escalated by repeated periods of 24 hr intermittent access.
Conclusions: The specific effect of LEV on alcohol, rather than sucrose, drinking suggests that LEV does not increase alcohol consumption by altering thirst or taste mechanisms. Rather, the increased alcohol consumption is consistent with the involvement of glutamatergic activity in the rewarding and reinforcing effects of alcohol. After LEV treatment, more alcohol may be required to potentiate the activity of the mesocorticolimbic circuit. Support: AA 018335 to CJM.

0367

EFFECTS OF NALTREXONE ON ETHANOL DRINKING FOLLOWING CHRONIC INTERMITTENT ETHANOL EXPOSURE

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As a first step in validating the use of the chronic intermittent ethanol (CIE) exposure paradigm for target assessment, we have examined the effects of daily naltrexone treatment on CIE induced excessive ethanol drinking. In mice, it has been shown that naltrexone administered immediately before ethanol availability in the Drinking-in-the-Dark model dose dependently decreased ethanol drinking (Kamdar et al., 2007). In terms of CIE, however, there do not appear to be any published results using mice. In alcohol preferring (P) rats naltrexone was shown to reduce operant ethanol self-administration in both control and vapor exposed (analogous to CIE model) animals to similar extents (Gilpin et al., 2008). These data suggest that naltrexone decreases the high innate alcohol drinking by P rats, but its effect is not exaggerated during alcohol dependence. In the present study, baseline two hour two-bottle choice ethanol drinking was determined in male C57BL/6J mice, they each were then assigned to an ethanol vapor group (3 days, 16 hr per day) or control group, and then two bottle choice ethanol drinking was reexamined following 3 days of abstinence. This entire cycle was repeated 2 additional times (for a total of 3 cycles). We examined the effects of 1 mg/kg naltrexone given once per day, 30 min prior to two-bottle choice testing for 5 consecutive days. As expected, saline injected CIE mice consumed more ethanol than saline injected control mice. Naltrexone significantly decreased ethanol drinking in both the control and CIE mice to similar extents on the first day of treatment. There was no effect of naltrexone treatment beyond this first day (i.e. days 2–5). Daily naltrexone injections were continued another two weeks in these mice as well as an age-matched ethanol-naïve group and anxiety-like behavior and cued and contextual fear conditioning were examined. Naltrexone significantly decreased anxiety-like behavior in ethanol-naïve mice and decreased fear conditioning in ethanol-experienced mice, suggesting that chronic naltrexone differentially affects behavior depending on ethanol history. These data do support the use of the CIE model to assess potential new targets for alcoholism treatment, while adding to the existing information concerning chronic naltrexone effects. Supported by the Integrated Neuroscience Initiative on Alcoholism (INIA)-West, 1U01 AA020893.

0368

AN EFFICIENT CHEMICAL SYNTHESIS OF NEUROKININ-1 (NK1) ANTAGONIST L822429, A USEFUL TOOL FOR PHARMACOLOGICAL STUDIES IN RODENT MODELS

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Neurokinin-1 receptor (NK1R) antagonists are anxiolytic, decrease alcohol consumption in mice, and can suppress alcohol cravings in alcoholics. The NK1R antagonist L822429 has been found to be a valuable tool for studying the behavioral effects of NK1R antagonism in rodent models. It selectively suppressed stress-induced reinstatement of alcohol-seeking in rats and had no effect on baseline alcohol self-administration, general locomotor activity, or self-administration of sucrose solution. In order to further investigate the role of the NK1 system for relapse-like behavior, a practical synthesis of chiral L822429 was required. Here, we report an efficient, eleven-step chemical synthesis of 2*S*,3*S*-L822429 from the readily available *p*-nitrophenol. The synthetic route features the cyclopropanation of a vinylphenol ether with a (halomethyl)zinc reagent as the key step. The identity and purity of target compound L822429 was confirmed by ^{1}H NMR, ^{13}C NMR, high resolution mass spectrum (HRMS) and combustion analysis. The optical purity was determined to be over 99% ee by derivatization of the intermediate, (2*S*,3*S*)-2-phenylpiperidin-3-amine with alpha methylbenzylisocyanate and ^{1}H NMR analysis. This synthesis of L822429 is shorter, simpler and an order of magnitude higher yielding (12% overall) than previous work. It is easily applicable to decigram scale laboratory synthesis of L822429 and thus enables future pharmacological studies in the rat.

0369

THE ROLE OF MICRORNA-9 AND MICRORNA-206 IN THE MEDIAL PREFRONTAL CORTEX OF ALCOHOL DEPENDENT RATS

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Background: Chronic ethanol exposure causes a large cascade of gene expression changes in the medial prefrontal cortex (mPFC). The global regulation exerted by miRNAs, and their ubiquitous nature may offer a mechanism behind the wide-ranging changes in gene expression. We previously identified in a microarray, miRNA-9 (miR-9) and miRNA-206 (miR-206) to be differentially regulated in the mPFC after chronic ethanol exposure. Here, we determined the functional role of miR-9 and miR-206 in alcohol dependence.
Methods: miRNAs were isolated using the mirVana miRNA Isolation kit. Quantitative real-time-PCR analysis of miRNA and mRNA expression levels were performed using the TaqMan assays. In situ hybridization was carried out using a standard procedure. Luciferase reporter assays to BDNF 3'UTR were created to determine binding potential of miR-206.
Results: miR-9 was confirmed by PCR to be significantly downregulated in the mPFC as well as the amygdala (AMG), but not in the ventral tegmental area (VTA) or cerebellum (CER) in rats with a history of alcohol dependence. miR-9 was also confirmed by PCR to be downregulated in the anterior cingulated cortex (ACC) of post-mortem human alcoholics showing differential regulation of miR-9 across mammalian species . *In situ* hybridization of miR-9 illustrated a ubiquitous downregulation of miR-9 specifically in the mPFC. miR-206 was confirmed by PCR to be significantly upregulated in the mPFC, but not in the VTA, AMG, or CER. *In situ* hybridization of miR-206 demonstrated a significant upregulation of miR-206 in the mPFC. Analysis using microRNA.org revealed 2 conserved target sites for miR-206 in the 3'UTR of BDNF. BDNF was found to be downregulated in our post-dependent rats by microarray analysis and PCR. BDNF expression was repressed by miR-206 but not miR-9 in a 3'UTR reporter assay.
Discussion: In conclusion, we have identified persistent, coordinated changes in the expression of miR-9 and miR-206 following alcohol dependence. We verified miR-9 expression across mammalian species and illustrated ubiquitous downregulation of miR-9 by *in situ.* We confirmed that miR-206 binds and inhibits the expression of BDNF. Assays are being finalized to determine the effect of miR-206 on BDNF-mediated dendritic spine density. Studies are also being currently executed to reverse dependent-like behavior using miR-9 overexpression vectors and miR-206 anti-miR vectors *in vivo* in the mPFC of post-dependent rats.

0370

EFFECTS OF LEVETIRACETAM ON ALCOHOL- AND COCAINE-RELATED BEHAVIORS IN C57BL/6J MICE

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The antiepileptic drug levetiracetam is under investigation as a possible treatment for alcohol use disorders, yet virtually no data are available on its preclinical pharmacology in animal behavioral models relevant to drug or alcohol abuse. The effects of levetiracetam on locomotor stimulation by acute and repeated administration of alcohol or cocaine and on acute potentiation of brain stimulation reward (BSR) were measured in male C57BL6/J mice. Levetiracetam alone (10.0 – 100.0 mg/kg i.p.) had no significant effect on total locomotor behavior, BSR threshold, or operant response rate. Pretreatment with levetiracetam (100 mg/kg i.p.) had no effect on acute locomotor stimulation by alcohol (2.0 g/kg i.p.) or cocaine (15.0 mg/kg i.p.). However, levetiracetam pretreatment independently blocked both development and expression of locomotor sensitization to alcohol. Levetiracetam also attenuated both potentiation of BSR by low-dose (0.6 g/kg p.o.) alcohol and the aversive effects of higher-dose (1.7 g/kg p.o.) alcohol on brain reward. In contrast, levetiracetam accelerated locomotor sensitization to cocaine over five consecutive days but did not affect sensitization after 10 days of withdrawal, and increased potentiation of BSR by acute cocaine. These data suggest that levetiracetam may have effects on the behavioral pharmacology of alcohol in preclinical models that predict its potential usefulness in the treatment of alcoholism. The findings are discussed in the context of the novel mechanism of action of levetiracetam as a presynaptic glutamate release inhibitor.

0371

GANAXOLONE AND THIP ALTER LIMITED-ACCESS ETHANOL INTAKE IN MICE

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The present study examined the role of a GABAergic neurosteroid agonist or an extrasynaptic $GABA_A$ receptor agonist on ethanol intake in a 2-bottle limited-access lickometer procedure. Male C57BL/6J mice (n=24) were allowed 2-hour access to either a 10% (v/v) ethanol solution (10E) or water beginning 2 hours into the dark cycle. In separate groups of mice, intake was measured following a systemic injection of the neurosteroid agonist ganaxolone (GAN; 0, 5, 10 mg/kg; n=12) or the extrasynaptic $GABA_A$ receptor agonist gaboxadol (THIP; 0, 2, 4, 8, 16 mg/kg; n=12). GAN dose-dependently decreased ethanol intake when compared to its within-subjects vehicle, with 10 mg/kg GAN decreasing intake by 18%. Bin analysis revealed a consistent decrease across the 2-hour span. There was no significant change in any of the bout parameters examined. THIP also dose-dependently decreased ethanol intake compared to its within-subjects vehicle, decreasing intake by 18% with 8 mg/kg THIP and by 83% with 16 mg/kg THIP. This decrease occurred primarily during the first hour of access, and bout analysis revealed that the change in intake was partly attributable to an alteration in bout frequency. Importantly, mice achieved physiologically relevant blood ethanol concentrations (GAN group: 1.15 ± 0.17 mg/ml; THIP group: 1.25 ± 0.21 mg/ml) at the end of the 2-hour session. These data extend previous studies showing an effect of neurosteroids and extrasynaptic $GABA_A$ receptor activation on ethanol intake in a variety of behavioral paradigms and contribute to literature highlighting extrasynaptic $GABA_A$ receptors as an important target in ethanol reinforcement.

3. PHYSIOLOGY C.N.S.
a. Electrophysiology 50–66 / 372–388

0372

STRESS AND ALCOHOL INDUCED PLASTICITY OF OPIOID SIGNALING IN THE EXTENDED AMYGDALA

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The bed nucleus of the stria terminalis (BNST) orchestrates physiological outcomes related to stress and anxiety. The BNST is a heterogenous structure with multiple cell types that receive glutamatergic inputs from the hippocampus, prefrontal cortex, paraventricular thalamus and basolateral amygdala and GABAergic inputs from the central nucleus of the amygdala. Kappa opioid receptors (KOR) have been previously shown to inhibit GABAergic signaling in the BNST, but their effect on glutamatergic transmission remains largely unexplored. The current study identified KOR-mediated modulation of glutamatergic signaling, and assessed plasticity in KOR-mediated effects on both GABAergic and glutamatergic transmission in the BNST following stress and alcohol exposure.
Whole-cell patch clamp experiments were conducted in brain slices containing the BNST from exposed mice 24 hours following manipulations. In the BNST, application of both the endogenous KOR agonist dynorphin, as well as the synthetic agonist U69,593 inhibited evoked excitatory post-synaptic currents (eEPSCs) and was blocked by pre-application of norBNI. These results indicate KORs play a role in regulating glutamatergic signaling in the BNST. Ongoing studies are exploring the signaling mechanisms underlying this KOR mediated inhibition, as well as the locus of action. We then examined the impact of repeated restraint stress and binge-like alcohol exposure on KOR modulation of synaptic transmission. We found that stress, but not binge-like alcohol exposure, impaired KOR modulation of GABA transmission. Future studies will examine plasticity in this KOR mediated inhibition of glutamatergic signaling following stress and alcohol exposure.

0373

MECHANISMS OF CORTICOTROPHIN RELEASING FACTOR NEURON REGULATION IN THE EXTENDED AMYGDALA: POTENTIAL IMPORTANCE FOR RELAPSE

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Relapse is a significant challenge to successful treatment of alcoholism. Corticotrophin releasing factor (CRF) mediated activation of the bed nucleus of the stria terminalis (BNST) and the central amygdala (CeA), two components of the extended amygdala, may play an important role in relapse behaviors. Previous reports suggest a serial circuitry in the BNST where drug-associated cues, via increased dopamine levels, or exposure to stress, via increased norepinephrine levels, may increase CRF levels in the BNST thereby precipitating relapse. However, there is little evidence confirming this hypothetical neurocircuit. Thus, we sought to determine if dopamine or the b-adrenergic receptor agonist, isoproterenol, can directly modify CRF neuron activity in the extended amygdala and if chronic intermittent ethanol (CIE) exposure may modulate this circuitry. Using a BAC-transgenic strategy to mark CRF-expressing neurons with a red fluorescent variant, CRF neuron activity was monitored using whole-cell patch-clamp electrophysiological methods. Acute application of dopamine and isoproterenol significantly depolarized BNST CRF neurons in persistent manner. In addition, dopamine and isoproterenol both significantly depolarized CeA CRF neurons, but in a reversible manner. CeA CRF neurons also appear to be distinct from BNST CRF neurons as CeA CRF neurons maintain a more depolarized resting membrane potential. In addition, 4–6 our withdrawal from CIE significantly enhanced basal BNST excitability compared to sham controls and reduced the ability of exogenous CRF to further enhance presynaptic glutamate release. Together with the finding that CRF enhances excitatory neurotransmission onto BNST neurons projecting to the ventral tegmental area (VTA) in naïve animals, these data suggest that both dopamine and isoproterenol may directly enhance CRF release from both local BNST and CeA sources, potentially precipitating relapse to alcoholism via enhanced signaling to VTA. Potential pharmacotherapies targeting this extended amygdala circuitry may be useful in the prevention of relapse to alcoholism. Funding: NIH grants AA020140 and AA019455

0374

ADENOSINE SIGNALING MODULATES EXCITIBILITY IN THE AMYGDALA AND IS ALTERED IN A RODENT MODEL OF EARLY LIFE STRESS THAT INCREASES ETHANOL DRINKING

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Adenosine (ADO) serves as an inhibitory neuromodulator in the mammalian CNS. ADO regulation of CNS excitability is mediated predominantly by presynaptic A1 receptors that decrease glutamate release and A2A receptors that may enhance GABAergic inhibition. Despite evidence that ADO regulates anxiety and ethanol drinking, little is known about ADO modulation of synaptic transmission in the basolateral amygdala (BLA), a region known to play an integral role in both anxiety disorders and addiction. To that end, we used whole-cell patch clamp recording methods to characterize the acute effects of ADO and theophylline (THEO), a non-selective ADO receptor antagonist, on GABAergic and glutamatergic synapses recorded from BLA pyramidal neurons in Sprague Dawley rats. We also conducted electrophysiological studies in Long Evans rats that had been socially isolated (SI) or group housed (GH) during adolescence (PD 28-70). ADO (20–40 μM) enhanced $GABA_A$ IPSCs and inhibited AMPA EPSCs recorded from BLA pyramidal neurons. Moreover, THEO produced the opposite effects, decreasing GABAergic inhibition and increasing glutamatergic excitation. These latter findings suggest that extracellular levels of ADO may tonically regulate BLA excitability. Adolescent social isolation significantly increased anxiety-like behaviors in the elevated plus-maze and also increased voluntary ethanol intake. To determine if the BLA ADO system was affected by the adolescent social isolation procedure, we conducted an electrophysiological analysis of a cohort of SI and GH rats, during a time period coinciding with the behavioral alterations induced by SI. These studies revealed that tonic ADO regulation of BLA excitation may be diminished in SI rats as THEO potentiation of AMPA EPSCs was significantly reduced in recordings from SI BLA pyramidal neurons, relative to GH recordings. Analysis of paired-pulse ratios also indicated a reduction in glutamate release probability onto BLA pyramidal neurons in SI rats. Taken together, these studies suggest that ADO modulates both GABAergic and glutamatergic transmission in the BLA and that ambient levels of ADO may dynamically regulate BLA excitability. These findings also suggest that tonic ADO signaling in the BLA may be reduced following adolescent social isolation and possibly contribute to the increased anxiety-like behavior and ethanol intake that are associated with this model of early life stress.
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0375

INTERACTIONS OF STRESS WITH CHRONIC ETHANOL TREATMENT ON ETHANOL INTAKE AND BNST PLASTICITY

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NMDA receptors (NMDARs) are key targets for the acute and chronic effects of ethanol on glutamate transmission. Our work has focused on evaluating how ethanol modulates glutamatergic transmission the bed nucleus of the stria terminalis (BNST), a region that is highly sensitive to stress and the negative affect associated with ethanol dependence. In the BNST, our work has demonstrated that chronic ethanol enhances plasticity via actions at synaptic and extrasynaptic GluN2B subunits of the NMDAR (Wills et al., 2012). In the course of this work an unexpected stress effect quantified by reduced long term potential (LTP) was discovered in air-controls exposed to chronic intermittent vapor chambers. The current work set out to investigate the potential contributors to this stress effect. We find that chronic pyrazole injections are sufficient to blunt LTP in BNST. Since chronic saline injections in combination with vapor chamber exposure produced normal LTP. Further, efforts to reduce the noise from air compressors used in ethanol vapor chambers were moderately effective in rescuing the blunted LTP in air-treated controls. In lieu of these stress effects associated with chronic inhalation approaches in the mouse, we set out to evaluate another method of chronic ethanol exposure, two bottle choice. Chronic intermittent two bottle choice produces substantial levels of ethanol intake and preference in C57 mice. One drawback to this method is that it relies on isolate housing of mice, which we know is a stressor that also blunts LTP in the BNST. To overcome this issue, we set out to develop new methods for the two bottle choice procedure that avoid isolate housing while retaining substantial levels of ethanol drinking. Here, we find that group housed mice (2 mice/cage) given 4 weeks of intermittent two bottle choice had significantly reduced ethanol intake and preference compared to previously published work in single housed mice. When sucrose was added to ethanol containing solutions in this paradigm, it produced increased levels of ethanol intake and preference. In a separate group we evaluated drinking in modified cages, which have a perforated clear divider to separate mice. Mice housed in these modified cages showed higher ethanol intake and ethanol preference than was seen in group housed mice. Future work will utilize these procedures to limit the effects of stress on chronic ethanol treatment when evaluating glutamate transmission in the BNST.

0376

DELTA OPIOID RECEPTOR SIGNALING IN THE VENTRAL TEGMENTAL AREA IN ETHANOL CONSUMING AND STRESSED RATS

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The opioid system has long been implicated in the motivational aspects of alcohol consumption, in particular through opioid activation of the mesolimbic dopamine system. We have recently found that ethanol consumption changes the function of both the mu (MOR) and delta (DOR) subtypes of opioid receptors in the ventral tegmental area (VTA): activating DOR in the VTA in drinking rats provides protection against elevated ethanol consumption through inhibition of GABA release onto VTA neurons. Further, acute stress also alters opioid receptor function in the VTA. In stressed rats, activation of DOR on VTA neurons causes trafficking of GABAA receptors to the postsynaptic membrane, augmenting the GABA-A R mediated inhibitory postsynaptic current. Understanding these changes in opioid receptor function in the VTA may direct development of improved treatments for alcoholism and anxiety and the prevention of stress-induced relapse.

0377

SEX AND AGE OF CHRONIC ETHANOL DRINKING AFFECTS ETHANOL INTAKE AND SYNAPTIC TRANSMISSION ONTO MEDIUM SPINY NEURONS IN THE STRIATUM OF THE RHESUS MONKEY

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As many as 1 in 12 adults abuse alcohol or are alcohol dependent. Studies suggest that alcohol-related problems and prevalence of binge or excessive drinking are highest among young adults (18–29 years). Similarly, the risk of alcohol dependence increases the younger the onset of drinking to intoxication. There are also differences in alcohol abuse and its effects due to gender. In general more men than women are alcohol dependent. However due to differences in drinking patterns as well as the effects of alcohol due to gender, women are at a greater risk to develop alcohol related problems.
Here we examine the effect of age of onset and gender on daily EtOH intake, pattern of drinking and the accompanying changes in synaptic transmission in MSNs of putamen, a brain region that we have previously discovered shows decreased GABAergic transmission that correlates with BEC/intake in chronic EtOH drinking monkeys. To examine age-of-onset effects on EtOH consumption and changes in synaptic transmission, young adult (age at drinking onset 5–6 years) and adult (age of onset drinking onset 7–11 years) male rhesus monkeys were trained to orally self-administer EtOH under ''open access'' for approximately one year. To examine potential sex differences, these young adult males were compared to age-matched females. Younger male monkeys had average daily intakes between 2.7 – 4.1 g/kg (yielding BECs 45.8–142.3 mg/dl) whereas older males averaged from 0.3 – 2.6 g/kg (yielding BECs 0–96.1 mg/dl). Young females, on the other hand, averaged between 4.1 – 5.6 g/kg (yielding BECs 47.0–99.4 mg/dl). This suggests that younger individuals drank more than older yielding higher BECs. What is interesting is that females drank more than their male counterparts yet had similar BECs. Our data suggests that this may be in part due to the pattern of drinking that differed between the sexes of rhesus monkeys. After necropsy, acute slices containing the dorsal striatum were obtained. Whole-cell patch clamp electrophysiology examined GABAergic miniature inhibitory postsynaptic currents (mIPSC) in putamen MSNs. Chronic EtOH drinking was associated with decreased mIPSC frequency in the putamen that correlated with EtOH intake. We are currently examining the interaction between gender and pattern of drinking with alterations in GABAergic transmission. The observed changes in striatal physiology may shed light on the increased risk for habitual EtOH drinking in younger onset and women drinkers.

0378

IN THE RAT, CHRONIC INTERMITTENT ETHANOL EXPOSURE DURING ADOLESCENCE, BUT NOT LATER, ALTERS THE ETHANOL SENSITIVITY OF TONIC INHIBITION IN ADULTHOOD

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Binge alcohol drinking by adolescents is a major public health concern because this pattern of ethanol exposure is associated with an increased risk of neurotoxicity and later development of alcohol use disorders. In adolescent rats, chronic intermittent ethanol (CIE) exposure, a model of binge drinking, produces a long-lasting maintenance of the adolescent high sensitivity to ethanol's amnestic effects. In this study, we determined if CIE exposure during adolescence, young adulthood, or full adulthood produced long-lasting changes in inhibitory neurotransmission in dentate granule cells (DGCs). Beginning at postnatal day 30 (adolescent), 50 (young adult), or 70 (adult), male Sprague-Dawley rats (Charles River) were given 5.0 g/kg ethanol (CIE) or an equivalent volume of saline (control) by gavage. Ethanol exposures were given in a 2-days-on, 2-days-off sequence; each animal received 10 gavage doses. After a 20- to 27-day post-exposure period, once all the age groups had achieved full adulthood, the animals were euthanized and brain slices were prepared. Whole-cell voltage clamp measurements of extrasynaptic $GABA_A$ receptor ($GABA_AR$)-mediated tonic inhibitory currents and inhibitory postsynaptic currents were made *in vitro* in DGCs from hippocampal brain slices. In control animals, baseline tonic current and the ethanol sensitivity of the tonic current varied with age. Baseline tonic current was largest in the youngest adults, i.e., those that began the study during adolescence, and ethanol potentiation of tonic current was lowest in these animals. CIE exposure significantly decreased the baseline tonic current in the youngest age group, but not in the two older groups. CIE exposure also significantly increased the ethanol enhancement of tonic current in the youngest age group, but not in the two older groups. Thus, CIE exposure during adolescence, but not young adulthood or adulthood, produced long-lasting changes in both baseline $GABA_AR$-mediated tonic inhibition and its ethanol sensitivity. This greater ethanol enhancement of tonic inhibition in adult DGCs after CIE is consistent with the greater sensitivity to ethanol-induced memory impairment in adult rats after adolescent CIE. This finding demonstrates a long-term, memory-related cellular effect of CIE during adolescence and could represent a conceptual step forward in understanding the vulnerability of the adolescent brain to alcohol.

0379

DIFFERENTIAL GLUTAMATERGIC METAPLASTICITY IN D1 AND D2 MEDIUM SPINY NEURONS OF THE NUCLEUS ACCUMBENS FOLLOWING CHRONIC INTERMITTENT ETHANOL EXPOSURE

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Glutamate receptor trafficking in the nucleus accumbens constitutes a neuroadaptation important for responding to a variety of positive and negative reinforcers. For instance, while conditioning stimulation of excitatory afferents to shell NAc medium spiny neurons (MSNs) induces synaptic depression (LTD) in slices from ethanol naïve mice, a 4-day bout of chronic intermittent ethanol (CIE) in vivo exposure induces synaptic potentiation (LTP) rather than LTD (Jeanes et al., JPET 2011). However, MSNs segregate into two functionally distinct populations based upon the subtype of DA receptor expressed and their function as part of the direct (D1) or indirect (D2) efferent MSN pathways. Therefore, here we extend our studies to compare synaptic responses and plasticity between D1 and D2 NAc MSNs of BAC transgenic mice (drd1-eGFP) using standard whole-cell voltage clamp recordings of fluorescent (D1) and non-fluorescent (D2) MSNs (Matamales et al 2009).
Intrinsic excitability of D1 NAc MSNs appeared greater than that observed in D2 MSNs as revealed by their greater basal mEPSC frequency, lower basal pair-pulse ratio and more hyperpolarized AP threshold. These factors may contribute to the marked differences in plasticity seen in D1 NAc MSNs versus D2 MSNs since the former displayed robust NMDA LTD (−31% baseline EPSC amnp) versus no apparent LTD in D2 MSNs (in agreement with a similar segregation of MSN populations seen in WT C57 mice). Interestingly, the expression of LTD appears regulated by endogenous opiate tone, since naltrexone (60 uM) completely prevented D1 MSN LTD whereas D2 MSN LTD now appeared very robust (−48% baseline EPSC amp). Differences in LTD following 4 day bouts of chronic intermittent ethanol were consistent with that seen in WT C57 mice. LTD was absent 24 hrs following the final vapor exposure in D1 MSNs (108% baseline EPSC amp), whereas one week following CIE, largely normal LTD was present (−24% baseline EPSC amp). Conversely, 24 hrs following CIE, D2 MSNs now displayed LTD in response to conditioning (−24% baseline EPSC amp) which returned back to control D2 LTD (100% baseline EPSC amp) one week later. Thus, passive ethanol experience modulates information processing differentially through the direct D1 and indirect D2 pathways with D1 MSNs primarily responsible for the metaplastic changes we previously reported (support: R01AA015167, U01AA016651 F31AA018941).

0380

ENHANCED CCL2 EXPRESSION PROTECTS HIPPOCAMPAL FUNCTION FROM THE EFFECTS OF CHRONIC ETHANOL EXPOSURE

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Several studies have shown that alcohol abuse can lead to immune dysregulation and alter the expression of several neuroimmune factors, such as the chemokine CCL2. CCL2 levels are upregulated in the brains of alcoholics (He and Crews, Exp. Neurol. 210, 2008) and elevated levels of CCL2 mRNA and protein are observed in the CNS of normal mice subjected to ethanol (Qin et al., J Neuroinflammation. 5:10, 2008). However, it is unknown if CCL2 produces neuroadaptive changes that affect the actions of ethanol within the central nervous system (CNS). The goal of our study was to address this issue by determining if elevated CNS levels of CCL2 altered the effects of chronic ethanol exposure on hippocampal synaptic function. Following repeated intermittent exposure to ethanol vapor, extracellular field potential recordings at the Schaffer collateral-CA1 synapse were used to compare synaptic transmission and plasticity in hippocampal slices from 7–9 month old transgenic mice that overexpress CCL2 (CCL2-tg; Huang et al., J. Neurosci. 22, 2002) and their non-transgenic littermates (non-tg). Mean BALs were 170±12 (non-tg, n=7) and 192±14 (CCL2-tg, n=6) mg/dl. For all studies, data from hippocampal slices from ethanol-treated animals were compared to data from hippocampal slices from control animals of the same genotype that were exposed to air vapor. Input/output (I/O) relationships for the population spike and field excitatory post-synaptic potentials were enhanced in non-tg hippocampal slices following chronic ethanol exposure, but no differences in the I/O relationships were observed in the CCL2-tg hippocampal slices. The presynaptic volley was not altered in either CCL2-tg or non-tg hippocampal slices following chronic ethanol exposure. No differences in paired-pulse inhibition and facilitation were observed in the CCL2-tg and non-tg hippocampal slices following chronic ethanol exposure. Synaptic plasticity induced by theta burst stimulation (15 bursts of 4 pulses at 100 Hz, with an inter-burst interval of 200 ms) was reduced following chronic ethanol exposure in non-tg hippocampal slices, an effect that was not observed in the CCL2-tg hippocampal slices. These results suggest that chronic in vivo exposure to CCL2 produces neuroadaptive changes that protect against the actions of chronic ethanol exposure on hippocampal function. Supported by NIAAA grant AA019261 and the Integrated Neuroscience Initiative on Alcoholism (INIA)-West grant AA020893.

0381

CHRONIC ETOH TREATMENT PRODUCES LAMINAR- & SYNAPSE-SPECIFIC ALTERATIONS IN THE MODULATION OF PREFRONTAL CORTICAL NEUROTRANSMISSION BY THE CB1 RECEPTOR

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Up-states are a form of network activity and are the cellular correlate of slow EEG rhythms that are often disrupted in alcohol-dependent patients. Up-states arise from balanced transmission at glutamatergic and GABAergic synapses in the cortex and they are influenced by various neuromodulatory substances. Of these, the endocannabinoid (EC) system may be particularly important as the cortex expresses high levels of CB1, the major receptor for the EC system in the brain, and levels of this receptor are altered following chronic exposure to EtOH. To test if CB1 expression and function is altered following chronic EtOH treatment, organotypic cultures of mouse prefrontal cortex (PFC) were chronically exposed to EtOH for 10 days. CB1 protein content was reduced in these cultures following a 4-day withdrawal from EtOH, and up-states recorded from EtOH-treated cultures had a longer duration than those in control cultures. To determine the functional role of CB1 receptors in modulating up-states, currents were recorded from EtOH treated and control cultures in the presence of the CB1 agonist WIN 55,212–2 (WIN; 1 μM). In control cultures, WIN significantly increased up-state amplitude consistent with a CB-1 mediated inhibition of GABAergic transmission that normally restricts the amplitude of up-states. In cultures previously treated with EtOH, the WIN-induced effect on up-state amplitude was significantly blunted. To determine the cortical layer and synapse type contributing to these effects, the effects of WIN on GABA- and NMDA-mediated currents were recorded from layer II/III or layer V/VI pyramidal neurons. WIN produced a significant reduction in glutamatergic transmission in both superficial and deep layers and this effect persisted following chronic EtOH treatment. In contrast to NMDA EPSCs, WIN-produced a greater inhibition of GABAergic transmission in layer II/III neurons from control cultures as compared to those in layer V/VI. After treatment with EtOH, the laminar specificity of this effect was reversed with layer V/VI IPSCs being more sensitive to WIN inhibition than layer II/III IPSCs. These data suggest that the sensitivity of up-state amplitude to WIN is governed by CB1 signaling at layer II/III GABAergic synapses, and that some of the changes in fronto-cortical physiology observed in alcohol dependent individuals may arise from altered function of the EC system. Supported by P50AA10761 and F31AA018908.

0382

ALCOHOL INDUCED SLEEP IMPAIRMENTS FOLLOWING WITHDRAWAL FROM CHRONIC INTERMITANT ETHANOL VAPOR INHALLATION

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Current theories of substance abuse maintain that neuropathological changes associated with repeated drug exposure and withdrawal establishes an allosteric state characterized by compulsive drug seeking, withdrawal, and relapse following prolonged abstinence. Insomnia is commonly observed during abstinence of many drugs of abuse. In the case of alcohol abuse, there is a correlation between risk of relapse and sleep disruption. Sleep impairments may contribute to a variety of cognitive deficits observed following alcohol abuse which are believed to be critical to relapse vulnerability. While studies in both humans and rodents have observed sleep deficits following ethanol exposure, the nature of the effects on sleep architecture have been inconsistent. The goal of this study was to examine sleep in rats exposed to chronic intermittent ethanol (CIE) exposure via vapor inhalation.
Electroencephalogram recordings from adult male Sprague-Dawley rats (n=7) were taken before and after alcohol exposure. Following 7 days of withdrawal, significant effects on sleep architecture were observed in all stages of sleep compared to pre-exposure. During the resting period (lights on), rats spent significantly more time awake and significantly less time in both NREM and REM sleep. During the active period (lights off) the rats spent significantly less time awake and significantly more time in both NREM and REM sleep. Preliminary analysis of later time points (14 days and 28 days) suggest recovery of some sleep deficits, but indicate that during the resting period there may still be an increase in waking and a decrease in NREM sleep. These results show that our rat model of alcohol dependence induces persistent impairments in sleep architecture during withdrawal, which is consistent with the human literature. These deficits likely contribute to cognitive dysfunction commonly observed during withdrawal. Future studies will use various behavioral tasks to assess the functional impact of these deficits and therapeutic strategies aimed to normalize the sleep/wake patterns following chronic alcohol exposure.

0383

THE EFFECT OF ACUTE ALCOHOL CONSUMPTION ON EVOKED DELTA FREQUENCY ELECTROENCEPHALOGRAPHIC RESPONSES (K-COMPLEX) DURING SLEEP

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Slow wave sleep (SWS) and delta frequency EEG are markers of sleep depth and quality and when increased reflect deeper more restorative sleep. Although acute alcohol consumption disrupts sleep overall, it somewhat paradoxically, increases SWS. It has been argued that, unlike increases in delta EEG activity during sleep after extended waking, the increased SWS following alcohol ingestion could be considered pathological and non-restorative. Stimuli presented during sleep can evoke an isolated EEG delta wave known as a K-complex (KC). KC's provide indices of delta amplitude [measuring the N550 component in the average evoked potential (EP) response] and triggering (KC elicitation probability & N550 latency). These measures are sensitive to changes in the sleeping brain's ability to generate normal delta EEG and parallel changes seen due to normal and pathological aging, or chronic alcoholism. No study has examined the acute effect of alcohol on evoked delta activity during sleep. Should the increase in SWS seen after alcohol reflect promotion of normal sleep processes then it would be expected that there should be a corresponding increase in KC measures; however, if the increase reflects non-restorative processes then KC measure increases should not be observed. We evaluated sleep EP's during stage 2 (N2) and SWS in 10 heavy (19.7±0.6yrs; 96.9±48.6 drinks in the previous month) and 9 light (20.0±0.9yrs; 9.5±7.9 drinks) drinking young men under two conditions. One with pre-sleep alcohol (Dosed for 0.09% peak BAC) and the other with a placebo beverage consumed over a 30 minute period one hour prior to bed after a standard meal. All had abstained from alcohol for 48hrs. BAC at lights out was 0.083±0.017% in the alcohol condition and 0.00±0.0% after placebo. KC elicitation did not differ between alcohol and placebo conditions (p=0.822). There were also no differences in N550 amplitude (p=0.399) or latency (p=0.578) in either N2 or SWS (Fz scalp site). Irrespective of alcohol condition and consistent with previous studies, N550 latency was shorter in SWS than N2 sleep (p<0.001) and did not differ in amplitude between N2 and SWS (p=0.447). Given that KC activity has been shown to parallel normal changes in SWS, be they due to experimental manipulation or pathology, these findings of no acute alcohol effects on the KC suggest that the increases in SWS and delta EEG after alcohol consumption may reflect different and possibly non-restorative sleep processes.

0384

PRENATAL ETHANOL EXPOSURE INCREASES GLUR2-LACKING AMPA RECEPTORS AT THE EXCITATORY SYNAPSES OF DOPAMINE NEURONS IN THE VENTRAL TEGMENTAL AREA

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Prenatal ethanol exposure (PE) leads to behavioral phenotypes associated with increased propensity for addiction. Evidence has shown that augmented excitatory synaptic transmission mediated by GluR2-lacking AMPA receptor expression in dopamine (DA) neurons in the ventral tegmental area (VTA) is a critical cellular mechanism underlying increased drug addiction propensity. The purpose of this study was to determine if PE rats have increased synaptic strength due to the expression of GluR2-lacking AMPA receptors. Briefly, pregnant rats were exposed to ethanol (0 or 6 g/kg/day) via intragastric intubation from GD8 - 20. Whole cell recordings were performed on 3–12-week-old male offspring.
AMPA receptor-mediated EPSCs (AMPAR-EPSCs) were evoked and recorded using a cesium methanesulfonate based intracellular solution containing spermine. To examine the impact of PE on the properties of AMPAR-EPSCs in VTA DA neurons, we constructed the current-voltage (I-V) curve and determined the rectification index (RI) in 4–8-week-old rats. We found that the PE profoundly increases the rectification index of AMPAR-EPSCs, suggesting that PE increased the proportion of GluR-2 lacking AMPARs at excitatory synapses of VTA DA neurons. Consistent with this notion, the selective GluR2-lacking AMPAR antagonist NASPAM reduced the amplitude of AMPAR-EPSCs in PE rats but not in control rats. The effect of NASPAM in PE rats was also observed in both developing (2-week-old) and adult (8–12-week-old) rats, suggesting that PE induces a persistent alteration in the subunit composition of AMPARs. We next examined the impact of PE on the overall strength of excitatory synaptic transmission by measuring the ratio of AMPAR/ NMDA receptor-mediated EPSCs at +50 mV. We found that PE reduced the AMPA/NMDA ratio in young rats (< 6 weeks) (PE=.367 ± .05, control= 0.946 ± 0.17) but not in older rats (> 6 weeks) (PE=.89 ± .17, control= 0.92 ± 0.17). Interestingly, similar results were also obtained using intracellular solution that does not contain spermine. Thus, it is likely that the PE-induced reduction of AMPAR/NMDAR ratio observed at +50 mV reflects an alteration of NMDAR-mediated synaptic currents. Experiments examining this possibility are currently underway.
In conclusion, PE caused a persistent change in the composition of AMPARs at excitatory synapses of VTA DA neurons, which might be an important cellular mechanism for increased addiction propensity caused by prenatal ethanol exposure.

0385

PRENATAL ALCOHOL EXPOSURE ENHANCES L- AND R-TYPE CALCIUM CHANNEL CURRENTS IN NEONATAL INFERIOR COLLICULUS NEURONS

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Alcohol consumption during pregnancy is one of the leading preventable causes of birth defect and neurobehavioral disorders in humans. In the most severe cases, these abnormalities make up a pattern of malformations termed fetal alcohol syndrome (FAS). This syndrome is associated with high prevalence of generalized tonic-clonic seizures and hearing disorders in neonates and children. Thus, alcohol exposure *in utero* is a potential factor for the etiology and mechanisms of enhanced seizure susceptibility in neonates with FAS. Evidence indicates that rodent subjected to gestational alcohol exposure exhibit altered auditory brainstem responses, which lasted into adulthood. The inferior colliculus (IC), the generator of auditory brainstem responses wave V, plays a critical role in the initiation of tonic-clonic seizures following alcohol withdrawal. Thus, alcohol-induced changes in IC neuronal excitability may contribute to the mechanisms of enhanced seizure susceptibility associated with FAS. Here, we examined the effects of prenatal alcohol exposure on firing and voltage-activated Ca^{2+} channel (Ca_v) currents in dissociated IC neurons obtained from neonatal rat offspring (P3–P7). Pregnant rats received a single dose of 5 g/kg body weight ethanol (95%) as a 30% (v/v) solution in Isomil by gastric intubation at gestational day 18. Control animals received only Isomil. IC neurons were recorded in whole cell patch clamp configuration for current- and voltage-clamp experiments. Ca_v currents were measured using 5 mM Ca^{2+}. Quantification shows that prenatal alcohol exposure elicits the occurrence of >2 action potentials (APs) evoked by depolarizing current injections. Such elevated responses were not seen in control IC neurons which only exhibited a single AP. Increasing extracellular (from 2 mM to 5 mM) Ca^{2+} concentration reversibly enhanced the number of APs in control IC neurons. Quantification also shows that Ca_v current density was significantly elevated in IC neurons following prenatal alcohol exposure. Pharmacological analysis reveals that $Ca_v1.2$/$Ca_v1.3$ and $Ca_v2.3$ contribute to the enhanced current density in neonatal IC neurons following prenatal alcohol exposure. These findings suggested that altered $Ca_v1.2$/$Ca_v1.3$ and $Ca_v2.3$ signaling may play important roles in the pathophysiology of FAS-associated diseases of neuronal excitability. Supported by NIH grants AA020073 (PN) and the NIAAA Division of Intramural Clinical and Biological Research (DML).

0386

PRENATAL ETHANOL PERSISTENTLY DOWN-REGULATES ENDOCANNABINOID SIGNALING AT GLUTAMTE SYNAPSES OF VENTRAL TEGMENTAL AREA DOPAMINE NEURONS

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Prenatal ethanol exposure (PE) is known to increase addiction propensity. Previous studies have shown that increased excitatory neurotransmission in dopamine (DA) neurons in the ventral tegmental area (VTA) plays an important role in addiction. In the present study, we examined the impact of PE on the synaptic plasticity of excitatory synapses of VTA DA neurons. To that end, pregnant rats were exposed to ethanol (0, 3, or 6 g/kg/day) via intragastric intubation from GD8 - 20. Whole cell recordings were obtained from DA neurons in brain slices obtained from 3–12 weeks old male offspring.

Endocannabinoid-mediated long-term depression (eCB-LTD) in VTA DA neurons was induced by pairing low frequency afferent stimulation (2 Hz) with moderate postsynaptic depolarization (−30 mV) for at least 5 min. We found that PE persistently abolished the induction of eCB-LTD in rats exposed to either 3 or 6 g/kg/day ethanol. Several mechanisms could mediate the PE-induced blockade of eCB-LTD. These include a persistent increase in eCB tone, which occludes the LTD induction, or a down-regulation of CB_1 receptors. To determine the mechanisms by which PE impairs eCB-LTD induction, we first examined the impact of CB_1 receptors antagonist AM 251 on the paired-pulse ratio of EPSCs. We found that AM 251 (3 mM) did not alter the amplitude of EPSCs or PPR in either the control or PE rats, suggesting that the eCB-LTD induction is unlikely to be occluded due to a persistent increase in eCB tone. We next examined the impact of PE on the function of CB_1 receptors by assessing the ability of CB_1 receptor agonist Win 55,212–2 to inhibit the amplitude of AMPAR-EPSCs. We found that PE significantly reduced the Win 55212–2-induced inhibition of AMPAR-EPSCs. Such a finding indicates that the PE-induced impairment of eCB-LTD induction is mainly caused by a down-regulation of presynaptic CB1 receptors.

In conclusion, the results of the present study indicate that PE induces a persistent impairment of eCB signaling at excitatory synapses of VTA DA neurons by a down-regulation of presynaptic CB_1 receptors. This effect could contribute to the augmented excitatory synaptic neurotransmission and increased addiction propensity after PE.

0387

PRENATAL ETHANOL EXPOSURE DISRUPTS ENDOCANNABINOID MODULATION OF DORSAL STRIATAL CIRCUITS GOVERNING HABIT FORMATION

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Prenatal ethanol (EtOH) exposure-induced changes in brain development are associated with impairments in learning and memory-related and activity-related behaviors governed by dorsal striatal regions in the basal ganglia. To investigate early life EtOH exposure effects on dorsal striatum function, we exposed mice to EtOH (yielding a BEC of ~80mg/dl) from embryonic day 0.5 through postnatal day 10, and assessed the ability to learn and execute dorsal-striatum dependent self-initiated actions in adulthood. Using a novel variant of an instrumental task, mice were trained to shift between performing the same action for the same reward in a goal-directed versus habitual manner. We found that while goal-directed actions were intact, prenatal EtOH exposure disrupted the ability to perform habitual actions. Since goal-directed and habitual actions depend upon dorsal medial (DMS) and dorsal lateral (DLS) striatum respectively, we then used *in-vivo* recordings of DMS and DLS neurons to examine activity changes. We observed that early life EtOH exposure disrupted shifts in circuit activity during learning and execution of habitual actions corresponding to impaired habit formation. Since habitual actions depend on cannabinoid type 1(CB1) receptors that are known to modulate DMS and DLS synaptic transmission and plasticity, we hypothesized that endocannabinoid modulation of dorsal striatal synaptic transmission may be altered following early life EtOH exposure. Indeed, early life EtOH exposure resulted in altered endocannabinoid modulation of DLS GABAergic transmission in adult mice. The CB1 agonist induced depression of mIPSC frequency seen in control mice was lost, while a CB1 receptor antagonist increased mIPSC frequency, and effect not seen in controls. These findings suggest that early life EtOH exposure increased ambient endocannabinoid levels. Immunohistochemistry suggested only slightly higher CB1 receptor expression, while binding studies showed a similar level of CB1 receptor binding. Altogether, these results suggest that early life EtOH exposure induces developmental adaptations in dorsal striatum resulting in increased endocannabinoid modulation of GABAergic synapses, leading to impaired habit formation. We are currently testing whether we can mimic this finding by increasing endogenous endocannabinoid levels, and whether we can rescue the EtOH-induced deficit in habit formation by altering CB1 receptor or endocannabinoid levels in the DLS.

0388

DORSOMEDIAL AND DORSOLATERAL STRIATUM SHOW DISTINCT PHASIC NEURONAL ACTIVITY DURING ALCOHOL SELF-ADMINISTRATION IN RATS

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The dorsal striatum is critical for addiction and reward reinforcement, underlying both motor activity and action selection. This area is thought to be regionally specialized, with the lateral aspect required for habit formation and the medial region important for goal-directed behavior. We investigated whether presumed medium spiny neurons of the dorsolateral striatum (DLS) and dorsomedial striatum (DMS) reflected lever presses and cues during alcohol-seeking behavior in their firing rates. We trained rats on one of two reinforcement schedules, simultaneously recording neuronal activity with microarrays implanted in the dorsal striatum. First, rats receiving ethanol rewards on a fixed-ratio (FR5) schedule modeled goal-directed behavior. We analyzed neuronal responses around the 1^{st} and 5^{th} of each set of 5 presses and found a consistent significant increase in DLS firing rates from the 1^{st} press to the 5^{th} press (in 15/49 cells), while the DMS demonstrated a brief, time-locked increase around the 5^{th} press and onset of cues and reinforcement (in 17/55 cells). Significant excitations were observed in the DMS at the presentation of start-of-session stimuli, which surprisingly increased in signal-to-noise ratio after administration of D1-antagonist. Next, rats trained on a 30-s variable interval (VI30) schedule exhibited more habitual response patterns (e.g., insensitivity to contingency degradation). When comparing reinforced to unreinforced lever presses, the strongest DLS responses were associated with the pre-press response epoch, with 13/44 cells excited before an unreinforced press and 10/44 excited before a reinforced press. In the DMS, however, the strongest response was observed after the reinforced press, with 23/66 cells significantly excited, compared to only 6/66 after the unreinforced press. As in the FR5 group, D1 antagonist administration increased the signal-to-noise ratio of the excitation associated with cues signaling the initiation of the session as well as the pre-press excitation. In summary, both DMS and DLS have activity related to FR and VI alcohol-seeking behavior but they may play different roles as the DLS showed greater excitation with lever press activity and the DMS showed greater excitation at cues and reinforcement, while all of these firing patterns are amplified by D1 receptor antagonism.

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4. ANIMAL BEHAVIOR

0389

A DEPRIVATION-LIKE EFFECT ON BOUTS IN EARLY ETHANOL DRINKING IN ALCOHOL PREFERRING (P) VS. WISTAR AND SPRAGUE DAWLEY RATS

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The goal of study was to compare an Alcohol Deprivation Effect (ADE) -like changes in early EtOH drinking in purpose-bred P with those inducible in progenitor Wistar (W) and non-related Sprague Dawley (SD) rats. P, W and SD rats (8 each) were trained to drink 15% v/v EtOH (15E) in choice with water respectively for 2 vs. 3 and 4 weeks, in 15-hr sessions. After this exposure EtOH intake was 4.0 vs. 2.5 and 2.8 g/kg in P, W and SD rats. In all groups 96–99% of intake was consumed in bouts that contained 0.55 vs. 0.32 and 0.34 g/kg EtOH in P, W and SD rats. Inter-bout interval (iBi) was 134 vs. 118 and 121 min in P, W and SD rats. However, in-bout time to accumulate 0.1cc 15E was 13.6 and 13.2 vs. 20.6 sec in P and SD vs. W rats. ADE like changes were induced by blocking EtOH access for several hours after completion of the first EtOH bout of a session. This in-session deprivation led P rats to increase the first post-deprivation bout (pdB-1) to ≥140% of normal bout; pdB-1 often appeared as an abnormally large ''super-bout'' where ≥1.25 g/kg EtOH was consumed in a several minutes. An increase of pdB-1 with generation of a ''super-bout'' started to appear at 6-hr deprivation, and peaked at 9 hrs when pdB-1 reached ∼200% of normal bout (1.06 g/kg). At 9 hrs, the pdB-1 was ∼150% of normal bout in Wistar (0.48 g/kg) vs. ∼200% in SD (0.66g/kg). Our findings are that: P rats develop a pronounced ADE-like effect by the 3rd week of choice EtOH drinking. The effect in P rat develops in the context of periodic timing of EtOH bouts with the base interval as short as 40–45 min and other iBi-s appearing as multiples of this period, interdependent with actual consumption. A maximum bout size in P rat found at a deprivation length about four times the average iBi. Daily intake, bout size and periodicity of spontaneous 15E drinking are similar in non-selected W and SD, and both differ from P rat. Progenitor Wistar rats have more within-bout delays, and exhibit a smaller ADE-like effect that P or SD. These data present a model of an 'early ADE' in P rat vs. Wistar vs. Sprague Dawley to study the 'normal' vs. 'elevated' anticipation, consumption and satiation of EtOH, and pronounced vs. blunted time dependency of EtOH drinking. Analysis of mesolimbic neural activity patterns during altered bout generation, and use of causal stimulation probes to explore CNS control during generation of abnormally high EtOH intake is now possible in controlled drinking states. (AA20676 to DJW)

0390

ALCOHOL DRINKING IN SOCIALLY MONOGAMOUS PRAIRIE VOLES (MICROTUS OCHROGASTER) AND NON-MONOGAMOUS MEADOW VOLES (MICROTUS PENNSYLVANICUS)

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Social relationships have important effects on alcohol (ethanol) drinking, and we have previously modeled social facilitation of alcohol drinking as well as effects of peer drinking in socially monogamous prairie voles (*Microtus ochrogaster*). One theory on the rewarding effects of alcohol and other drugs of abuse is that they act on natural reward pathways, which are vital for social bonds. Here we examined whether meadow voles (*Microtus pennsylvanicus*), a closely related species with different social behaviors and social reward neurocircuitry, would exhibit differences in alcohol drinking levels. We tested adult prairie and meadow voles' alcohol drinking in limited access sessions over four days. Subjects had access to alcohol (10%, V/V) and water four hours per day in an apparatus where a same-sex cagemate was separated by a wire divider that allowed visual, auditory, olfactory, and limited physical contact. The drinking tubes were available for half the session in a 'social drinking' condition where the voles could drink near each other, and for the other half of the session the tubes were on opposite ends of the cage, called the 'nonsocial drinking' condition, and the order was counterbalanced across pairs. One week after alcohol intake, voles were given 2.5 g/kg ethanol IP and euthanized 90 minutes later to collect trunk blood for blood ethanol concentration (BEC) in order to determine whether any difference in alcohol elimination rate exists between the species. There was a main effect of drinking condition, and no interaction with species on alcohol intake, indicating that both prairie and meadow voles drank more alcohol in the social condition. While meadow voles had a similar preference for alcohol over water when compared to prairie voles, they drank significantly lower doses, and we observed greater signs of intoxication even with the lower dose of alcohol. Indeed, meadow voles had significantly higher BECs after the same dose of alcohol was injected, indicating that they may not metabolize alcohol as efficiently. However, the magnitude of the difference was not so great that this should preclude future studies of alcohol drinking in this species. Species differences in social reward circuitry may explain differences in alcohol intake observed here, but direct comparisons of alcohol drinking between these vole species, must be cautioned against due to potential differences in alcohol metabolism.
AA019793 to AER and AA020136 to AMJA.

0391

MODELING ALCOHOL RELAPSE IN THE MONOGAMOUS PRAIRIE VOLE (MICROTUS OCHROGASTER)

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There is robust evidence for a protective role of interpersonal factors such as social support and marital status against alcohol relapse. However, research on the mechanisms the social environment may be acting on to effectively protect individuals against relapse is lacking. Given high rates of alcohol relapse, it is of critical importance to understand the biological mechanisms underlying relapse-like behaviors and to identify target treatments for improving rates of remission. The monogamous prairie vole displays selective social attachments (''pair bonds'') and freely self-administers ethanol without sucrose fading. Our laboratory has begun to characterize a bi-directional relationship between social environment and alcohol drinking in prairie voles. Therefore this species is an ideal model for understanding interactions between social behavior and alcohol use, including relapse. Relapse can be modeled in the alcohol deprivation effect, in which alcohol-exposed subjects show increased motivation for and intake of alcohol following repeated abstinence periods. We have developed a similar procedure in prairie voles. Adult male and female voles were either mesh-housed with a same-sex sibling or housed alone. Animals were given 4 weeks of continuous access to each 10% ethanol and water in a 2-bottle choice paradigm. Alcohol was then removed for a 72-hour forced abstinence period, then access was resumed for an additional 24 hours. Upon restoring ethanol access, subjects showed an increase in alcohol intake (8.1 vs 9.6 g/kg; $F_{1,21}$=7.3, p=0.01) and preference (0.50 vs. 0.59; $F_{1,21}$=6.0, p=0.02) relative to the final week of initial access. Socially housed animals had higher alcohol intake (p=0.03) and preference (trend only: p=0.06) than isolated animals during the initial access period, consistent with previous findings in our lab. There was only a trend for an effect of housing during the re-exposure period for ethanol consumption (p=0.07) and no difference in preference (p=0.44), suggesting that social influences on abstinence-induced drinking may be disrupted. Future research will explore the role of social relationships on relapse-like behavior, and the neural underpinnings of this interaction. Funded by NIH AA019793 & T32AA007468-24.

0392

SOURCE (VENDOR) OF WISTAR RATS IS AN IMPORTANT VARIABLE IN THE INTERMITTENT ACCESS TO ALCOHOL (IAA) MODEL OF INCREASED VOLUNTARY ALCOHOL DRINKING

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The IAA model has been reported to produce daily voluntary alcohol intake by outbred Wistar rats that is similar to intake commonly reported for selectively-bred alcohol-preferring (P) rats. However, some applications of this model have produced much lower intake. One potential contributor to this variability is illustrated by a recent study (Palm et al., 2011) in which Wistar rats from 5 different European vendors exhibited profound differences in IAA alcohol intakes. Consequently, we obtained male Wistar rats from Charles River Labs (Hollister, CA); Simonsen Labs (Gilroy, CA); and Harlan Labs (Livermore, CA); along with Long-Evans rats from Harlan Labs (Indianapolis, IN) for comparison (10 rats/group). These rats were housed in standard plastic shoebox cages with fluids delivered via ball-bearing sippers. Additional Wistar rats were obtained from Harlan Labs (Indianapolis) and divided into two sets of 10 rats each, one housed the same as the rats from the other vendors and the other in hanging metal cages with glass drinking tubes with a horizontal opening for fluid access. All rats were individually housed in the same room and compared simultaneously in the IAA protocol, with 3X/week (M, W, F) 24-h 2-bottle choice of 20% alcohol *vs* water, for 6 weeks starting at 55–60 days of age. The pattern of daily alcohol intake was highly variable among the vendors. The Charles River Wistar rats exhibited highest initial alcohol intake (4.0±0.9 g/kg/24 h), which did not increase over the 6 weeks IAA. Wistar rats from Harlan (Indianapolis) increased alcohol intake progressively across the 6 weeks, achieving final intakes of 6.1±0.8 g/kg/24 h when housed in shoebox cages with sippers and 7.6±0.9 g/kg/24 in hanging cages with drinking tubes. Wistar rats from Harlan (Indianapolis) achieved markedly higher final alcohol intakes than Wistar rats from Simonsen (6.1±0.7 *vs* 2.6±0.2, p<0.001). Final alcohol preference in the Harlan Wistar rats (from both Indianapolis and Livermore; 38±4 and 38±7%, respectively) was also higher (p<0.01) than in the Simonsen Wistar rats (22±2%). These results confirm that supplier of Wistar rats is an important factor in IAA studies, suggesting that genetic and/or early developmental housing and/or husbandry differences between vendors may confound comparisons between IAA studies. Supported by resources from VA Puget Sound Health Care System, VISN 20 MIRECC and NIH AA017839, AA010567.

0393

INTERMITTENT ACCESS TO ALCOHOL RESULTS IN VOLUNTARY, DEPENDENCE-LIKE DRINKING IN MICE AND RATS: ROLE OF GLUTAMATE AND CRF

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Rationale: Further development of the intermittent access protocol begins to define essential features that lead to voluntary and dependence-like drinking in outbred and inbred strains of mice and rats.
Methods: In the current studies 20% w/v ethanol was offered in one of two bottles on alternate days of the week to single-housed male or female CFW or C57BL6/J mice or Long-Evans rats. The other bottle contained water.
Results: (1) CRFR1, microinjected in the DRN and VTA of B6 mice or Long-Evans rats selectively attenuate escalated ethanol drinking as a result of intermittent access. (2) After 4–8 weeks of intermittent access, signs of withdrawal become evident (e.g., HIC, escalated aggression) in outbred and inbred strains of mice, possibly due to hyperglutamatergic activity; and (3) acute injections of memantine amplifies the escalated aggression in outbred mice that are withdrawing from intermittent access to alcohol.
Conclusions: Taken together, these results suggest that intermittent ethanol access escalates drinking in part as a result of a withdrawal-induced hyperglutamatergic state that is modulated by CRFR1receptors and monoaminergic pathways.

0394

BEHAVIORAL PROFILING FOR VOLUNTARY ETHANOL INTAKE AND ETHANOL SEEKING IN MALE OUTBREED RATS

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The development of alcohol use disorder (AUD) is dependent on the interaction between genetic and environmental components. Between, and within, outbreed rat strains there are great individual differences with regards to voluntary ethanol intake and seeking. Here, we used the Novel Cage Test to evaluate the emotional reactivity and stress coping styles of three outbreed rat strains (Rcc Han Wistar (Harland, Netherlands), Lister Hooded (Charles River, UK) and Long Evans (Charles River, UK)) before given access to ethanol. Each rat was placed for 5 minutes in an empty Plexiglas box and the latency time, frequency and duration of locomotor, explorative, risk assessment and anxiety-like behaviors were calculated. The rats were thereafter subjected to two models of voluntary ethanol consumption; (a) intermittent-access 20% ethanol two-bottle-choice paradigm and (b) operant self-administration of 20% ethanol. The results from the Novel Cage Test were correlated with voluntary ethanol intake and ethanol seeking behavior through a pattern recognition analysis - the prinicipal component analysis (PCA). The PCA showed that Wistar rats had the highest voluntary ethanol consumption of the three strains in the two-bottle-choice paradigm and they were cautious, proactive stress copers, with high emotionality. However, nearly half of the Wistar rats did not perform any ethanol seeking behavior in the operant paradigm. In contrast, Lister Hooded had the lowest voluntary ethanol intake, but the highest level of ethanol seeking behavior of all strains. These rats were very explorative with low emotionality. The Long Evans rats were anxious, reactive stress copers with high emotionality and had a low degree of both voluntary ethanol consumption and seeking behavior. In conclusion, the rats that had the highest ethanol intake in a two-bottle-choice setting had a proactive stress coping style and a higher level of emotionality compared to rats with a high level of ethanol seeking behavior, which were more explorative. Being too emotional or anxious in combination with a reactive stress coping style decreased the initiative to voluntary ethanol consumatory behavior significantly. Early identification of high ethanol consuming or seeking individuals would reduce cost of long-term experiments needed for studying AUD. The presented behavioral profiling has potential to be a valuable tool in the prediction of high or low individual responders in preferred AUD models.

0395

INTERMITTENT ETHANOL ACCESS INCREASES ETHANOL INTAKE IN DIVERSE MOUSE GENOTYPES

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Considerable research has been aimed at identification of the behavioral, physiological and genetic factors regulating free-choice (i.e., 2-bottle) ethanol intake under conditions of continuous 24-hour access. Nevertheless, the clinical relevance of such studies is limited by the fact that rats and mice rarely achieve intoxicating blood ethanol levels during free-choice drinking, nor do they typically show signs of dependence when ethanol access is terminated. In recognition of this limitation, researchers have developed a number of procedures designed to engender "excessive" levels of voluntary ethanol intake that might more closely resemble human alcohol use disorders. Perhaps the simplest way to increase voluntary ethanol intake is to impose limitations on ethanol availability. Thus, schedules of intermittent 24-hour ethanol access reliably lead to escalation of ethanol intake in both rats and mice. While a number of rat lines have been tested under intermittent-access procedures, to date such studies have been conducted only in C57BL/6 mice, an inbred strain known for its high levels of voluntary ethanol intake. The present study was designed to explore the effects of intermittent access on voluntary ethanol intake in a range of mouse genotypes characterized by diverse ethanol-related phenotypes. We therefore assessed the effects of intermittent ethanol access in high-drinking C57BL/6J and low to moderate-drinking C3H/HeJ inbred mice, in selectively-bred "High-Drinking-in-the-Dark" (HDID1) and HS/Npt control mice, and in selectively-bred Withdrawal-Seizure-Prone (WSP2) and Withdrawal-Seizure-Resistant (WSR2) mice. All genotypes displayed robust escalation of ethanol intake under both one-day-per-week and three-days-per-week access schedules, indicating that the effects of intermittent ethanol access are broadly generalizable. Nevertheless, C3H/HeJ mice showed the most dramatic effect of any of the lines tested, characterized by a 3–4-fold increase in ethanol drinking, while the WSP and WSR lines showed the least dramatic effect, characterized by an approximate 30% increase in drinking. Surprisingly, there were no differences in escalation between HDID and HS/Npt mice nor between WSP and WSR mice, indicating that alleles contributing to escalated drinking under intermittent ethanol access are largely independent of those underlying both binge-like drinking and withdrawal severity.

0396

HABIT FORMATION ACROSS MULTIPLE REINFORCERS IN A FIXED-RATIO SCHEDULE ANIMAL MODEL

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Different schedules of reinforcement can generate different behavioral patterns. Ratio schedules of reinforcement that supply a reward based on the amount of an operant behavior generate goal-directed behaviors; these behaviors are traditionally defined as sensitive to changes in both reward value and the action-outcome contingency (the relationship between behavior and reward). Conversely, more inflexible habit-associated behaviors are insensitive to changes in reward value and action-outcome contingency. In a previous study, we found that rats trained to self-administer 10% ethanol on an FR5 reinforcement schedule were goal-directed, while rats similarly trained to self-administer 1.5% sucrose were insensitive to reward devaluation. This insensitivity could reflect either habit formation or a characteristic of the reinforcer that is resistant to devaluation. Thus, this study compared the development of habit-like reward seeking in rats trained to self-administer 1.5% sucrose and 10% sucrose. After 4 weeks of FR5 operant training, habitual responding was evaluated by 3 satiety-specific devaluation tests over 6 weeks. Finally, habitual behavior was additionally assessed before and after contingency degradation training that dissociated the lever press from reinforcement delivery. Additional groups of 10mM MSG and 10% ethanol were added to compare additional reinforcers.
Satiety-specific devaluation revealed habit-like behavior in the 1.5% sucrose group (n=5) and goal-directed behavior in the 10% sucrose group (n=7). The 1.5% sucrose group displayed insensitivity to outcome devaluation across devaluation tests, with a significant interaction between pre-treatment fluid and test ($p<0.01$). The 10% sucrose group (n=7) displayed a main effect of pre-treatment fluid ($p<0.05$), with reduced pressing after preexposure to 10% sucrose as compared to a control solution. In contrast, a 2-way ANOVA of group by time showed that both groups reduced pressing in response to degradation training (main effect of time, $p<0.01$), consistent with goal-directed behavior. Studies with MSG and ethanol reinforcement are ongoing. These data suggest that two tests of "habit" – satiety specific devaluation and contingency degradation – do not always yield consistent results, and we speculate that weak sucrose concentrations that support operant behavior may not devalue after home-cage exposure.
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0397

TOLERANCE IS PROPORTIONAL TO THE LEVEL OF ALCOHOL DRINKING IN CROSSED HIGH ALCOHOL PREFERRING MICE FOLLOWING 3, BUT NOT 5 WEEKS OF FREE CHOICE DRINKING

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In some animal populations, a transient increase in drinking known as the alcohol deprivation effect (ADE) is sometimes seen following a period of abstinence and is considered a model of relapse. Less is known, however, about the recently developed crossed High-Alcohol Preferring (cHAP) mouse line, which unlike these prior models, reaches high BECs (260 mg/dl) during continuous free-choice access (Matson and Grahame, 2012). Moreover, these mice steadily increase alcohol consumption during the first 2 weeks of free-choice drinking. However, it is unknown what drives this increase, or how a period of abstinence affects drinking.

To begin investigating these issues, 60 cHAP mice were divided into four groups. All mice had access to 10% alcohol and water in the home cage. Two groups had Continuous Access for either 2 or 3 weeks (Groups CA2 and CA3, respectively) prior to the first test point. One group (ADE1) drank freely for 2 weeks and had their alcohol bottles removed for one week. Water Controls (WC) had only water access during this initial 3-week period. At Test 1, all groups were given free-choice ethanol access for 7 hours and tested for ataxia prior to having bloods drawn. All mice then received free-choice ethanol access for 2 more weeks. Then, half of all mice with a history of alcohol drinking were deprived of alcohol for one week, while the other half had continued alcohol access. Alcohol was then reintroduced at Test 2, at which time motor ataxia was also tested after a 1.75 g/kg injection of alcohol.

Results at Test 1 indicated that a week of alcohol deprivation decreased alcohol consumption in Group ADE1 to the level of drinking shown in naïve mice. However, drinking returned to peak levels again with 7 days subsequent access. Furthermore, while ataxia was similar among groups, mice that had been continuously drinking for 3 weeks showed a modest ataxia to ingested alcohol at a much higher BEC (~200 mg/dl) than groups without alcohol exposure or with deprivation (~70 mg/dl and ~100 mg/dl), suggesting tolerance dissipates following deprivation. In Test 2, drinking levels failed to decrease following 5 weeks of drinking and a week of abstinence, but tolerance again dissipated with abstinence. These results indicate that tolerance and drinking are initially related after 3, but not 5 weeks of drinking, and lend preliminary evidence to drinking instating itself as a habitual behavior after long periods of exposure. AA07611 to D. Crabb.

0398

ETHANOL PRE-EXPOSURE ALTERS ETHANOL PREFERENCE AND AVOIDANCE IN CAENORHABDITIS ELEGANS

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Drug addiction is a chronic and relapsing mental illness characterized by compulsive drug use despite serious negative consequences. Animal models allow for the investigation of neuronal alterations and behavioral changes associated with the exposure of drugs of abuse such as ethanol (EtOH). *Caenorhabditis elegans* (*C. elegans)* provides a simple animal model which has many highly conserved molecular systems that are present across many species including humans. The purpose of this study was to examine approach/avoidance behavior to a range of EtOH concentrations [CONCs] as determined by a simple choice test in *C. elegans,* and then determine how pre-exposure to EtOH changes the behavior. Pre-exposed worms were moved from their maintenance plates 4 hours prior to testing and placed on EtOH-treated plates (0 mM or 250 mM) with food. Lifetime pre-exposed worms were maintained from hatching until testing on EtOH-treated plates (0 mM or 150 mM) with food. For EtOH preference testing, agar plates were constructed so one half of the plate had EtOH-exposed agar (9 final CONCs in a range between 0 and 400 mM EtOH) and the other side control agar (water-exposed). Approximately 100 age-synchronized, EtOH-exposed or control adult N2 worms were transferred to the center of the test plate and allowed to roam freely for 30 minutes. Each side of the plate was photographed at 30 minutes and the worms counted. The results indicate that *C. elegans* were able to sense EtOH on agar plates and moved towards or away from the EtOH-exposed side, and this occurred in the presence or absence of food. For the 4-hour EtOH pre-exposure, a 2-way ANOVA revealed a significant effect of pre-exposure CONC where worms pre-exposed to 250 mM EtOH showed decreased preference for the EtOH side compared to controls, $F(1, 65) = 7.18$, $p < .01$. Further, there was a significant effect of preference CONC where low CONCs (~100–250 mM) were preferred over control (0 mM) and high CONCs (> 300 mM), $F(7, 65) = 3.84$, $p < .01$, producing inverted U-shaped CONC-response curves. Lifetime pre-exposure to 150 mM EtOH elicited an opposite effect where EtOH preference in adulthood increased over controls, $F(1, 190) = 26.96$, $p < .001$. These results suggest that EtOH exposure during development, or the duration of pre-exposure, alters future preference for EtOH in *C. elegans*. Thus, *C. elegans* may provide a good model for investigating how pre-exposure changes vulnerability for future abuse of EtOH. Supported by AA07462

0399

SIMULTANEOUS ANALYSIS OF APPETITIVE AND CONSUMATORY SELF-ADMINISTRATION BEHAVIORS IN RATS FOLLOWING PHYSICAL DEPENCENCE TO ETHANOL

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The transition from alcohol use to dependence and abuse is theorized to occur via a cycle of preoccupation/anticipation, binge/intoxication, and withdrawal/negative affect. Operant self-administration is a highly validated and frequently utilized animal model for the binge/intoxication stage of this addiction cycle. Previous work with physically dependent animals has focused primarily on the appetitive/seeking aspect of ethanol operant self-administration. In contrast, measurement of the consummatory behaviors has been relatively unexplored. In the current study, we have used the Samson Sipper Model of operant self-administration to evaluate the impact of physical dependence on both appetitive and consummatory behavior. Daily ethanol seeking and consumption by Long-Evans rats was measured with six hour sessions consisting of a FR1 schedule reinforced with an eight-second presentation of a sipper tube. Sessions included both an ethanol-reinforced lever which delivered a sipper tube containing 10% ethanol in water and a ''water only''-reinforced lever. Following a baseline period, we induced ethanol dependence using a ten day chronic intermittent vapor exposure; animals were subsequently placed back in the daily operant sessions 72hr after withdrawal from the ethanol vapor. In a preliminary study, we found that dependence increased both the total number of ethanol-reinforced lever presses and the average number of consecutive ethanol-reinforced lever presses. Water reinforced responding was not significantly altered by ethanol dependence. Chronic intermittent ethanol significantly increased both the total number licks but not the number of licks per reinforced lever-press. This suggests that the eight-second access period during each reinforced presentation may have been too brief to measure any dependence-related changes in consumption. However, total ethanol intake significantly increased from ~0.4g/kg/session to ~1.4g/kg/session after the CIE exposure. In roughly half the animals, only ~70% of the ethanol-reinforced lever presses resulted in consumption of the ethanol solution; and this was increased to ~90% by physical dependence. In summary, this preliminary study has shown that physical dependence can increase both appetitive and consummatory behaviors. The model may permit extensive investigation of the mechanisms controlling consumption following physical dependence. This work was supported by NIH grant #AA014445.

0400

REVISITING INTRAVENOUS ETHANOL SELF ADMINISTRATION IN THE P RAT USING A MULTIPLE SCHEDULE OF REINFORCEMENT

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Intravenous (IV) self-administration of ethanol (EtOH) allows for controlled and precise dosing, bypasses first order absorption kinetics allowing for faster onset of pharmacologic effects, and eliminates the confounding ''non-pharmacological'' effects associated with oral consumption. Dissociating these effects is essential to untangling the neurologic underpinnings of alcohol abuse and dependence. IV self-administration of EtOH has been reliably demonstrated in both mouse and human experimental models; however, consistent IV self-administration of pharmacologically relevant EtOH exposures remains elusive in the rat. Our previous work has demonstrated reliable elevated IV EtOH self administration using an oral sucrose and IV EtOH compound reinforcer. The present study sought to elucidate the role of each reinforcer in this complex using an operant multiple schedule study design. Male P rats had free access to both food and water during all IV self-administration sessions with all testing performed in conjunction with the onset of the dark cycle. Once animals achieved stable responding on two levers for orally delivered 1% sucrose (1S) on a FR4 schedule, animals were surgically implanted with an indwelling jugular catheter. Animals were then trained to respond on a multiple FR4-FR4 schedule composed of alternating 2.5 minute components across 30 minute sessions. During one component only oral 1S was presented, while in the second component a compound reinforcer of oral 1S + IV 20% EtOH was presented (25 mg/kg/injection). Both levers were extended during the session, with the active lever alternating as the session progressed across components. Average total EtOH intake was 0.47 ± 0.04 g/kg (range 0.04 – 1.05 g/kg). We found a significantly higher level of sucrose-only reinforcers earned as compared to the compound reinforcer, and greater sucrose-lever error responding (i.e., perseverative responding relative to ethanol errors). Together, these response patterns suggest that sucrose, not EtOH, was responsible for driving overall responding. The current findings add to a body of literature indicating that the existing IV EtOH self-administration techniques do not overcome the aversive/punishing qualities of this route of administration in the rat. Supported by IUPUI DRIVE grant to AEK and T32 AA007462.

0401

DEPENDENCE INDUCED ENHANCEMENT OF INTRAGASTRIC ALCOHOL CONSUMPTION (IGAC) PERSISTS OVER A 2-WEEK ABSTINENCE

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Intermittent passive ethanol (EtOH) exposure has been shown to produce later increases in IGAC in several mouse genotypes, an effect attributed to alleviation of withdrawal (i.e., negative reinforcement) and/or tolerance to aversive post-absorptive EtOH effects (Fidler et al., 2011). This interpretation is supported by data showing that dependent DBA/2J (D2) mice increase choice IGAC after abstinence periods up to 5 days when mice receive access to ethanol during the first 24-h of withdrawal (Cunningham et al., 2011). In this experiment, we investigated whether the increased IGAC would persist over an even longer abstinence. Adult male D2 mice were surgically implanted with IG catheters. After recovery, mice received 5 consecutive days of passive water or 10% v/v ethanol infusions (3 infusions/day; 3–5 g/kg/infusion) followed by 2 no-choice days during which one Kool-Aid flavor (S+) was available and licks produced IG EtOH infusions. This cycle of passive infusions and no-choice IGAC was repeated and then mice were returned to their home cages for a 2-week abstinence period. During the post-abstinence test, a second flavor (S-) was also available and licks on this flavor were paired with infusions of water. As in previous studies, EtOH-exposed mice showed significantly greater choice EtOH intake (8.5 ± 0.5 g/kg/d) and EtOH preference (80.0 ± 8.0%) than water-exposed control mice (1.2 ± 0.5 g/kg/d; 15.5 ± 9.0%). Intakes by the EtOH-exposed group were elevated relative to controls on each of the 5 days of the choice phase. These data suggest that enhanced EtOH intake and preference are persistent across long periods of abstinence, an outcome that mimics the increased motivation for ethanol seen in abstinent alcoholics. Supported by INIA AA13479.

0402

ASSESSMENT OF PHENOTYPES CHARACTERISTIC OF MODELS OF DEPENDENCE IN C57BL/6J MICE WITH A PRIOR HISTORY OF BINGE-LIKE ETHANOL DRINKING

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Binge drinking, defined as excessive ethanol intake over a short period of time that generates elevated blood ethanol levels (80 mg/dL or greater), has become a serious health problem both in the United States and world-wide. Binge drinking has been linked to heart disease, high blood pressure, liver cirrhosis, pancreatitis, and type 2 diabetes. Perhaps most alarming, longer-term binge drinking has been implicated in the subsequent development of ethanol dependence. ''Drinking in the dark'' (DID) procedures have recently been developed to model excessive binge-like ethanol consumption in C57BL/6J mice. Here we used DID procedures to determine if a history of binge-like ethanol drinking promotes behavioral phenotypes characteristically associated with dependence-like drinking models, including anxiety-like behaviors and 24-h voluntary (two-bottle choice) ethanol consumption. We used a 4-day DID procedure in which male C57BL/6J were given 20% (v/v) ethanol in place of water beginning 3 hours into the dark cycle. Mice had limited access to ethanol for 2 hours on days 1–3, and for 4 hours on day 4. Separate groups of mice experienced 1, 3, or 6 cycles of binge-like ethanol drinking (4 days per cycle, and each cycle separated by 3 days). Relative to water drinking controls, mice that had a history of 6 binge-like drinking cycles exhibited a subsequent increase of two-bottle (water versus ethanol) voluntary ethanol consumption over a range of ethanol concentrations (10 to 20%). Voluntary ethanol consumption was not altered in mice with a history of 1 or 3 binge-like drinking cycles, and none of the binge-like drinking groups demonstrated subsequent alterations of anxiety-like behavior (assessed by elevated plus maze and open-field tests). The present results show that 6 repeated cycles of binge-like ethanol drinking promotes increases of subsequent voluntary ethanol consumption but does not trigger changes in anxiety-like behaviors. We are currently assessing the effects of a history of up to 10 binge-like drinking cycles on subsequent voluntary ethanol intake, anxiety-like behaviors, and ethanol withdrawal-induced behaviors (rotarod assessment of ataxia and/or handling induced convulsions). (Supported by NIH grants AA013573 and AA015148).

0403

ACOUSTIC STARTLE AMPLITUDE PREDICTS VOLUNTARY ALCOHOL INTAKE DURING SUBSEQUENT INTERMITTENT ACCESS TO ALCOHOL (IAA)

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After extensive review of the literature, Begleiter and Porjesz (1999) proposed that hyperexcitability is the key feature of the simplest model of the neuronal milieu underlying a predisposition to alcoholism. This hypothesis is consistent with recent evidence that hyperexcitability reflected in enhanced acoustic startle response is characteristic of abstinent alcoholics, selectively bred alcohol preferring (P) rats, and post-dependent rats experiencing either acute alcohol withdrawal or prolonged alcohol abstinence. Enhanced startle is associated with increased brain noradrenergic activation mediated by α1-adrenergic receptor mechanisms (which also contributes to increased voluntary alcohol drinking), is correlated with increased anxiety (a risk factor for alcohol abuse), and is high in individuals at high family history risk for anxiety disorders. Accordingly, we hypothesized that acoustic startle response could predict acquisition of elevated voluntary alcohol intake. Basal startle responses to 10 presentations each of 90, 95 and 100 dB 40 msec white noise stimuli in counterbalanced semi-randomized order, 30 second intervals between stimuli, were tested in 22 alcohol-naïve young adult male Wistar rats (Simonsen Labs) before stable voluntary alcohol intake was established with 2-bottle choice (water *vs* 20% ethanol) alcohol access 24 h/day, 3 days (M, W, F) / week – i.e., IAA. The response to 95 dB stimuli correlated with subsequent IAA alcohol intake ($p<0.01$, Pearson Product Moment correlation analysis, $r=0.59$). Responses to 100 dB tended to correlate with subsequent IAA-induced alcohol intake ($p=0.07$) but results were skewed by exceptionally high startle in one rat (if this rat was excluded, $p<0.01$). Grouping the rats on high *vs* low 95 dB startle response (median split, n=11/group) confirmed that the pre-IAA high startle group subsequently developed increased alcohol drinking relative to the pre-IAA low startle group ($p<0.01$, Student t-test). These results demonstrate that basal acoustic startle amplitude can predict subsequent voluntary IAA alcohol intake and suggest that hyperexcitability and associated factors, such as increased noradrenergic activation and anxiety, may be responsible for this correlation and may be useful as predictive indices of vulnerability to alcohol abuse. Supported by resources from VA Puget Sound Health Care System, VISN 20 MIRECC and NIH AA017839, AA010567.

0404

EFFECTS OF 7-NITROINDAZOLE IN BEHAVIORAL SENSITIZATION BETWEEN STRESS AND ETHANOL IN MICE

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Introduction: Behavioral sensitization (progressive augmentation of locomotor activity following repeated drug administration) is considered a model of neuroplasticity associated with addiction, and can also be induced by the interaction between drugs of abuse and stress. Adolescence is a critical period of brain remodeling, and increased evidence has linked this period with high vulnerability to drug addiction and to stress. Initiation of ethanol abuse in humans may be due to either the excitatory effects of ethanol or stress-relief properties of this drug. Nitric oxide (NO) plays an important role in regulating behavioral processes, and also in various effects of ethanol, including ethanol-induced behavioral sensitization. We have shown that stress increases neuronal nitric oxide synthase (nNOS) activity.
Aim: Study the effects of 7-nitroindazole (7NI), a selective nNOS inhibitor, on NO mediation in adolescent (ADL) and adult (AD) Swiss mice submitted to chronic unpredictable stress (CUS) and subsequent ethanol challenge.
Methods: Mice were exposed to 11 days of CUS or received either a saline or ethanol injection (1.8 g/kg). All groups (N=10 each) were challenged with 1.8 g/kg ethanol on the 12^{th} day of treatment and the locomotor activity was measured during 10 min, immediately after the ethanol injection. Three other groups of mice were treated with 15 mg/kg 7NI 30 minutes before the injections or once a day in CUS group. One CUS group received 7NI in drinking water. All groups were challenged with ethanol on the 12^{th} day of treatment.
Results: The results showed cross-sensitization between stress and ethanol. Pretreatment with 7NI decreased locomotor activity in both ages.
Conclusions: (1) stress induces behavioral sensitization to ethanol; (2) 7NI was able to decrease locomotor activity in adolescent and adult mice, signaling that NO is required to addiction.
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0405

THE IL-1 RECEPTOR MAY INFLUENCE ALCOHOL CONSUMPTION AND STRESS INDUCED DRINKING IN C57 MICE

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Proinflammatory activity plays an increasingly recognized role in behavioral responses to stress and addictive processes. IL-1 beta is a key proinflammatory cytokine that is induced by stress as well as alcohol exposure, and has been suggested to modulate stress- and alcohol-related behaviors. Here, we investigated a potential role of the receptor for IL-1 beta, the IL-1R, in regulation of alcohol consumption and stress related drinking behaviors, using IL-1R KO mice. Alcohol intake was measured using a two bottle free choice paradigm. Intake of an ethanol solution of stepwise increasing concentration revealed that IL1R KO mice drink significantly less at pharmacologically active concentrations ($p < 0.02$). This effect was still present during repeated cycles of deprivation (24 hr access to the ethanol-solution after 6 days of deprivation; this was repeated in 3 cycles), although both groups escalated their consumption (main effect of cycle, $p < 0.005$; no genotype x cycle interaction). Ongoing experiments examine whether IL-1R deletion moderates the consequences of social defeat stress on voluntary alcohol consumption, and the effects of alcohol exposure on the expression of a broad range of immune system transcripts. In summary, we show that the IL-1R is involved in regulating voluntary drinking in mice and we further hypothesize that it may also regulate stress-induced drinking.

0406

SEX DIFFERENCES IN THE EFFECT OF BINGE DRINKING HISTORY ON ALCOHOL PREFERENCE AND ANXIETY-LIKE BEHAVIOR IN C57BL/6J MICE

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Almost 7% of those who use alcohol recreationally develop an alcohol use disorder (Grant et al., 2004). This shift from use to abuse and dependence is influenced by a number of factors. The striking sex difference in the temporal progression of alcohol use disorders suggests biological sex may play a role in mediating the drug's abuse potential. A number of animal models of voluntary alcohol consumption support and extend these clinical findings. Using a modified version of the DID-MSA procedure our lab has previously described sex differences in the development of escalated drinking in C57BL/6J (B6) mice, with females showing a 122% increase in intake across 14 days (Melón et al., RSA 2011). In the present set of experiments, adult male and female B6 mice were given access to alcohol (or water) using the DID-MSA procedure for 3, 7 or 14 days to assess whether the escalated intake previously described for females is related to a faster development of preference for alcohol and/or a greater vulnerability to behavioral adaptations following binge drinking. Mice had 3-hourly access periods to a 20% ethanol solution per day. Signs of withdrawal-induced anxiety were measured 7–8 hours following their final day of binge access using the Light-Dark box. There was no significant change in anxiety-like behavior following 3 or 7 days of DID-MSA binge-like drinking for males or females. However, after 14 days of access, female (but not male) binge drinkers displayed a surprising 25% reduction in withdrawal-induced anxiety-like behavior. Two-bottle (24-hour) choice drinking was initiated 16 hours following the last binge access period (at the start the next dark cycle) and maintained for 3 weeks. For females, 3 days of binge drinking was sufficient to develop significantly greater preference for alcohol than their water-drinking counterparts. In contrast, male B6 mice required 14 days of binge drinking to display significant increases in their daily alcohol consumption and preference, over that of their water drinking controls. These results support a telescoped development of problem drinking for B6 females. Future studies will assess the role that alcohol-induced dysfunction to the estrous cycle-linked regulation of both neurosteroid synthesis and GABAA receptor expression may play in this sexually dimorphic vulnerability to binge drinking. This work was supported by NIH grants AA016789 (SLB) and AA07462 (LCM), as well as the Indiana Alcohol Research Center.

0407

INCREASED SELF-ADMINISTRATION OF ETOH IN MICE IN RESPONSE TO IMPEDENCE OF A RUNNING WHEEL: MODULATION BY SEX AND B-ENDORPHIN

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The gender gap in alcohol use disorders (AUDs) seems to be diminishing (Bjork, et al., 2008; Keyes et al., 2011) increasing the need for better understanding sex-specific motivational factors. Females are well known to be more sensitive to stress (Bekker & vanMens-Verhulst, 2007), and stress is also known to modulate drinking, thus it is possible that changing rates of AUDs are related to increases in exposure to environmental stressors. However, the neural mechanisms mediating the association between stress and drinking are not well understood, in part because reliable animal models have been hard to come by. Scheduling or controlling access to positive reinforcers induces stress (Grant, et al., 2008 for review) and in animal studies has the advantage of taking place in the subject's home cage environment where alcohol (EtOH) can also be made available. We evaluated limited access, 2-bottle free choice drinking (20%) in the subject's home cage where there was also 24 hr access to a running wheel. After establishing baseline drinking behavior we blocked rotations of the running wheel every other day for 10 days. This had the effect of increasing self-administration, particularly in females. To begin to explore the mechanisms underlying this effect, we tested mice that had limited or no capacity to synthesize b-endorphin. Again female but not male mice who lacked the capacity to synthesize b-endorphin increased their consumption; in fact, with decreasing b-endorphin the sex difference in frustration-induced drinking got larger. Thus the relationship between stress and b-endorphin may differ in males and females.

0408

PRAZOSIN, AN α1-ADRENERGIC RECEPTOR ANTAGONIST, BLOCKS THE EFFECT OF STRESS ON ANXIETY BEHAVIOR DURING SUBSEQUENT ALCOHOL WITHDRAWAL

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It has previously been demonstrated that stress facilitates the anxiety-like behaviors that occur during alcohol withdrawal. Since anxiety is mediated, in part, by excessive activity of the central noradrenergic system, we hypothesized that the CNS-active α1-adrenergic receptor antagonist, prazosin, would block stress-induced facilitation of alcohol withdrawal-induced anxiety. We employed a stress paradigm that has been demonstrated to increase anxiety-like behavior during alcohol withdrawal in rats selectively bred for alcohol preference and high voluntary alcohol drinking (alcohol preferring or ''P'' rats). Adult male P rats received 3 cycles of 5 days of voluntary alcohol drinking interrupted by 2 days of alcohol deprivation, with or without 1 h restraint stress introduced at 4 h after the start of each of the first 2 alcohol deprivation cycles. Prazosin (1.0 or 1.5 mg/kg, IP) or vehicle was administered before restraint stress in each of the first two alcohol deprivation cycles. Additional groups of untreated control rats, rats receiving constant alcohol access, and rats receiving cycles of alcohol access and deprivations without stress were also included (n=6–7/group; total n=40). Rats that received constant access to alcohol, or cycles of alcohol drinking and deprivation without stress, did not exhibit increases in anxiety-like behavior during the third and final deprivation. In contrast, rats that had been stressed at the start of the first two alcohol deprivations exhibited increased anxiety-like behavior during the third and final deprivation when compared with control rats (elevated plus-maze: $p<0.05$ for open arm time, $p<0.01$ for open arm entries; social approach/avoidance: $p=0.05$). This demonstration that stress increases anxiety-like behavior during subsequent alcohol withdrawal is similar to the findings of a prior study also conducted with P rats (Overstreet et al, 2007). Prazosin treatment before each of the two stresses blocked this stress effect. These results suggest that clinical treatment with prazosin to decrease α1-adrenergic signaling during alcohol withdrawals may help prevent increases in anxiety during subsequent withdrawal that can contribute to alcohol relapse. Supported by resources from VA Puget Sound Health Care System, VISN 20 MIRECC and NIH AA018604, AA017839 (Rasmussen); AA018604, AA007611 (Froehlich).

0409

ELEVATED EXPRESSION OF NEURONAL PENTRAXINS IN THE MEDIAL AMYGDALA DURING ETHANOL ABSTINENCE IN DEPENDENT AND STRESS-EXPERIENCED RATS

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Ethanol dependence and a history of stress both yield increased ethanol intake, suggesting that common neuroadaptations may subserve both conditions. Neuronal pentraxins, activity-induced proteins that strengthen glutamatergic synapses by clustering AMPA receptors at the cell surface, have been implicated in withdrawal from multiple drugs of abuse. We hypothesized that expression of neuronal pentraxins in the amygdala or medial prefrontal cortex might likewise be modulated by acute ethanol withdrawal or stress history. Ethanol dependence was generated by 5 weeks of daily cycles of ethanol vapor and withdrawal (vapor 14h on/10h off, peak BAL=175–200 mg%). To investigate the effect of stress history, separate rats were subjected to 3 daily, 30-minute sessions of 60 inescapable cued footshocks (stressed) or light cues alone (controls). Both stress history groups were then allowed to self-administer ethanol (10% v/v) in an acquisition (13 sessions) – extinction (15 sessions) - relapse (10 sessions) design. Brain tissue was collected after 8 h of withdrawal (dependent rats), or 24 h after the final self-administration session (stress history rats), and mRNA levels for neuronal pentraxins 1 and 2 (*Nptx1/2)* were determined via qPCR. During acute ethanol withdrawal, we found significantly elevated *Nptx1/2* levels in the medial amygdala and infralimbic prefrontal cortex, a trend towards increased *Nptx2* in the basolateral amygdala and unchanged levels in the central amygdala, prelimbic prefrontal cortex and nucleus accumbens. Medial amygdala *Nptx1* expression was also increased in stress history rats 24 h after their final ethanol self-administration session, with a similar trend observed for *Nptx2* mRNA levels. In contrast, stress history did not alter *Nptx1/2* mRNA levels in the infralimbic prefrontal cortex. Together, the results implicate neuronal pentraxins in the medial amygdala, as well as its afferent pathways, as a potential common locus for neuroadaptations that underlie behavioral changes associated with ethanol dependence or a history of stress.

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0410

ROLE OF SEROTONIN 2C RECEPTOR SIGNALING IN THE BNST IN ETHANOL-INDUCED ANXIETY-LIKE BEHAVIOR

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Anxiety is a coresymptom of ethanol withdrawal that is associated with relapse and ethanol dependence. Several lines of evidence suggest that the serotonin 2c receptor (5HT2cR) plays a key role in anxiety and may be altered following ethanol exposure. Preliminary data from our lab suggests that chronic intermittent ethanol (CIE) increases both 5HT2cR mRNA and anxiety-like behavior in mice. Furthermore, the 5HT2c/b agonist mCPP increases anxiety in detoxified alcoholics (Krystal, 1994). The mechanism of 5HT2cR-induced anxiogensis is unknown, but some evidence suggests that CRF neurons in the bed nucleus of striaterminalis (BNST) areinvolved.Our goal was to determine if1) 5HT2cR antagonists reduce CIE-induced anxiety and 2) 5HT2cRs modulate CRF neurons in the BNST.For CIE studies, male DBA/2J mice pretreated with pyrazole (1 mmol/kg, i.p.) were exposed to ethanol vapor or room air for 5 days, 16 hr/day. After withdrawal (24 hr and 1 week), mice received the 5HT2cR antagonist SB242,084 (3 mg/kg, i.p.) 1 hour before the social interaction test. We found that SB 242,084 significantly attenuated anxiety-like behavior in the social interaction test in CIE mice, but not in controls. Using ex vivo electrophysiology, we studied the effects of mCPP (20 μM) on CRF neurons in the BNST in a CRF reporter mouse. The effect of mCPP (5 mg/kg, i.p.) on neuronal activity (i.e. FOS-IR) in the BNST was examined in DBA/2J mice using immunohistochemistry (IHC). We found that mCPPdepolarized CRF neurons in the BNST, an effect which was completely blocked by SB 242,084. Likewise,mCPPincreasedFOS-IR in the oval nucleus of the BNST, which contains a high density of CRF neurons.The anxiolytic effect of SB 242,084 in CIE, but not control mice, indicates that 5HT2cR signaling may be altered following CIE exposure. This is supported by data from our lab showing that 5HT2cR mRNA is upregulated following CIE, and we are following up on this finding with Western blots. Upregulation of 5HT2cRs following CIE, together with electrophysiological data showing that 5HT2cRsmodulate CRF neurons in the BNST, may partially explain the anxiety in CIE mice and the anxiolytic effects of 5HT2cR antagonists. Studies are underway to determine if mCPP increases FOS-IR in CRF neurons in the BNST using the CRF reporter line.Taken together, our findings suggest that 5HT2cR actions on CRF systems may represent a novel molecular target for intervention of anxiety associated with alcohol abuse.

0411

ACUTE STRESS DECREASES IMPULSIVITY IN HIGHLY IMPULSIVE RATS

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Alcoholism is associated with increased impulsivity, characterized by preference for immediately available rewards over delayed but more valuable rewards (Mitchell 2006). Acute stressors are implicated in relapse in abstinent alcoholics and cause reinstatement of ethanol seeking in animal models (Breese 2005, Le 1998). The neural mechanisms through which stress increases drug seeking are not fully understood, but drug seeking may result from a stress-induced increase in preference for immediate rewards. Thus, stress may cause abstinent alcoholics to become more impulsive, leading to preference for alcohol consumption (i.e., immediate reward) over continued abstinence (i.e., delayed rewards, such as improved health). Here, we address the hypothesis that a pharmacological stressor (yohimbine) increases impulsive behavior.

Male Sprague Dawley rats (n=16) were trained in a delay discounting task, in which rats chose between a small, immediate (100 uL of 4% intralipid) or a large, delayed reward (400 uL of 4% intralipid; delay times of 0, 10, 20, 30, and 40 seconds). Yohimbine (0.6, 1.25, 2.5, or 5 mg/kg, IP) or vehicle was administered 30 minutes prior to task performance. Percent preference for large reward across blocks was analyzed and used as a measure of impulsive behavior.

Yohimbine did not significantly alter decision making in the population as a whole ($p>.05$). However, the effect of yohimbine varied as a function of baseline impulsivity. A median split was used to classify rats as ‘‘High Impulsivity’’ or ‘‘Low Impulsivity.’’ Surprisingly, yohimbine decreased impulsivity in the High Impulsivity group (ANOVA, $F(1,7)=2.7$, $p<0.05$), but had no effect on the Low Impulsivity group.

Paradoxically, these results suggest that pharmacological stress reduces impulsivity in a subset of highly impulsive rats. We speculate that this outcome may stem from a suppression of goal-directed behavior in favor of habit-driven behavior, which is manifested as decreased impulsivity in the delay discounting task. Future experiments will specifically address this possibility.

0412

ANXIETY-LIKE BEHAVIOR IN A HIGH DRINKING IN THE DARK SELECTED MOUSE LINE

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The High Drinking in the Dark (HDID) mouse line has been selectively bred for a binge drinking-like phenotype wherein animals reach a high blood ethanol concentration (BEC) following limited access to an ethanol solution. Over successive generations this line has shown significant divergence from the unselected HS/Npt control line for both the selected measure of BEC and also for the g/kg body weight dose of ethanol consumed, and these animals readily drink to intoxication in a limited access procedure. In this study, we examined whether HDID-1 mice would drink a sufficient amount of ethanol during the Drinking in the Dark (DID) test to produce anxiolysis as assessed on the elevated zero maze (EZM). Female HDID-1 mice were given a 2-day DID test with either water or ethanol access and then tested on the EZM immediately following the end of drinking on the final day. HDID-1 mice provided with ethanol consumed on average 6.3 g/kg in a 4 hour period, and achieved a mean BEC of 1.4 mg/ml. Mice drinking ethanol also showed significantly more open arm entries as a percent of total entries, a greater percent of total time spent on the open arms, and more line crossings than the mice drinking water. These results show that HDID-1 mice will consume a sufficient dose of ethanol during the DID test to produce both locomotor stimulation and a reduction in anxiety-like behavior, and suggest that the anxiolytic effects of ethanol may play a role in the high-drinking phenotype of the HDID mice. Supported by AA13519, AA10760, and a grant from the US Department of Veterans Affairs. AB-L is supported by AA007468, and the Achievement Rewards for College Scientists Foundation.

0413

ADOLESCENT INTERMITTENT ETHANOL EXPOSURE INCREASES SOCIAL ANXIETY AND RETAINS ADOLESCENT-TYPICAL SENSITIVITY TO ACUTE ETHANOL IN MALE RATS

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Alcohol use is initiated during adolescence, with adolescents often demonstrating a binge pattern of drinking (i.e., consuming large amounts that bring blood ethanol concentrations to levels > 80 mg/dl). Surprisingly, there has been little basic research investigating lasting consequences of adolescent intermittent ethanol exposure (AIE) on later behavioral function, despite the significant proportion of adolescents who engage in risky patterns of drinking. The present study was designed to test whether AIE alters baseline levels of social behavior as well as sensitivity to the social consequences of ethanol in adulthood. Male and female adolescent rats were given 3.5 g/kg or water via gavage every other day from postnatal days (P) 25 to 45. On P70, ethanol-, water-exposed and non-exposed control animals were subjected to a modified social interaction test in a familiar context. Thirty min prior to the test, animals were challenged intraperitoneally with one of four doses of ethanol (0, 0.5, 0.75, 1.0 g/kg) or left non-injected for the assessment of changes in baseline levels of social behavior AIE at levels well in the range of binge consumption (BECs around 200 mg/dl) decreased baseline levels of social investigation and social preference in males, suggesting increases in social anxiety. These AIE-induced decreases in social investigation were sensitively reversed by acute ethanol. AIE preserved adolescent-typical patterns of ethanol sensitivity in males, with male adult animals exposed to ethanol, but not to water or non-manipulated as adolescents, demonstrating facilitation of play fighting following acute ethanol challenge. Surprisingly, AIE produced few, if any, effects in females. Although the possible contribution of pharmacokinetics to these sex differences in AIE effects are still being examined, these results demonstrate long-lasting changes in social motivation/behavior and in the social consequences of ethanol in males following chronic intermittent exposure to ethanol during adolescence, including retention into adulthood of adolescent-typical sensitivities to the socially facilitating effects of ethanol. Supported by U01AA019972-NADIA Project.

0414

ASSESSMENT OF ANXIOLYTIC AND MOTOR STIMULANT EFFECTS OF ETHANOL IN ADOLESCENT AND ADULT WISTAR RATS

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Background: It is important to assess age-related differences that may put adolescents at risk for developing alcohol-related problems. Ethanol-induced motivational effects (appetitive, aversive and anti-anxiety consequences) are important modulators of ethanol-seeking and intake. In the present study we assessed anxiolytic and motor behavioral stimulant effects of ethanol in adolescent and adult outbred Wistar rats.
Methods: On postnatal day 28 or 74 (adolescents and adults, respectively), male and female animals were given ethanol (0.0, 0.5, 2.5 or 3.25 g/kg) and then assessed in an open field (size: 30 x 30 x 30 cms, and 50 x 50 x 50 cms; for adolescents and adults, respectively) for 7 minutes (post-administration time: 5–12 min). Total duration of forward locomotion and time spent in the center of the open field were measured. The former was considered as a measure of drug-induced activation, whereas the latter is thought to reflect an anxiety-like response. Time spent rearing and wall-climbing were also assessed.
Results: ANOVAs indicated that overall forward locomotion was significantly higher in adult than in adolescent rats and in female than male rats. Ethanol induced significant motor activation, particularly at 3.25 g/kg, and this stimulant effect was fairly similar in adolescent and adult rats. Time spent in the center of the open field was similar in adolescents and adults treated with vehicle (0.0 g/kg). Adults given 2.5 and 3.25 g/kg ethanol, however, exhibited significantly less time in the center of the arena when compared with vehicle-treated counterparts. High (i.e., 3.25 and 2.5 g/kg) but not low (0.5 g/kg) ethanol-dose induced a significant decrease in both rearing and wall-climbing.
Preliminary conclusions: Under the present experimental conditions there were no age-related differences in the motor stimulating effects of ethanol. Ethanol, however, seemed to induce anxiety-like behavior in adult but not in adolescent rats. The latter result is consistent with previous findings of adults, but not adolescents, exhibiting ethanol-induced social anxiety (Varlinskaya & Spear, 2002).

0415

CHRONIC CORTICOSTERONE INDUCES NEUROADAPTIVE CHANGES IN THE ACCUMBENS AND IMPACTS SENSITIVITY TO THE INTEROCEPTIVE EFFECTS OF ALCOHOL VIA MGLUR5

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Metabotropic glutamate receptors-subtype 5 (mGluR5) in the nucleus accumbens (NA) functionally regulate sensitivity to the interoceptive/subjective effects of alcohol and alcohol self-administration in rats. We have shown that chronic exposure to the stress hormone corticosterone (CORT) in the drinking water results in reduced sensitivity to the interoceptive effects of alcohol and increased alcohol self-administration. We sought to investigate whether CORT exposure alters the expression of mGluR5 in the NA. Long Evans rats were given CORT in the drinking water (0.3 mg/ml) or water for 7 days. On Day 7, rats were sacrificed and brains processed for mGluR5 immunoreactivity (IR). A significant decrease in mGluR5 IR in the NA (core and shell) was observed in CORT-exposed rats, while no change in mGluR5 IR was found in the caudate putamen (positive control region). To confirm specificity of the change to mGluR5, mGluR2/3 IR in the NA was examined and no change was observed. In addition, IR of phosphorylated extracellular regulated kinase (pERK1/2), a downstream target of mGluR5, showed a parallel decrease to mGluR5 in the NA. Next, we assessed whether CORT exposure altered glutamate synaptic function in the NA and found significant elevations in spontaneous excitatory post-synaptic current (sEPSC) frequency, but no change in amplitude or AMPA/NMDA ratio, suggesting increased glutamate release within this brain region. To begin to examine whether mGluR5 plays a functional role in the decreased sensitivity to the interoceptive effects of alcohol following CORT, we assessed whether pharmacological manipulation of mGluR5 could restore sensitivity to alcohol. Briefly, rats trained to discriminate alcohol from water (1 g/kg, IG) underwent CORT exposure. On Day 7, rats were injected with the mGluR5 positive allosteric modulator CDPPB (10mg/kg, IP) prior to alcohol (1 g/kg, IG). CDPPB restored sensitivity to alcohol (1 g/kg), suggesting the functional involvement of this receptor in modulating sensitivity to alcohol following CORT. Together these data show specific neuroadaptive changes in mGluR5 and synaptic function in the NA following chronic CORT exposure which may contribute to decreased sensitivity to alcohol, and possibly to increased alcohol self-administration. Further, manipulation of mGluR5 may be a viable target for restoring sensitivity to alcohol following a stressful episode, which may have therapeutic value. Supported by the ABMRF and AA019682.

0416

ENHANCED CORTICOSTERONE RESPONSE EVOKED BY NOVEL ENVIRONMENT STRESS IMPOSED DURING WITHDRAWAL IN SPRAGUE-DAWLEY RATS

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It has been shown that ethanol withdrawal is associated with reduced activity, anxiety, and other signs of stress. Data from our laboratory demonstrated that the hypothalamic-pituitary adrenal (HPA) axis response to a mild stressor (e.g. novelty, restraint) is increased when stressor exposure occurs during the early phase of withdrawal from acute alcohol exposure (Buck et al., 2011), but the persistence of this enhanced stress reactivity has not been explored. The goal of the present study was to characterize the corticosterone (CORT) response to a stress challenge (exposure to a novel environment) at various time points following acute ethanol exposure in adult male Sprague-Dawley rats (N = 42). Ethanol (4 g/kg, 20% v/v) was administered intragastrically (i.g.), with vehicle-exposed animals intubated with tap water. Rats were then exposed to a mild stressor either 14, 24, 48, or 72 hr after the injection (8–9:30 am), with the stressor consisting of placement in a novel environment with automated locomotor activity sensors for 15 min. Blood samples were taken from the tail immediately before (as baseline measurement) and immediately after the stress challenge in order to assess CORT levels (via ELISA) and BECs. Exposure to a novel environment led to an enhanced CORT response 14 hrs after alcohol intubation (~3 hr after ethanol clearance), with higher levels of CORT both before and after stress exposure when compared to other time points and the control group. HPA axis enhancement was not observed when stress was imposed at 24, 48 or 72 hr after ethanol exposure, suggesting that the enhanced CORT response is only present within the first few hours after ethanol clearance. BECs measured at the 14 hr time point confirmed no significant levels of ethanol in the blood. Behavioral assessment during the locomotor activity test revealed significant decreases in horizontal and vertical activity, as well as increases in resting time when animals were exposed to stressor at the 14 hr time point. These behavioral alterations were no longer apparent by later time points. The results from this study confirm previous results from our laboratory, indicating decreased activity and a hyper-responsive HPA axis during withdrawal from acute alcohol exposure. Current and future studies will examine potential mechanisms involved in sensitization of the HPA response, including alterations in expression of central or peripheral cytokines due to ethanol-induced inflammation.

0417

RELATION BETWEEN CORTICOSTERONE AND FEAR-RELATED BEHAVIOR IN MICE SELECTIVELY BRED FOR HIGH OR LOW ALCOHOL PREFERENCE

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In humans, there is a high rate of co-morbidity between alcohol use disorders (AUDs) and post-traumatic stress disorder (PTSD). Alterations in hypothalamic-pituitary-adrenal (HPA) axis functioning have been linked with genetic (familial) risk for both disorders and cortisol response to stress or trauma has been suggested to be a biological risk factor for the development of PTSD and AUDs. Mouse lines selectively bred for high (HAP) or low (LAP) alcohol preference may be a relevant model of genetic risk for co-morbid AUDs and PTSD in humans. HAP mice show greater fear-potentiated startle (FPS), a model used to study PTSD, than LAP mice. In this study, we explored the relation between corticosterone and FPS behavior in three experiments. Naïve male and female HAP2 and LAP2 mice were randomly assigned to either a fear-conditioned (paired light+shock) or control (unpaired light+shock) group and blood was sampled from the submandibular vein to assess corticosterone (CORT) content at various time points before and after fear-conditioning (Experiment 1) and FPS testing (Experiment 2). For Experiment 3, HAP2 mice received one of 4 CORT doses (0, 1, 5, and 10 mg/kg) 30 min before fear-conditioning and blood was sampled in the same manner as in Experiment 1. The data showed lower CORT response in fear-conditioned HAP2 than LAP2 mice after fear-conditioning (Experiment 1) and FPS testing (Experiment 2). In Experiment 3, the highest dose of CORT (10.0 mg/kg) increased the expression of FPS. However, CORT levels in the 10.0 mg/kg dose group were significantly lower than the 0 mg/kg dose group vehicle control group (measured at the end of the 2-hr conditioning session and 2.5 hrs after CORT injection), reflecting negative feedback inhibition of the HPA axis. These results are consistent with other data in humans and rodents indicating that lower cortisol/CORT levels after stress are associated with greater PTSD/PTSD-like behavior. Overall, these findings in the HAP/LAP model suggest that a lower CORT response to stress and/or greater negative feedback inhibition of the HPA axis may be a biological risk factor for greater susceptibility to develop PTSD in individuals with increased genetic risk for AUDs.
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0418

SOCIAL ISOLATION DISRUPTS EXTINCTION OF FEAR LEARNING AND ENHANCES ADRENOCEPTOR ANTAGONIST-MEDIATED INHIBITION OF ETHANOL DRINKING IN LONG EVANS RATS

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Prior studies by us and others have shown that adolescent social isolation in rats can result in enduring increases in anxiety-like behaviors and ethanol self-administration. The purpose of these studies was to investigate the effect of adolescent social isolation on the acquisition and extinction of fear learning, and to determine the role of the adrenoceptor (AR) system in moderating drinking behaviors induced by prolonged exposure to this early life stress. Briefly, socially isolated (SI) and group housed (GH) Long Evans rats were trained to pair a neutral light stimulus with the delivery of a noxious footshock. Following this fear conditioning procedure, fear learning was assessed using a standard auditory startle assay in which a series of 109 dB tones were delivered either alone or preceded by the light stimulus that was previously associated with the shock. After acquisition of fear learning, the light was presented repeatedly in the absence of the shock (extinction training) and the fear-potentiated startle assay was repeated. No differences in basal auditory startle responsivity or fear-potentiated startle were noted between SI and GH animals. However, SI rats exhibited a significant impairment in extinction of fear learning. Furthermore, using an intermittent two bottle choice procedure (20% ethanol/water, Mon-Wed-Fri), systemic administration of an α1-AR antagonist (prazosin, 1.5 mg/kg) dose-dependently decreased total ethanol intake and ethanol preference in SI animals during the first 30 minutes of ethanol availability, but had no effect on either measure in GH subjects. Likewise, systemic administration of the β1/2-AR antagonist propranolol dose-dependently inhibited ethanol intake in SI animals (1.25 and 2.5 mg/kg), while only the highest dose of this drug decreased ethanol intake in GH animals. These results suggest that early life stress not only leads to increases in anxiety-like behaviors and ethanol consumption, but may also disrupt extinction of fear-related memories, a behavioral phenotype also observed in individuals afflicted with post-traumatic stress disorder. Furthermore, our data also suggest that antagonism of α1- and β1/2-ARs has a greater effect on ethanol consumption in SI rats, suggesting that alterations in AR signaling may contribute to the deleterious behavioral sequalae associated with early life stress.
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0419

EFFECT OF SOCIAL DEFEAT STRESS ON VOLUNTARY ETHANOL INTAKE IN ETHANOL DEPENDENT AND NON-DEPENDENT C57BL/6J MICE

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Repeated cycles of chronic intermittent ethanol (CIE) exposure produces escalation of voluntary ethanol drinking in C57BL/6J mice. Previous studies have also indicated that social defeat (SD) stress can increase intake in mice. This study evaluated the effect of repeated SD on voluntary ethanol intake in ethanol-dependent and control non-dependent mice. C57BL/6J mice were trained to drink 15% (v/v) ethanol using a limited access (2 hr/day) 2-bottle choice paradigm. Once stable intake was established ($\sim$2.6 g/kg/day), mice received 4 weekly cycles of chronic intermittent exposure (16 hr/day x 4 days) to ethanol vapor (EtOH group) or air (CTL group), with each exposure cycle alternating with a week of limited access drinking test sessions. Separate groups of EtOH and CTL mice experienced SD stress either during every ethanol intake test, only during the last (fourth) test cycle of ethanol intake, or were not exposed to stress. During SD stress sessions, each C57BL/6J mouse was placed in the home cage of a resident CD1 mouse for 30 min (5 min of interaction, 25 min separated by a wire mesh) at 4 hr before each ethanol intake session. As expected, EtOH mice that did not experience SD showed a significant increase in ethanol intake (up to $\sim$3.4 g/kg/day) compared to CTL no stress mice that evidenced relatively stable intake across all test cycles. EtOH mice that experienced SD stress during every test cycle did not show an increase in ethanol intake above baseline levels while CTL mice showed a significant decrease in intake during the first two test cycles compared to baseline (down to 1.9 g/kg/day). EtOH mice that experienced SD stress only during the last test cycle showed a reduction in intake to baseline levels while CTL mice that experienced SD stress during the last test cycle did not show a change in ethanol intake. In summary, these results indicate that SD stress does not increase ethanol consumption in C57BL/6J mice. However, SD stress did differentially impact ethanol intake in ethanol-dependent and control (non-dependent) mice. SD stress reduced ethanol intake in control non-dependent mice and prevented the escalation of drinking in ethanol-dependent mice.
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0420

EFFECTS OF YOHIMBINE AND ALCOHOL DEPRIVATION ON ETHANOL- RELATED BEHAVIORS IN ALCOHOL-PREFERRING (P) AND HIGH-ALCOHOL DRINKING (HAD-2) RATS

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Stress has been shown to increase alcohol drinking during periods of use and to contribute to relapse during periods of abstinence. The present experiments sought to determine the role of stress in ethanol seeking and self-administration during continuous or intermittent ethanol access under binge-like operant and free-choice homecage access conditions in lines of rats selectively bred for high alcohol intake. In both experiments, male P and HAD-2 rats were given 6 weeks of ethanol access prior to 3 cycles of 1-week periods of ethanol deprivation interspersed with 1-week periods of ethanol self- administration. During the deprivation periods, or at similar timepoints in rats given continuous ethanol access, rats were exposed either to the pharmacological stressor yohimbine (YOH) or to vehicle. In Experiment 1, rats trained to self-administer ethanol were injected with YOH prior to an extinction session to measure the effect of stress on ethanol-related appetitive responding. Rats resumed ethanol self-administration the following day. In Experiment 2, rats given homecage ethanol access were injected with YOH every other day (3 injections/week) during the deprivation periods. Rats were tested in the elevated plus maze prior to the resumption of ethanol access during the final cycle to assess stress- and deprivation-related changes in anxiety-like behavior. YOH did not alter ethanol-motivated responding or drinking in Experiment 1, but increased ethanol drinking in Experiment 2, suggesting that the timing of YOH exposure and drinking paradigm are important in stress-related changes in ethanol-motivated behaviors. Ethanol deprivation produced modest increases in ethanol intake in both experiments. However, anxiety-like behavior was not altered as a function of YOH or ethanol deprivation in Experiment 2. Regardless of treatment, P rats showed less anxiety-like behavior and responded more for ethanol than HAD-2 rats in the present experiments. While YOH increased ethanol intake in Experiment 2, overall, these studies do not support the hypothesis that stress enhances anxiety due to ethanol deprivation, which provides a mechanism for enhanced subsequent ethanol seeking and consuming. Further investigation into the complex relationship amongst stress, anxiety, and alcohol consumption might identify conditions that confer sensitivity to stress in alcohol-related behaviors and lead to further development in treatments aimed at reducing alcohol drinking and relapse.

0421

OREXIN RECEPTORS MODULATE YOHIMBINE-INDUCED REINSTATEMENT OF ETHANOL SEEKING AND GABAERGIC TRANSMISSION IN THE CENTRAL AMYGDALA

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Rationale: The central amygdala (CeA) is a critical brain area important in processing anxiety-related behaviors and voluntary ethanol consumption. The hypocretin/orexin system is a key component of arousal and stress response, and has been recently implicated in addictive behaviors. The central amygdaloid projections regulate the Hypothalamic-Pituitary-Adrenal (HPA) axis and innervate orexin-containing neurons in the lateral hypothalamus. Dense orexinergic innervation from the hypothalamus is also observed in the CeA. Therefore, the orexinergic system is ideally positioned to play a significant role in stress-induced reinstatement of reward-seeking. In this study, we use yohimbine, a pharmacological stressor, to invoke stress-induced reinstatement of ethanol-seeking and employ electrophysiological techniques to examine the role of orexin receptor subtypes on GABAergic transmission in the CeA.
Methods: Long-Evans rats were trained to self-administer (SA) 20% ethanol (30 min/day). Following 4 weeks of SA training, lever responding was extinguished. Almorexant (dual orexin receptor antagonist) was administered 30 min prior to yohimbine (0 or 2 mg/kg, i.p.) to examine reinstatement behavior. Whole-cell patch-clamp electrophysiology was performed on naïve adult rat CeA neurons to measure evoked GABAergic IPSCs. Orexin-A and receptor antagonists were bath applied to study the effect of orexins on evoked GABAergic IPSCs.
Results: Systemic (10 and 15 mg/kg, n=11) administration of almorexant before yohimbine exposure (2 mg/kg i.p.) significantly reduced yohimbine-stress induced reinstatement of ethanol-seeking. Orexin-A (100 nM, n=8) significantly depressed evoked GABAergic IPSCs in the neurons of the central medial (CeM) nucleus of the CeA. Orexin R_2 receptor antagonist, CB-7893933 (1μM, n=6), significantly blocked the orexin-A induced depression of evoked IPSCs in the CeM.
Conclusions: The orexinergic system mediates stress-induced reinstatement of ethanol-seeking with the CeA as a potential site of action.
Acknowledgements: The work was supported by TATRC grant (W81XWH-10-1-0247) awarded to S.E.B

0422

EXAMINING THE RELATIONSHIP BETWEEN ANXIOUS AND AGGRESSIVE BEHAVIOR AND HEAVY DRINKING IN FEMALE RHESUS MONKEYS

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Anxiety is associated with heavy drinking in humans. However, it is unclear whether anxiety is a risk or a consequence of heavy drinking. The current study assessed anxiety using a human intruder test (HIT) and a novel objects test (NOT) in a group of female rhesus monkeys (n=6) prior to introducing them to ethanol. These tests have reliably been shown to assess individual differences in anxiety and the stress response in primates. The HIT assesses three different conditions: acclimation, profile (stranger stands on side of the cage without facing monkey, with profile towards monkey), and stare (stranger stares at monkey while maintaining eye contact). The NOT sequentially measures responses during three conditions: a novel food offer, a novel object test, and a novel object with familiar food test. Ethanol self-administration was induced via a schedule induced polydipsia procedure, which consisted of daily induction of specified volumes of water or 4% ethanol. Every thirty days, the consumed dose was increased by 0.5 g/kg/d up to a final dose of 1.5 g/kg/day. Following this induction procedure, ethanol (4% w/v) and water were available concurrently 22 h/d.
The HIT consisted of two anxiety-inducing conditions; the stare and profile phases. During these phases, 100% of the monkeys displayed anxious and/or aggressive behavior.
Significant correlations were found between several measures of anxiety and drinking, such as the positive correlation between teethgrinding during the stare phase and 22 hour ethanol intake (g/kg) over 6 and 12 month periods (r_s = 0.94, p = 0.005). During the NOT, latencies to touch the novel objects ranged from 1 second to 300 seconds, with latencies of more than 90 seconds indicating anxiety in response to the object. The same monkeys tended to exhibit anxious behavior across the NOT phases, with monkeys showing increased latency to inspect one novel object also showing increased latency to inspect the other novel objects. Monkeys were characterized as having high or low levels of anxiety based on their responses during the NOT, and non-significant differences in their ethanol consumption were found. When instead characterized based on their aggressive-anxious behaviors during the HIT, significant differences in their blood ethanol content were found (t = 3.2, p =0.03), indicating higher ethanol consumption in the aggressive-anxious group. An aggressive-anxious temperament may predict heavier ethanol consumption.

5. PATHOLOGY: HUMAN/ANIMAL

0423

IMPAIRED SILIBININ (MILK THISTLE) CLEARANCE IS ASSOCIATED WITH ETHANOL-DEPENDEDNT HEPATOCELLULAR CARCINOMA (HCC) PROGRESSION IN MALE MICE

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Background: We previously reported dietary silibinin, a plant-derived antioxidant, selectively potentiates ethanol-dependent HCC progression (an effect mirrored in human patients) in male mice. Mice maintained on dietary silibinin and ethanol (E) displayed increased hepatic injury, disrupted REDOX status and tumor burden compared to controls and pair-matched females. Silibinin exerts differential effects on androgen and estrogen; hormones that influence severity and progression of chronic liver disease. This study aimed to explore potential mechanisms as to why males fed dietary silibinin are more susceptible to ethanol-dependent HCC progression than females, and how sex steroid hormones influence these effects.
Methods: Diethylnitrosamine (D, 1 mg/kg, i.p.) was used to initiate hepatocyte transformation in infant male (m) and female (f) B6C3 mice. AIN93M mouse chow (+/– 0.5% (*w/w*) S) was administered at 15 or 39wks for 9wks. Animals were randomized to an E-drinking water regime at 16 or 40wks (10/20% (*v/v*); alternate days) for 8wks. Serum was pooled from each treatment group and liver tissue prepared for analysis. Total silibinin (silybin A and silybin B) from conjugated and unconjugated fractions was measured utilizing UPLC-tandem MS following chromatographic separation. Serum testosterone (T) and estrogen (Es) were measured by ELISA.
Results: Impaired S clearance was observed in m DES mice at 48wks (+2.4 fold, tissue,+1.8 fold, serum) *vs.* S, (+4.3 fold, tissue, +1.5 fold, serum) *vs.* pair-matched f mice; associated with previously reported increased ALT levels, oxidative stress, necrosis and hepatic immune cell infiltration in m *vs.* f DES mice (48wks). While measurement of circulating T showed no significant difference in control *vs.* DES m mice at 24wks, a significant increase in Es was observed. At 48wks both T and Es levels were significantly increased in DES compared to S controls.
Conclusions: Impaired silibinin clearance/increased accumulation is associated with exacerbated hepatic injury/oxidative stress and immune cell infiltration observed in male DES mice compared to females, indicating ethanol alters silibinin conjugation within the liver. Additionally, a potential silibinin-sex steroid hormone interaction may also contribute to ethanol-dependent HCC progression, as ethanol is known to induce feminization in males and exacerbate injury in chronic liver disease.

0424

ALCOHOL AND DIET-INDUCED OBESITY SYNERGIZE TO PROMOTE HEPATOCELLULAR CARCINOMA IN MALE MICE

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Hepatocellular carcinoma (HCC) is the most rapidly increasing type of cancer diagnosed in the USA and represents a major health burden globally. Obesity is an emerging potential risk factor for HCC development, particularly in developed nations. Other risk factors for HCC act synergistically to increase HCC incidence. Therefore, we investigated the effects of diet-induced obesity and chronic ethanol feeding in a diethylnitrosamine (DEN) mouse model of HCC progression. Methods: Juvenile (21–24 day) male C57BL/6 mice were injected with either vehicle (olive oil) or DEN (5mg/kg). At 5wks mice were randomized to 10% kcal% fat control diet (CD) or 60% kcal% high fat diet (HFD). At 34wks mice were weaned on to either 10%/20% ethanol (EtOH) in drinking water (alternating days) or maintained on drinking water (H_2O) alone. 8wks later mice were sacrificed and tissue/serum collected and analyzed.
Results: HFD resulted in significantly higher body weights than CD. No effect on body weight was observed with EtOH feeding; however, mice injected with DEN had lower body weights in HFD (H_2O and EtOH) than their vehicle-injected counterparts. At necropsy no HCC were detected in CD non-initiated groups regardless of ethanol feeding; however, HCC formed in 30% of HFD H_2O and 10% of HFD EtOH mice. In DEN-initiated animals small (1–3mm) tumors were visible in 60% of CD H_2O mice (6/10). In DEN mice on HFD + H_2O a significantly higher incidence (89%) of larger tumors (3–9mm) was detected. Chronic EtOH feeding reduced visible tumor lesions in CD mice (1/10) but did not significantly affect tumor incidence in HFD mice (90%). Histologically, HFD + H_2O resulted in increased steatosis, necrosis and inflammation versus LFD counterparts, effects blunted in vehicle-injected, and exacerbated in DEN-injected animals. Similarly, alanine transaminase increased in HFD H_2O and EtOH (Veh- and DEN-injected) mice compared to LFD counterparts. Conclusions: These data suggest DIO can independently promote HCC incidence and tumor size compared to low fat diet (CD). However, ethanol was noticed to modestly suppress tumor formation in CD-fed animals (6/10 CD EtOH H_2O vs. 4/9 CD EtOH DEN). Notably, DIO can independently promote HCC formation both in the absence (3/10, HFD H_2O Veh) and presence of an initiating agent such as DEN (8/9, HFD H_2O DEN). Taken together, these data suggest obesity is a stronger risk factor for HCC incidence and progression than ethanol in this model of HCC progression.

0425

ETHANOL POTENTIATES HIV-INDUCED APOPTOSIS OF HEPATITIS C VIRUS RNA REPLICATIVE HUMAN HEPATOMA CELLS

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Abusive chronic alcohol consumption worsens the outcome of hepatitis C virus (HCV) infection as well as its co-infection with human immunodeficiency viral infections (HIV). The host response is triggered when a pathogen-associated molecular pattern (PAMP) presented by the infecting virus is recognized by specific PAMP receptor factors. For RNA viruses, protein and nucleic acid products have been identified as viral PAMPs and are each engaged by specific Toll-like receptors (TLRs), which serve as PAMP receptors. In the case of HCV, the viral RNA contains each of these PAMP signatures, and is sufficient to trigger the host response when introduced into naive cells. Our study analyzes interactions between HCV-HIV and alcohol by using an *in vitro* model that allows autonomous HCV replication in human liver cells. Function and morphology of hepatocytes are altered in the cells harbouring HCV replicon in the presence of HIV infected mononuclear cells and that the alcohol may exacerbate the damage. Our previous studies demonstrated EtOH exposure induced apoptosis of primary human hepatocytes in vitro, thus mirroring alcohol-induced hepatocellular apoptosis in humans. Objective: To characterize *in vitro* EtOH-signaling and the apoptotic response in Huh7 human hepatoma cells and Huh7 cells harboring an HCV subgenomic RNA replicon in the presence of absence of mononuclear HIV-infected cells. Methods: Experiments were conducted in Huh7-cells harbouring an HCV subgenomic replicon, and in parental Huh7 cells that lack the HCV replicon in the presence or absence of HIV viremia. Cell cultures were exposed to 100 mM EtOH, and apoptosis was assessed. In addition the presence of the interferon system was assessed. The non-structural protein (NS5A) in replicon system was studied Results: HCV RNA replication was associated with a dose and time-dependent increase in EtOH-induced apoptosis as well as PAMP inhibition. Exposure to ETOH doubled the amount of apoptosis observed in the replicon cells versus the same treatment in the parental Huh7 cells lacking the HCV replicon. In addition, HIV-infection increased significantly apoptosis in replicon cells when compared to cells non-HIV-infected. Exposure to antiviral cytokine Interferon reduced apoptosis significantly. Conclusions: HIV/HCV RNA replication significantly exacerbates the apoptotic effects of EtOH exposure. Modulation of PAMP signatures by EtOH may have implications both HIV and HCV pathogenesis.

0426

COMPARISON OF NFKB GENOME-WIDE TARGETING BETWEEN CHOW-FED AND LIEBER-DECARLI ISOCALORIC PAIR-FED RATS DURING LIVER REGENERATION

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Analyzing the effects of chronic alcohol use on liver regeneration can provide insight into the effect of ethanol on the liver's gene regulatory network and how its deregulation can lead to alcoholic liver disease. In this study, we use the Lieber-DeCarli pair-feeding protocol to assess the extent to which the molecular processes underlying liver regeneration in the calorie restricted pair-fed controls, in which ethanol calories were replaced by carbohydrates (CHO), are similar to those in the normal chow-fed rats. In both dietary groups, we obtained liver tissue samples at 0hr, 1hr, and 6hr post partial-hepatectomy (PHx). We employed Chromatin Immunoprecipitation followed by Roche NimbleGen promoter microarray assay to identify genome-wide localization of NFkB. We performed a novel pattern analysis to identify sets of target genes with similar or altered binding between the dietary groups as a function of regeneration time. We identified $\sim$1600 target genes unique to CHO-fed rats and $\sim$3300 target genes unique to chow-fed rats. The former set included genes associated with mitochondrion, protein catabolism, positive regulation of caspase activity, ribosome, protein complex assembly, and apoptosis. The target gene set unique to chow-fed rats included genes associated with extracellular space, signaling, positive regulation of organelle organization, nuclear lumen, positive regulation of cell growth and size, ribosome, response to hormone stimulus, and cytoskeleton.We also identified genes with a delayed increase in NFkB binding activity in chow-fed rats, including genes related to cell adhesion, and genes with an early increase in NFkB binding activity, including genes related to acetyltransferase activity, glucose metabolism, and the cell cycle. In summary, our analysis indicates significant differences in the genome-wide targeting of NFkB activity between chow-fed and isocaloric pair-fed rats. Given the similarity of physiological response in the two dietary groups, it is likely that the differences in NFkB binding are compensated for elsewhere in the global regulatory network driving liver regeneration. Research Support: NIH AA018873, AA017261, and T32 AA007463.

0427

C/EBPβ MEDIATED GENOME-WIDE COMBINATORIAL TRANSCRIPTIONAL REGULATORY DYNAMICS DURING EARLY ONSET OF LIVER REGENERATION AND CHRONIC ALCOHOL INTAKE

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The primary objective of this study is to characterize effects of chronic alcohol consumption on genome-scale transcriptional regulatory network dynamics during the early phase liver regeneration after 70% partial hepatectomy (PHx) at 6h post 2/3rd PHx in the rat. Rats were fed liquid diet containing 36% of total calories derived from ethanol for 5 weeks, controls were pair-fed an isocaloric liquid diet with carbohydrate replacing ethanol. Genome-wide binding targets C/EBPβ were detected by ABI SOLiD sequencing approach and qPCR validation. Our results indicate significant differences in the binding profiles of C/EBPβ in chronic ethanol samples compared to isocaloric controls, at baseline as well as in response to PHx. Major component of the difference consisted of missing binding activity in the chronic ethanol group, for baseline as well as PHx induced activity. Pathway analysis of these gene sets revealed several cellular processes such as regulation of cell proliferation, regulation of cell cycle, lipid biosynthetic process, response to hormone stimulus, lipid catabolic process, MAPK signaling pathway. C/EBPβ was detected during liver regeneration at the gene promoters of key regulatory pathways such as (1) positive regulation of cell cycle, regulation of programmed cell death, regulation of cAMP biosynthetic process, positive regulation of RNA metabolic process, MAPK signaling pathway etc common to chronic ethanol and control groups; (2) mitochondrion, negative regulation of cell death, Insulin signaling pathway, cell adhesion etc showing missing activity in the ethanol group (3) regulation of transcription, protein kinase activity, VEGF signaling pathway etc showing novel binding in the ethanol group. We employed qPCR to validate a limited set of genomic loci with missing increase in C/EBPβ activity in the ethanol group. We used our PAINT and TRANSFAC bioinformatics software to predict combinatorial regulatory modules containing co-localized binding sites for NF-κB, STAT3, cFos, cJun, C/EBPα and C/EBPβ, on key genes promoter regions, e.g., Mt1a, G0s2, iNOS, Sod2, etc. This indicates potential for C/EBPβ to coordinate with other key transcriptional regulators active during early phase of liver regeneration. Based on these findings, we propose that significant reduction of genome-wide binding activity of C/EBPβ underlies chronic alcohol-mediated deficiencies in liver regeneration response to PHx. Research Support: NIH AA018873 and AA017261.

0428

COMBINATORIAL GENEOME-WIDE TARGETING OF NFKB AND C/EBPβ DURING THE EARLY PHASE OF LIVER REGENERATION IN ETHANOL-FED RATS

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The central objective of this study is to identify the effects of a chronic ethanol diet on the patterns of genome-wide binding of two key transcriptional regulators, NFkB and C/EBPβ, during the early phase of liver regeneration after partial hepatectomy(PHx). The complexity of the regeneration process involves interactions of multiple transcription factors in the activation and regulation of target genes. Transcription factors activated within 1 to 6 hrs after PHx are involved in regulating expression of genes that are associated with homeostasis and stimulating cells to reenter cell cycle and proliferate. We employed Chromatin Immunoprecipitation followed by Roche NimbleGen ChIP-ChIP microarray platform to detect NFkB targets, and ABI SOLiD ChIP-seq platform to detect C/EBPβ targets, in liver samples obtained at 6h following PHx. We performed dynamic pattern analysis to identify gene sets with correlated binding evolution of NFkB and C/EBPβ. Our results indicated that targeting by C/EBPβ alone is the dominant aspect in both ethanol and isocaloric pair-fed carbohydrate control groups. Within this pattern, C/EBPβ binding at a significant number of gene promoters were novel in the ethanol group. However, a similar number of targets showed common C/EBPβ binding without NFkB binding between the two dietary groups. These sets were enriched for processes regulating cell cycle, transcription, cell proliferation, cell death, apoptosis. We found subtle patterns reflecting combinatorial post-PHx binding in both the factors. For eg: in control data set, a group of genes transiently binding to NFkB targets followed by C/EBPβ binding at 6hr time point were associated with processes such as cell proliferation, protein transport, chemical homeostasis, regulation of fatty acid metabolic process etc. Relatively fewer genes were targeted by both NFkB and C/EBPβ at 6h post PHx. The majority of these genes showed altered binding activity in the ethanol group. Based on these results, we conclude that chronic ethanol effects are mediated through individual as well as combinatorial targeting by key transcriptional regulators during liver regeneration. Research support: NIH AA018873 and AA017261.

0429

CNS IMMUNE RESPONSE IN RATS WITH LIVER DAMAGE

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Hepatic encephalopathy (HE) can accompany liver disease and include disturbances such as altered cognitive and motor function. The aim of this work was to assess whether recruitment of the peripheral or central nervous system (CNS) immune system occurs in a rodent model of chronic liver injury that can cause HE. We chose rat bile duct ligation (BDL), a model recommended by the International Society for HE. Accordingly, 16 Sprague-Dawley (SD) rats underwent surgery for bile duct catheterization; 5 SD rats were controls. At baseline, all rats underwent blood collection and in vivo magnetic resonance imaging (MRI) for brain structural measurement and spectroscopy (MRS) for neurometabolite measurement. Following baseline assessment, catheters were ligated for induction of biliary cirrhosis. Three weeks after ligation, all rats underwent behavioral assessment, blood collection, MRI, and MRS before euthanasia for harvesting of livers and brains. BDL rats weighed up to 25% less than their controls (CON). Physiological signs included piloerection (present in n=15 BDL rats), hypothermia (n=10), and high respiration (n=8); signs of HE included reduced activity (n=9), hunched back (n=11), and altered gait (n=10). While MRS metabolite T2s did not differ between groups at baseline or terminal scans, the T2s of N-acetylaspartate (p=.0002), creatine (p=.01), and choline (p=.01) increased between the baseline and terminal scans for BDL but not CON rats; longer T2s may reflect neuronal edema. At baseline, but not at termination, BDL animals had higher levels of alanine- (p=.01) and aspartate- (p=.01) aminotransferase in their serum. At the time points assessed, ammonia and C-reactive protein levels were not elevated in BDL rats. Left lateral lobe liver specimens of BDL but not CON rats revealed hepatic necrosis, inflammation, bile duct proliferation, and bridging fibrosis. Levels of cytokines IL-1b, IL-6, MCP-1 (i.e., CCL2), and TNF-a were assessed in the liver and 6 unilateral (left) brain regions: prefrontal cortex (PFC), striatum, hippocampus, hypothalamus, anterior vermis, and cerebellum. IL-1b was higher (p=.018) and IL-6 (p=.003), MCP-1 (p=.02), and TNF-a (p=.004) were lower in BDL compared with CON livers. Only the PFC showed group differences in cytokine levels: BDL rats had lower levels of MCP-1 (p=.02). Together, these data suggest that liver disease can lead to CNS changes including edema and neuroimmune involvement.
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0430

CIRCADIAN DISRUPTION EXACERBATES ALCOHOL-INDUCED INTESTINAL PERMEABILITY AND LIVER PATHOLOGY

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Introduction: Alcohol-induced pathologies occur in only a subset of individuals; thus, identification and a better understanding of underlying susceptibility factor(s) may prevent disease development/progression. Hypothesis: Since Circadian rhythm disruption promotes a variety of disease states, we hypothesized that chronic environmental disruption of circadian rhythms would exacerbate alcohol-induced intestinal permeability and liver damage.
Methods: Mice were kept on a regular 12h/12h light:dark (L:D) cycle or shifted (once weekly 12h L:D inversion) for 12 weeks to induce a chronic circadian disruption which occurred before and continued throughout the duration of the alcohol-feeding phase. For the 10 week alcohol-feeding phase, mice were administered an alcohol containing diet or a calorically matched dextrose control diet. Intestinal permeability was assessed at baseline (prior to initiating the alcohol or control diet), and after 1, 4, and 8 weeks into the alcohol-feeding phase. For in vivo measurements of gut permeability, macromolecules that are neither metabolized nor actively transported across intestinal epithelial cells (i.e., sucrose, lactulose, mannitol, and sucralose) were orally administered as a bolus and were subsequently measured in urine. At the end of the 10 week alcohol-feeding phase, liver tissue was harvested.
Results: Alcohol increased intestinal permeability, an effect which was increased by 67% by chronic circadian disruption; furthermore, chronic shifting increased intestinal permeability in control-fed mice by 50% (Week 8, urinary sucralose excretion: Non-shifted control-fed (n=12), 0.55±0.06%; Shifted control-fed (n=12), 1.09±0.20%; Non-shifted alcohol-fed (n=15), 1.20±0.21%; Shifted alcohol-fed (n=14), 1.77±0.23%, one way ANOVA p=0.001). These results indicate that circadian disruption promotes intestinal hyperpermeability and markedly exacerbates alcohol-induced permeability; a result which may have significant consequences for the development/progression of alcohol-induced pathology in the liver. Liver pathology associated with alcohol consumption was indeed augmented by circadian disruption (i.e., steatosis, inflammation, cell death, and ballooning degeneration).
Conclusion: These results suggest that chronic circadian disruption may be a predisposing factor for alcohol-induced liver pathology, an effect which may be the consequence of increased intestinal permeability. Supported by NIAAA, AA020216 to AK.

0431

MLCK ACTIVATION IS ELEVATED IN INTESTINAL EPITHELIAL CELLS FOLLOWING ACUTE ETHANOL EXPOSURE AND BURN INJURY

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Independently, both ethanol exposure and burn injury cause an elevation in intestinal inflammation and permeability. Previous work done in our lab and others indicates that after the combined insult there is significantly greater intestinal morphological damage, IL-6 release and bacterial translocation than in animals given either treatment alone. Changes in permeability and inflammation coincided with less ZO-1 and occludin localizing to tight junctions in the intestinal epithelial cell layer. Furthermore, MLCK knockout or PIK (permeant inhibitor to MLCK)-treated wild type mice did not exhibit alterations in morphological and inflammatory parameters following ethanol and burn injury. Since the phosphorylation of MLC leads to cytoskeletal contraction and can promote barrier dysfunction, we examined whether ethanol and burn injury influences the activation of MLC. Our findings suggest that, 3 hours after insult, intestinal epithelial cells from mice in the combined injury group had higher levels of both MLCK and its phosphorylation target, myosin light chain (pMLC). This increase of MLCK and pMLC found in mice exposed to ethanol and burn was greater than found in mice given either insult alone. Six hours after the combined insult, the elevation in pMLC persisted; however, total MLCK levels were not different between groups at this time point. No differences in pMLC levels were observed in injured MLCK knockout mice regardless of ethanol exposure. Interestingly, treatment with a specific inhibitor to MLCK, PIK, also reduced levels of pMLC in the intestinal epithelial cells of mice exposed to ethanol and burn injury. These data suggest that elevated activation of the MLCK pathway may cause the morphologic and immunologic alterations seen in the intestine after exposure to ethanol and burn injury. In addition, greater inactivation of myosin light chain phosphatase may also have a role in the increase in pMLC observed. This possibility is part of our focus for future studies. [This work was supported by NIH R01AA012034 (EJK), T32 AA013527 (EJK), F31 AA019913 (AZ), R01DK06271 (JRT), and Marian C. Falk Medical Research Trust.]

0432

ALTERED ADRP AND RAB 18 CONTENT IN ISOLATED LIPID DROPLETS (LDS): CONTRIBUTION TO ALCOHOL-INDUCED FATTY LIVER IN RATS

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Background: Lipid droplets (LDs), cytoplasmic organelles that serve as storage compartments for triglycerides and cholesterol esters, consist of a core of neutral lipids, surrounded by a monolayer of phospholipids with attached or embedded proteins. The LD proteome contains structural proteins, lipid-synthesis enzymes, lipases and membrane-trafficking proteins. In the present study we wanted to determine the effect of ethanol administration on the content of a Rab GTPase (Rab 18) and a known LD surface protein, ADRP (adipose differentiation-related protein) in LD fractions. ADRP has been shown to be one of the major LD-associated proteins that can act to attenuate lipolysis. Rab 18, on the other hand, is thought to mediate the association of LDs with the endoplasmic reticulum (ER) in order to mobilize lipid esters stored in LDs.
Methods: Male Wistar rats were pair-fed Lieber-DeCarli diet with or without ethanol for 5 to 7 weeks. Livers were excised and portions of tissue used for TG analysis, histology, and LD isolation. To visualize LDs *in situ*, frozen liver sections were stained with BODIPY and analyzed microscopically. Immunohistochemical staining for ADRP was determined in paraffin-embedded sections. Protein contents for Rab 18 and ADRP were determined by Western Blot (WB) analysis using the appropriate antibodies.
Results: Ethanol administration increased the TG content by 2–3 fold in both whole liver and isolated LDs. In frozen liver sections using BODIPY staining, we observed strong lipid accumulation, characterized by larger vacuoles in ethanol-fed rat livers compared to controls. Immunohistochemical staining and WB analysis showed that alcohol feeding increased ADRP content by 1.5–3 fold in both isolated LDs and in whole liver. In contrast, Rab 18 content was unchanged in whole liver, but showed 50–75% decreases in isolated LDs from ethanol-fed animals.
Conclusions: Chronic alcohol consumption significantly increased the expression of ADRP, while Rab 18 content was decreased in isolated LDs. Since ADRP is known to stabilize LDs, while Rab 18 is involved in LD mobilization, these two changes would work in concert to contribute to the alcoholic fatty liver; indeed, altered ADRP/Rab18 ratios are known to reflect varying degrees of steatosis. Further studies such as these will aid in the development of therapeutic targets to decrease steatosis, and thus contribute to the prevention of its progression to alcoholic hepatitis.

0433

DIETARY FATS DIFFERENTIALLY MODULATE FATTY ACID PROFILE AND LIPID METABOLISM IN THE LIVER OF RATS CHRONICALLY FED ALCOHOL

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Alcohol consumption causes fatty liver, and the progression of alcoholic fatty liver has been shown to be halted by dietary saturated fat in comparison with unsaturated fat. The objective of this study was to determine if dietary fats modulate fatty acid profile and lipid metabolism in the liver. Male Sprague Dawley rats were pair-fed with liquid alcohol diets and isocaloric maltose dextrin diet for 8 weeks. The liquid alcohol diets were consisted of either corn oil (enriched in unsaturated fatty acids, USFAs), cocoa butter (enriched in long chain saturated FAs) or medium chain triglycerides (MCT, enriched in medium chain saturated FAs). Alcohol feeding induced significant lipid accumulation in the livers of corn oil group, but only minor lipid accumulation was found in the livers of cocoa butter or MCT group. The concentrations of hepatic triglycerides, cholesterol esters and free fatty acids (FFAs) were significantly higher in corn oil group than that of cocoa butter or MCT group. Analysis of fatty acid profile of the liver total lipids and triglycerides demonstrated that alcohol feeding with corn oil as fat source increased almost all kinds of fatty acyl species in the liver, in particular, the abundant 18C:1, 18C:2, 20C:1 and 20C:4 USFAs. Alcohol feeding with cocoa butter or MCT as fat source increased the saturated FAs, but did not remarkably affect the abundant USFAs in both liver total lipids and triglycerides. The effects of dietary fats on the fatty acid profile of liver phospholipids and FFAs were not remarkable, compared to those of liver total lipids and triglycerides. To determine the mechanism of how alcohol feeding with corn oil causes lipid dyshomeostasis, oxidation of unsaturated fatty acids and the major regulator, peroxisome proliferator-activated receptor α (PPARα), were determined. Hepatic accumulation of PUFAs in corn oil group was associated with a decreased protein level of dodecenoyl-Coenzyme A delta isomerase, a key mitochondrial enzyme involved in beta-oxidation of unsaturated fatty acids. In accordance, the protein levels of PPARα were significantly decreased in corn oil group but not in cocoa butter or MCT group. The plasma fatty acid profile was also affected by dietary fats, but not as remarkable as in the liver. These results demonstrated that alcohol consumption suppresses hepatic oxidation of unsaturated fatty acids, leading to a metabolic switch from fatty acid oxidation to synthesis and accumulation of lipid.

0434

DIETARY SUPPLEMENTATION WITH ZINC ALLEVIATES ETHANOL-INDCUED LIVER INJURY THROUGH PREVENTING GUT LEAKINESS AND ENDOTOXEMIA

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Zinc deficiency has been documented in alcoholic liver disease. The present study was undertaken to determine whether dietary supplementation with zinc provides beneficial effects on ethanol-induced liver injury. Male Sprague Dawley rats were pair-fed the Lieber-DeCarli liquid diets containing ethanol or isocaloric maltose dextrin for 8 weeks. Zinc sulfate was added to the ethanol diet at 60 mg elemental zinc/kg BW. Chronic ethanol feeding caused liver damage as indicated by elevated plasma alanine aminotransferase activities and liver histopathological alterations including lipid accumulation, neutrophil infiltration and hepatocyte necrosis. Dietary supplementation with zinc alleviated ethanol-induced liver damage. Chronic ethanol feeding elevated the plasma endotoxin levels by 2.5-fold, which were normalized by zinc supplementation. In accordance, chronic alcohol exposure significantly increased hepatic expressions of CD14 and LBP, and elevated the mRNA levels of CINC-1 and MCP-1. Dietary supplementation with zinc prevented ethanol-induced endotoxemia and the consequent endotoxin-chemokine signaling in the liver. To define the mechanisms of how zinc prevents endotoxemia, intestinal barrier function was accessed by measuring the mRNA expressions of ileal and colonic major tight junction proteins. Ethanol feeding remarkably decreased the intestinal distributions of Claudin-1, Claudin-5 and ZO-1. Surprisingly, dietary supplementation with zinc dramatically up-regulated the mRNA levels of tight junction proteins. Furthermore, the concentrations of ethanol and acetaldehyde in the intestinal luminal contents were measured by headspace GC/MS. Ethanol feeding elevated both ethanol and acetaldehyde concentrations in the luminal contents. Zinc supplementation did not affect the luminal ethanol concentrations, but attenuated acetaldehyde accumulation in the ileal luminal contents. These results demonstrated that attenuation of gut leakiness and endotoxin signaling in the liver contributes to the protective effects of zinc against alcoholic liver damage. This study suggests that dietary zinc supplementation might be an attractive therapy for alcoholic liver disease.

0435

INHIBITION OF ETHANOL-INDUCED GASTRIC MUCOSAL DAMAGE BY *GYMNEMA SYLVESTRE* IN MALE WISTAR ALBINO RATS: POSSIBLE BIOCHEMICAL CONSEQUENCES

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Gastric mucosa is a likely target of the regular consumption of ethanol The present study was designed to investigate the possible protective effects of *GymnemaSylvestre (G. sylvestre)* leaves aqueous extract against chemically induced gastric mucosal injury.The effects caused by pylorous ligation accumulated gastric acid secretions and ethanol-induced changes in gastric mucus secretions, levels of proteins, nucleic acid, malondialdehyde (MDA) and non-protein sulfhydryl groups (NP-SH) in the stomach wall were investigated in male Wistar albino rats. The gastric ulcers were induced by oral administration of one mL of 80% ethanol. *G. sylvestre* at doses of 100, 200 and 400 mg/kg body weight given orally 60 min before the ethanol provided dose-dependent protection against the damage caused by ethanol administration.*G. sylvestre* pretreatment afforded a significant inhibition of pylorous ligated accumulation of gastric acid secretions. Ethanol administration caused depletion in stomach-wall mucus, total proteins, nucleic acids, and NP-SH concentrations. Pretreatment with *G. sylvestre* showed protection against these depleted levels in a dose-dependent manner. Lipid peroxidation marker, malondialdehyde(MDA), was significantly increased by ethanol ingestion that was inhibited following *G. sylvestre* pretreatments in dose-dependent manner. Ulcer protection in *G. sylvestre* treated rats was confirmed by histopathological screening. *G. sylvestre* leaves extract has a protective effect on chemically induced gastric wall mucosa damage which may be mediated through its effects on mucus production, on non-protein sulfhydryl concentrations, free radical scavenging ability and/or possible cytoprotective properties.

0436

NEURAL CONSEQUENCES OF REPEATED BINGE ALCOHOL EXPOSURE: EFFECTS OF EXERCISE

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This study assessed long-term neural consequences of repeated binge alcohol exposure and potential neurorestorative effects of exercise. Rodent models show that binge alcohol exposure damages the brain, particularly the hippocampus, where it kills cells and inhibits neurogenesis. Because human binge drinking involves repeated intoxication and withdrawal, we examined the long-term effects of a second binge. Exercise promotes brain health and enhances neurogenesis, therefore, the present study investigated whether exercise could mitigate binge-induced suppression of hippocampal neurogenesis.

Adult female Long-Evans rats underwent 0, 1 or 2 binge episodes. Rats in the 1 or 2 binge groups were gavaged with ethanol (25% w/v) in nutritionally complete diet every 8 hours for 4 days. Control animals (the 0 binge groups) received isocaloric control diet. Recent evidence from a rodent model suggests that the hippocampus is undergoing self-repair during the first week following a single binge, so we timed the second binge to begin on day 6 of abstinence, in order to disrupt ongoing neurorestoration. Animals in the exercise groups had access to running wheels 5.5 hours per day, for 28 days, beginning 7 days after the final binge. Rats were sacrificed 35 days after the end of the final binge.

Compared to rats that underwent 1 binge, 2-binge animals took longer to reach peak intoxication levels, and withdrawal symptoms were more severe. For all binge groups, there was a positive correlation between behavioral intoxication and severity of withdrawal symptoms. Prior binge alcohol exposure had no effect on distance run. Stereological analysis of dentate gyrus cells positive for doublecortin (DCX, an early neuronal marker) revealed no effect of a single binge, but a second binge significantly reduced the number of DCX+ cells. As has been previously shown, exercise increased the number of DCX+ cells in control animals. However, there was no increase in DCX+ cells in exercising single binge animals, indicating a binge-induced suppression of the neurogenic effect of exercise. The effect of exercise after a second binge episode on DCX+ cells is currently being investigated.

We conclude that repeated binge alcohol exposure causes a lasting suppression of neuronal differentiation in the hippocampus, and that exercise, which promotes neurogenesis in the alcohol-naïve brain, may have limited ability to do so in the binge-exposed brain.

0437

INFLAMMASOME ACTIVATION MEDIATES IL1-ß INCREASE IN THE BRAIN OF CHRONIC ALCOHOL-FED MICE

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Introduction: Ethanol is known to exert neurodegenerative and neuroinflammatory effects. Interleukin-1 beta (IL-1ß) is an important inflammatory mediator, which is increased in chronic ethanol feeding in liver and brain tissue. Pro-IL-1ß is cleaved by caspase-1 upon activation of the multiprotein inflammasome complex and becomes mature, functionally active IL-1ß.
Aim: We aimed to evaluate the role of inflammasome activation in the brain in chronic ethanol-fed mice.
Methods: C57BL6/J (WT), toll-like receptor-4 (TLR4) and p47phox knock out (KO) mice were fed with Lieber-deCarli (EtOH) or isocaloric diet (PF) for 5 weeks. Microglia activation (Iba1) and astrocyte (GFAP) markers were evaluated by immunohistochemistry. Inflammasome, caspase-1 and IL-1ß mRNAs, IL-1ß protein, caspase-1 activity and endotoxin were measured.
Results: We found microglia activation and astrogliosis in brains of EtOH-fed mice. Messenger-RNA expression of inflammasome components (NALP1, NALP3, NLRC4, ASC, pannexin-1, pro-caspase-1) and IL-1ß was increased in the brain in EtOH- compared to PF-fed mice. Inflammasome activation was evident by increased caspase-1 activity and IL-1ß protein in the brain of EtOH- compared to PF-fed mice. Serum-endotoxin level was increased in EtOH-fed mice compared to PF controls. The TLR4 mediated inflammatory pathway has been implicated to be involved in the alcohol-induced pathophysiology of the liver and brain. The expression of inflammasome components was significantly attenuated in TLR4 KO compared to WT mice upon EtOH feeding however caspase-1 activity and IL-1ß protein levels were comparable betweenTLR4 KO and WT mice. There was no difference in endotoxin levels among PF and EtOH-fed animals in the brain, suggesting other signals for inflammasome activation. Reactive oxygen species have been shown to trigger NALP3 priming and activation. Deficiency of the NADPH oxidase component, p47phox, resulted in significantly decreased NALP3 expression and prevented the ethanol-induced caspase-1 activation although IL-1ß protein levels in the brain were comparable to WT controls.
Conclusion: Our novel findings show upregulation and functional activation of the inflammasome complex in chronic ethanol-fed mouse brains. Our data suggest that TLR4 is involved but it is not the sole mediator of upregulation of inflammasome and ROS production also contributes to inflammasome activation in ethanol-fed mice in the brain.

0438

COMBINED USE OF IBUPROFEN AND ETHANOL INCREASES CELL DEATH IN NEURONAL SH-SY5Y CELLS

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Background: Ibuprofen, a non-selective nonsteroidal anti-inflammatory drug (NSAID), is one of the top 200 over-the-counter (OTC) analgesics prescribed for the treatment of acute pain. Although a few recent studies have shown positive outcomes of NSAID treatment on brain functions, such as Alzheimer's disease, the use/abuse of OTC NSAIDS, when taken with ethanol (E) remains a cause of great concern, because of the possible effects of the two agents together on the liver and kidneys. As of this date, however, no published work has addressed the combined effects of Ibuprofen and E on the brain. Therefore, this study investigated the effect of stepped doses of Ibuprofen (20–300μM), in the absence and presence of low (10mM) and high (88mM) levels of E, in cultured human SH-SY5Y neuronal cells.
Methods: The effects of these two drugs on the cells were assessed visually, using confocal microscopy, and by measurement of their mitochondrial respiration and cell viability, using MTT assays. In addition, cellular oxidative stress levels were determined by fluorometry and confocal microscopy with cells that were labeled with the free radical marker DCFDA. Cell death was analyzed by poly-(ADP-ribose) polymerase (PARP) cleavage, and by release of cytochrome c, detected using Western blotting.
Results: Cells treated either with low or high doses of E, used alone, exhibited no significant change in viability relative to untreated controls. Moreover, very low doses of Ibuprofen, used alone, had no effect on cell survival in culture. However, as expected, cells treated at higher ibuprofen concentrations showed significant dose-dependent loss in cell viability, with 100μM ibuprofen causing death of 40% of the cells. Interestingly, when E was also present, dramatic increase in PARP cleavage and cytochrome c release also occurred.
Conclusion: These results show that Ibuprofen alone, at concentrations of 100μM or higher, kills cultured neuronal cells. However, a combined treatment with high concentrations of Ibuprofen and E causes significantly more cell damage and death. These results suggest that use of Ibuprofen soon after heavy E consumption, e.g. for headache relief for hangovers, may damage the brain.

0439

CHRONIC BINGE ALCOHOL DIFFERENTIALLY MODULATES BRAIN GENE EXPRESSION IN SIV-INFECTED MACAQUES; PRELIMINARY COMPARISON WITH HIV+ & HIV ENCEPHALITIS

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The persistence of human immunodeficiency virus (HIV) encephalitis (HIVE) in spite of antiretroviral therapy underscores the importance of continued research focused on the neurobiology of HIV. Alcohol use disorders have been reported in as many as 41% of HIV-infected patients. Previous studies using a non-human primate model of chronic binge alcohol (CBA) and simian immunodeficiency virus (SIV) infection showed greater behavioral deficits in CBA/SIV than either CBA or SIV alone. The underlying molecular mechanisms involved in CBA/SIV accentuated neurobehavioral dysfunction and their relevance to HIVE development remain to be determined. We determined and contrasted the gene expression profile of brains (n=2–3/group) obtained at necropsy from CBA and isocaloric sucrose control SIV+ and SIV- rhesus macaques with that obtained from brains of HIV-, HIV+, and HIVE. The control group was used as reference for the analysis (sucrose/SIV- for the rhesus and HIV- brain for the human study). Based on the differential gene expression, the ratio between the groups (SIV/CBA vs.SIV and HIVE vs. HIV) was obtained. Using the ''Compare experiments'' algorithm in GeneGo 1710 common genes were found between HIVE and CBA/SIV profiles. Further analysis revealed the list of pathways and networks in which those genes participate. The most significant pathways included those associated with oxidative phosphorylation, translation & regulation of translation initiation, cell cycle regulation, antigen presentation by MHC class I, spindle assembly & chromosome separation, and cytoskeletal remodeling. Expression of 427 genes was preferentially upregulated in the CBA/SIV, and 166 genes were preferentially upregulated in HIVE. Further analysis revealed these genes to be preferentially involved in immune response, development, cytoskeleton remodeling, and regulation of lipid metabolism. These results indicate the relevance of the SIV model to HIV neurobiological studies. Furthermore, they indicate the strong similarity between mechanisms affected by CBA and those that are eventually disrupted in HIVE. The genes included in the most relevant pathways identify further areas of needed research. Supported by AA-09803, MH 079751, AA-07577, AA-11290

0440

SHORT TERM ETHANOL EXPOSURE INDUCES CALPAIN DEPENDENT A-SPECTRIN PROTEOLYSIS AND NEURODEGENERATION IN THE HIPPOCAMPUS

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The calpain family of cysteine proteases is crucial to the initiation, regulation and execution of cell death and is implicated in neurodegenerative states such as stroke and traumatic brain injury. The present studies examined accumulation of the calpain-dependent 145kDa α-spectrin breakdown product (SBDP) and changes in the neuronal markers NeuN, MAP-2, and propidium iodide (PI) following 1, 3 or 5 days of binge-like exposure to EtOH (50 mM) in organotypic hippocampal slice cultures. Western blot analysis demonstrates time-dependent accumulation of the 145kDa SBDP in homogenized hippocampal tissue with significance observed after 5 days of EtOH exposure. Uptake of the non-vital marker PI was increased in the pyramidal cell layers of the CA1 and CA3 and the granule cell layer of the DG of the hippocampus following 1 day of exposure to EtOH, with increases evident in the granule cell layer on day 3 as well. Immunoreactivity (IR) of MAP-2, a known calpain substrate, showed time-dependent decreases in each subregion, while NeuN IR was significantly reduced in all subregions after 5 days of EtOH exposure. These data suggest the activation of calpains with prolonged exposure to binge-like EtOH concentrations and the associated development of neurodegeneration within the hippocampus. In sum, the calpain family of cysteine proteases may represent a novel therapeutic target for the treatment of ethanol abuse disorders. Supported by NIAAA.

0441

IS THE PRESENCE OF ALZHEIMER TYPE II ASTROCYTES A CONFOUNDING FACTOR FOR HUMAN POSTMORTEM BRAIN TISSUE QUALITY?

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A previous study by the NSW Tissue Resource Centre (NSWTRC) showed the presence of cirrhosis of the liver and more so, hepatic encephalopathy (HE), adversely affects the integrity of postmortem brain tissue. The aim of this study was to devise a rating scale to assess the severity of Alzheimer type II astrocytosis, the pathological hallmark of HE, and to examine the effect of these ratings on brain pH and RNA integrity.
Method: Fifty cases with a history of substance abuse of alcohol were obtained from the NSWTRC. Paraffin embedded blocks of frontal cortex, caudate, putamen and pons were sectioned at 7μm and stained with hematoxylin and eosin. The presence of Alzheimer type II astrocytes were assessed and rated as follows: nil; mild where Alzheimer type II astrocytes were present in one or more fields examined, but not in all fields; moderate: two to three Alzheimer type II astrocytes were found in each field; and severe: the majority of astrocytes showed Alzheimer type II change. Inter-rater reliability was performed on 5 cases. Brain pH and RNA integrity were measured using the standard protocols of the NSWTRC.
Results: Inter-rater reliability was 85% (17/20 sections). The brain pH mean (± SD) for those with nil Alzheimer type II astrocytes was 6.58 (± 0.26), mild 6.40 (± 0.32), moderate 6.30 (± 0.28) and severe 6.15 (± 0.21). There was a significant difference between the group of mild, moderate and severe groups when compared to those with no Alzheimer type II astrocytes; p = 0.047, p = 0.046 and p = 0.042, respectively. The brain RIN mean (± SD) for nil was 7.42 (± 2.05), mild 6.89 (± 0.96), moderate 6.78 (± 0.73) and severe 6.70 (± 1.84). There was no significant difference in RIN between groups.
Conclusion: The increasing severity of Alzheimer type II astrocytes correlates with a decrease in brain pH but not RIN.

0442

THE EFFECTS OF CHRONIC ALCOHOLISM ON PROLIFERATION IN THE HUMAN SUBVENTRICULAR ZONE

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Proliferation continues in the adult mammalian subventricular zone (SVZ) throughout life. SVZ-derived neuroblasts migrate to the olfactory bulb (OB) where the majority of survivors become integrated as interneurons in the granule cell layer (GCL). The functions of these interneurons are unknown but they are thought to contribute to odor discrimination. Chronic alcoholism results in focal neurodegeneration that manifests clinically as cognitive dysfunction and hyposmia. Rodent models have shown that the deleterious effect of chronic alcohol intoxication on neurogenesis contributes to neurodegeneration but no studies have been carried out in humans. Using postmortem brain tissue from the NSW Tissue Resource Centre we compared mitotic events in the SVZ of a well-characterized cohort of 20 chronic alcoholics and 20 age- and gender-matched controls. There was no difference in the number of proliferating cell nuclear antigen (PCNA)-immunopositive cells between alcoholics (mean +/− SD = 4104 +/− 3992 cells/mm^3) and controls (4379 +/− 2655 cells/mm^3, p = 0.66) in the SVZ. We then investigated PCNA immunoreactivity in the OB of a subset of six alcoholics and eight controls. Again there was no difference in PCNA-positive cells in the GCL of alcoholics (197.4 +/− 65.4 cells/mm^3) or controls (405.1 +/− 184.3 cells/mm^3, p = 0.06), but there was a 25% decrease in granule cell numbers in alcoholics (285272 +/− 49051 cells/mm^3 versus 382508 +/− 59290 cells/mm^3, p = 0.007). Granule cells were also inversely correlated with both lifetime (r^2 = 0.34, p = 0.04) and peak daily (r^2 = 0.29, p = 0.04) alcohol consumption. Our findings suggest that chronic alcohol consumption does not affect proliferation in the human SVZ or OB but that OB granule cells are particularly susceptible to the neurotoxic effects of alcohol. The latter may account for the deficits in odor discrimination seen in chronic alcoholics.

0443

HIPPOCAMPAL CELL DEATH AND ASTROCYTE ACTIVATION OBSERVED IN FEMALES BUT NOT MALES FOLLOWING CHRONIC ETHANOL EXPOSURE

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Chronic alcoholism is known to produce lasting changes in brain structure and function. It is proposed that changes in gene expression and are fundamental to the high rate of relapse in recovering alcoholics. We are interested in the role played by genetic factors and gender (biological sex) in the changes caused by chronic ethanol (EtOH) exposure, and have used a genetic model of high withdrawal severity (Withdrawal Seizure Prone, WSP) and low withdrawal severity (Withdrawal Seizure Resistant, WSR) to elucidate the interplay of genetics and sex in the response to alcohol. Male and female WSP and WSR mice were chronically exposed to 72hr of vapor EtOH. Following 5d of withdrawal from EtOH, mice were perfused and brains collected for histological analysis. Changes in the hippocampus (HIP) were evaluated given that the HIP is a target in alcoholics and important in both reward and seizure circuitry. Using H&E staining techniques, we identified dead or dying cells based on their eosinophillic nature and shrunken cell bodies. The total numbers of dead cells were counted using stereology and a thresholding method. For each animal, at least 4 separate sections were counted to determine an average number of dead cells. Our analysis shows increased dead cell counts in the HIP of female WSP at 5d of withdrawal from chronic ethanol exposure ($p<0.05$; n=5–12). In contrast, no significant changes were detected in males of either selected line (n=7–11). Given our previous analysis of gene expression changes which identified astrocytes as a target of chronic EtOH, we also evaluated potential astrocyte activation in the HIP using GFAP immunohistochemistry. Notably, significant increases in GFAP expression were again observed in WSP females ($p<0.05$; n=7–15), with no significant changes in males of either line (n=10–15). The same observation was made in B6D2F2 mice, with females showing significant increases in GFAP expression but no significant changes in the males. These findings are in agreement with our previous analysis in the parietal cortex at 10d of withdrawal and with microarray analyses during peak withdrawal (8hr) showing cell death/apoptosis signaling pathways were targeted in females but not males in WSP and WSR mice. Collectively, these findings support the hypothesis that sex is a more important factor than genetic background during the early stages of withdrawal and that sex-specific astrocyte activation after withdrawal may play a role in neurotoxicity.

0444

SEX DIFFERENCES IN ASTROCYTE FUNCTIONALITY DURING CHRONIC ETHANOL EXPOSURE AND WITHDRAWAL WOULD MAKE FEMALES MORE VULNERABLE TO BRAIN DAMAGE

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Chronic alcohol abuse is associated with brain damage in a sex-specific fashion. We have characterized the influence of biological sex on the effects of chronic ethanol (EtOH) exposure and withdrawal, and have previously published analysis that revealed a strong contribution of sex to the transcriptional response in the prefrontal cortex. Significantly regulated transcripts included many genes that are predominantly or exclusively expressed in astrocytes, suggesting that a strong component of the neuroadapative response in the brain reflects changes in astrocyte gene expression. To better characterize the contribution of astrocytes, genetically non-identical B6D2F2 males and females were chronically exposed to EtOH and withdrawn for 5 days. *In vivo* analyses from brain slices used GFAP immunohistochemistry as a marker of activated astrocytes, while H&E staining was used to identify dead cells. In hippocampus, males had a significant decrease in dead cells after withdrawal ($p<0.05$) while females showed a trend for an increase in dead cells, similar to our previous findings in prefrontal cortex and other genetic backgrounds. In addition, females had significantly elevated numbers of activated astrocytes after withdrawal ($p<0.05$), which was not seen in males. Given this result, an *ex vivo* primary astrocyte culture model using male vs. female pups was used to characterize the direct effects of chronic EtOH exposure (100mM) for 4 days, followed by withdrawal for 5 days with qPCR gene expression and biochemical analyses. Chronic exposure in male cultures resulted in significantly increased glutamate transporter expression (both *Eaat1* and *Eaat2;* $p<0.05$) compared to control cultures, while females showed no significant difference. Glutamate uptake was also determined. By 2-way ANOVA, male cultures showed more robust glutamate uptake than females during EtOH exposure (main effect of sex ($F(1,43) = 5.10$; $p=0.029$)). While there were no changes in cell viability (MTT) in either male or female cultures, both sexes showed a 70% reduction in lactate dehydrogenase activity during EtOH exposure ($p<0.001$), indicating that EtOH exposure modulates cellular energy status. There were few changes in any marker after withdrawal. These results suggest that males may be less vulnerable to EtOH insult than females because of an increased ability of male astrocytes to remove glutamate *in vivo*, and thus less glutamatergic excitotoxic brain damage.

0445

ADOLESCENT INTERMITTENT BINGE ETHANOL ALTERS NEURONAL ACTIVATION BY ETHANOL IN THE CEREBRAL CORTEX OF ADULT RAT BRAIN

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Binge drinking is common in adolescent humans. The current study examined the effect of adolescent intermittent binge ethanol (AIE; 2 days alcohol-5 g/kg, i.g., 2 days off; P25–P55) compared with water controls on neuronal activity marker c-Fos in adult (P80) rat brain. Male Wistar rats were bred and reared in our vivarium. On the day following birth (P1), litters were culled to 10 pups. At weaning on P21, male offspring were weight matched and pair-housed. The challenged water or ethanol (2 or 4 g/kg, i.g.) neuronal activation was determined using c-Fos immunohistochemistry (IHC) 2 hours after challenge. There were no significant differences on the basal expression of c-Fos+IHC in the cortical regions of interest. In control adults (P80), both challenge doses of ethanol (2 g/kg and 4 g/kg, i.g.) increased c-Fos expression in the orbitofrontal (OFC, 205% $p<0.01$ and 342% $p<0.001$), infralimbic (IL, 100% $p<0.01$ and 103% $p<0.01$), prelimbic (PrL, 183% $p<0.001$ and 247% $p<0.001$), piriform (Pir, 67% $p<0.05$ and 78% $p<0.01$), cingulate area 1 (Cg1, 74% $p<0.05$ and 87% $p<0.05$), cingulate area 2 (Cg2, 68% $p<0.05$ and 67% $p<0.05$), secondary motor (M2, 78% and 155% $p<0.001$), ectorhinal (Ect, 232% $p<0.001$ and 316% $p<0.001$) and perirhinal (PRh, 105% $p<0.05$ and 176% $p<0.001$) cortex. AIE treated adults (P80-25 days after AIE) showed a different ethanol challenge response. In AIE groups, ethanol-induced c-Fos was reduced in OFC (44 and 56%, $p<0.05$ or 0.001), PrL (38 and 47%, $p<0.05$ or 0.001) with 2 and 4 g/kg Ethanol doses respectively. Similarly, the increase in c-Fos expression with high dose ethanol (4.0 g/kg) was decreased in AIE animals in IL ($p<0.05$), Pir ($p<0.01$), Ect ($p<0.05$) and PRh ($p<0.05$) cortex. However, ethanol-induced c-Fos expression was not affected by AIE in Cg1, Cg2 and M2 areas. The results of co-labeled c-Fos and Tbr1 showed that c-Fos cells of around 45% in IL and PrL expressed $Tbr1^+$ in adult controls. Ethanol challenge increased the co-labeled cells in IL and PrL of adult brain, and the increases were reduced in AIE. These finding has indicated that adolescent intermittent binge ethanol alters the cell functioning of the cerebral cortex in adult rat brain, and decreases activity in brain behavioral control regions. However, there are the different impacts on different functional subregions of the cortex. Further, the different types of neuron in the cortex for producing c-Fos protein will be investigated. (Supported by the NADIA from NIAAA).

0446

MECHANISMS OF ALCOHOL-INDUCED THIAMINE DEFICIENCY IN BRAIN PATHOGENESIS: THERAPEUTIC ROLE OF ACETYL-L-CARNITINE

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Background: Thiamine (vitamin B1), an essential micronutrient plays a pivotal role for the conversion of glycolytic end-product pyruvate to acetyl coenzyme A. Thiamine deficiency causes neuropathy known as the Wernicke-Korsakoff syndrome in chronic alcoholism. Our goal is to understand the mechanisms of alcohol-induced thiamine deficiency in the brain and to prevent this associated neurotoxicity by acetyl-l-carnitine (ALC) therapy.
Methods: We determined the uptake and distribution H^3-thiamine in most internal tissues (intestine to brain) in animal model of thiamine deficient diet (TDD) intake with/without ethanol. Alterations in the expression of thiamine transporter protein-1 (THTR-1) and THTR-2 validated the changes in H^3-thiamine distribution in these organs. We also analyzed the effects of alcohol on thiamine pyrophosphokinase (TPK), thiamine-pyrophosphate (TPP), and pyruvate dehydrogenase (PDH) in TDD-induced brain pathogenesis.
Results: Feeding of TDD diets developed atrophy, foot-drop, and impaired body coordination with ultimate death within 6 weeks. Combination of TDD and 4% ethanol liquid diets exacerbated the symptoms and reduced the life span to 4 wks. Supplementation of acetyl-L-carnitine (ALC, 1 mg/mL liquid diets) in TDD or TDD+ethanol diets delayed the onset of symptoms and life span to 9–11 weeks. Alcohol intake diminished the uptake of thiamine by intestine, livers, kidneys, heart and brain. Thus, thiamine depletion in alcoholic brain appeared to result from inhibition of thiamine transport in intestine/brain endothelium and accumulation of thiamine in the livers during chronic alcohol intake. Blockade of thiamine uptake by intestine/brain tissues in alcohol intake was validated by reduction of THTR-1 and THTR-2 protein compared with pair fed controls. As expected, the uptake of thiamine was significantly increased in the intestine and brain tissues of TDD animals, suggesting that THTR-1/THTR-2 was not impaired in the absence of alcohol. We also uncovered the mechanism of thiamine-associated neuropathy in alcoholism. Alcohol interfered the synthesis of TPP (a co-factor for PDH) by impairing TPK; thereby PDH was unable to convert pyruvate to acetyl co-enzyme A effectively for bio-fuel production in the brain.
Conclusion: We provide the underlying tissue organ, pharmacological, and biochemical mechanisms of alcohol-related neuropathy as well as therapeutic circumvention for improvement of neurological complications in alcohol abusers.

0447

ENDOPLASMIC RETICULUM-TARGETTED BCL-2 RESCUES SH-SY5Y NEUROBLASTOMA CELLS FROM ETHANOL TOXICITY.

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Ethanol is a well-documented inducer of apoptosis, though the precise cellular mechanism of its toxicity remains unknown. It has recently been demonstrated that endoplasmic reticulum (ER) –localized Bcl-2 is involved in regulating ethanol-induced apoptosis in immortalized CHO695 cells, a non-neuronal hamster cell line. The present study sought to investigate Bcl-2 mediated rescue from ethanol in a more relevant cell line, namely SH-SY5Y human neuroblastoma cells. Ethanol responsiveness of SH-SY5Y cells was first determined. SH-SY5Y cells were cultured in the presence of varying concentrations of ethanol for 24 hours. MTT cell viability assay was performed to quantify surviving cells. Similarly to published studies in CHO cells, relatively high concentrations of ethanol were required to kill this immortalized cell line. A linear ethanol dose response was found, with a 20% reduction in cell viability at 500 mM ethanol, 40% at 750 mM and 80% at 1000 mM. After determining ethanol sensitivity, we next sought to investigate rescue from ethanol toxicity by wildtype Bcl-2, mitochondria-targeted Bcl-2 and ER-targeted Bcl-2. SH-SY5Y cells were cultured for 24 hours then transfected with cDNA constructs encoding GFP-tagged wildtype or organelle-localized Bcl-2. Localization was verified by fluorescence microscopy. Cells were then treated with varying concentrations of ethanol for 24 hours, followed by MTT assay. Overexpression of ER-targeted Bcl-2 rescued SH-SY5Y cells from ethanol at higher rates than wildtype or mitochondria-targeted Bcl-2, even at the highest concentration tested. Indeed, cells treated with 1000 mM ethanol showed only a 20% reduction in cell viability when ER-Bcl-2 was overexpressed, compared with a 40% reduction for wildtype Bcl-2, a 70% reduction for mitochondrial Bcl-2 and an 80% reduction for controls. In conclusion, the present study shows that SH-SY5Y cells are rescued by ER-targeted Bcl-2 much like hamster cells and sets the stage for further investigation of ER-dependent ethanol toxicity mechanisms in a more relevant human neuroblastoma cell line.

0448

SIGNAL OR NOISE? NON-PHASE-LOCKED THETA EVENT-RELATED OSCILLATIONS DISCRIMINATE LONG-TERM ABSTINENT ALCOHOLICS FROM CONTROLS

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Decades of research searching for event-related potential (ERP)-based biological markers for alcoholism have focused on measures extracted from averaged ERP data (i.e, data averaged across trials so that the phase-locked activity is accentuated and the background, non-phase-locked, ''noise'' is averaged out). There is overwhelming evidence that reduced amplitudes of the P3b ERP complex is reduced in individuals with a genetic vulnerability to alcoholism (and other externalizing disorders). This phenomenon can be looked at either in the time domain (e.g. the P300) or in the frequency domain where it appears as a reduction in delta and theta oscillations in the P300 time window of the evoked response. Recently, we have shown that there may be important alcohol-related information contained in the non-phase-locked EROs (called induced EROs, in contrast to evoked EROs), i.e. that there may be an important signal in the data which has previously been discarded as noise. Results from our lab in California indicated that event-related theta band synchronization (ERS; an increase in non-phase-locked ERO power relative to a pre-stimulus baseline period) is larger in long-term abstinent alcoholics (LTAA) than age and gender comparable controls, and that this effect is independent of the endophenotypic effect seen in the evoked (i.e., time-locked) data. The present study examined these phenomena in new age- and gender comparable LTAA and control samples in Hawaii. The evoked response to target stimuli was reduced in LTAA relative to controls, and this effect was present whether it was examined in the time or frequency domain. Theta ERS was significantly higher in LTAA than controls, and this effect was independent of the effect on the evoked (i.e., time-locked, averaged) response. The results replicate our earlier findings, showing that theta ERS is sensitive to alcoholism-related variance, and that this effect is independent from and opposite in direction to that of the evoked ERP/ERO measures (LTAA's induced theta power was *increased* in LTAA vs. controls, while P3b amplitude and evoked theta are both *reduced* in LTAA vs. controls). The event-related activity that was most sensitive to alcoholism-related variance in the ERP – the induced theta activity – was part of what is typically considered noise in ERP studies. Future studies will address whether this induced theta effect reflects an index of genetic vulnerability or if it is an effect of alcohol abuse itself.

6. FETAL ALCOHOL SYNDROME / DEVELOPMENT
a. Cell Biology **127–142/449–464**

0449

COMPONENTS OF THE BMP SIGNALING PATHWAY INTERACT WITH ETHANOL, PERTURBING PROPER EMBRYONIC JAW DEVELOPMENT IN ZEBRAFISH
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Fetal Alcohol Spectrum Disorders (FASD) describe a myriad of ethanol-induced developmental defects, including lower jaw hypoplasia. Cranial neural crest cells generate the majority of the craniofacial skeleton, including the lower jaw. Complex interactions between neural crest cells and epithelia, notably endoderm and oral ectoderm, are essential for craniofacial morphogenesis. These interactions are orchestrated by several signaling pathways, including the Bone Morphogenic Protein (Bmp) pathway. Because evidence suggests a genetic component to FASD, these pathway members are promising candidates for genes that interact with ethanol. In a zebrafish genetic screen, we identified synergistic gene-ethanol interactions in members of the Bmp signaling pathway. While *bmp2b* homozygous mutant embryos die before our analyses occur, *bmp2b* heterozygous embryos and *bmp4* homozygous mutant embryos (together termed Bmp-pathway mutants) undergo normal craniofacial development. However, when exposed to tissue levels of approximately 0.1% ethanol from 10–24 hours post fertilization (hpf), Bmp-pathway mutants display defects to the embryonic lower jaw. Knock down of Bmp signaling at 14 hpf via a dominant-negative Bmp receptor recapitulates these ethanol-induced lower jaw defects, indicating that ethanol perturbs Bmp signaling. Analysis of Bmp activity through a Bmp response transgenic line demonstrates that from 10–18 hpf the endoderm receives Bmp signaling, suggesting that Bmp signals directly to the endoderm. Mutation of the sphingosine receptor, *s1pr2,* causes strikingly similar lower jaw defects to those observed in ethanol-treated Bmp-pathway mutants. Lower jaw defects in *s1pr2* mutants are due to disrupted morphogenesis of the anterior pharyngeal endoderm. These data suggest a model where Bmp pathway members synergistically interact with ethanol, perturbing endoderm morphogenesis through an *s1pr2*-dependent mechanism. Overall, this work will provide greater insight into the gene-ethanol interactions that lead to the variability of craniofacial defects in FASD and will allow for better diagnosis and treatment.

0450

IMPAIRMENT OF ALVEOLAR MACROPHAGE MIGRATION IN FETAL ALCOHOL EXPOSURE: AN IN VITRO MODEL
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Alcohol-related birth defects are present in approximately 1% of all US births, and fetal alcohol exposure has been well defined as a contributor to neonatal lung injury and infection. This pathology is thought to be modulated in large part by the alveolar macrophage (AM). The AM defends the lung against foreign particles and infection by initiating an immune response–through chemotaxis and phagocytosis–and by regulating the subsequent inflammatory reaction. While it has been shown that phagocytic functions of the AM are impaired by ethanol (ETOH) exposure, its effects on AM chemotaxis are relatively unexplored. Therefore, we hypothesize that ETOH exposure compromises AM migration, a key factor in the immune response of the neonatal lung.

To mimic chronic ETOH exposure, rat AMs were placed in modular chambers and incubated for 4 days with 0.08% ETOH. Control cells were similarly incubated without ETOH. After four days of exposure, cells were seeded onto the apical surface of transwell chambers with chemoattractant added to the bottom chamber. After four hours, cells that had successfully migrated across the transwell membrane were fixed in formalin and their nuclei were stained. Cells were counted and quantified as number of cells per high-powered field (expressed as mean ± SEM).

After four days of exposure to ETOH, AM migration toward the chemoattractant was decreased by approximately 50% as compared to control (Control: 9.2 ± 2.0 cells/hpf vs. ETOH: 4.4 ± 0.5 cells). Preliminary results suggest that ETOH exposure impairs AM chemotaxis. This data augments previous studies of macrophage function by suggesting that, in the setting of chronic ETOH exposure, the immune response is first compromised by the decreased ability of the AM to migrate toward the invading agent. Further studies will focus on elucidating the mechanisms of this impaired function.

0451

BRAIN-DERIVED NEUROTROPHIC FACTOR DECREASES ETHANOL-INDUCED OXIDATIVE STRESS AND APOPTOSIS IN HYPOTHALAMIC NEURONS: ROLE OF MICROGLIA
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We have previously shown that ethanol exposure during early life causes a long-term structural and functional deficiency of hypothalamic neurons, including beta-endorphin neurons due to apoptotic death. However, the mechanism by which ethanol activates the death pathway is not well understood. Because ethanol is known to cause oxidative stress and since oxidative injury is known to result in microglia-mediated inflammation, we hypothesize that inflammatory molecules from microglia might be involved in the ethanol-induced death of developing neurons. We also postulate that ethanol's suppression of cAMP production reduces the availability of neurotrophic factors that causes oxidant/antioxidant imbalance and activation of microglia. Hence, we hypothesize that activation of this cell signaling molecule via brain-derived neurotrophic factor (BDNF) will prevent ethanol-induced oxidant/antioxidant imbalance and the neurotoxic action. We show here that ethanol decreases production of BDNF from neurons. Addition of BDNF in cultures suppressed ethanol ability to induce apoptotic death of neurons. Furthermore, BDNF decreases the intracellular free radicals (ROS and O2) and the nitrite levels and increased the antioxidant status in cultured hypothalamic neuronal cells, exposed to ethanol-activated microglia media. These data suggest that BDNF inhibits both apoptosis and oxidative status caused by ethanol-activated microglia in cultured fetal hypothalamic neuronal cell. (Supported by NIH grant R37 AA08757).

0452

EFFECTS OF NMDA AND GLUTAMIC ACID ON ETHANOL'S NEUROTOXIC ACTION ON HYPOTHALAMIC NEURONS: ROLE OF MICROGLIA-ACTIVATED OXIDATIVE STRESS
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Induction of apoptosis by ethanol has been implicated in the complications related to fetal alcohol syndrome and in ethanol-induced brain injury. Oxidative stress plays a role in the mechanisms of ethanol's neuronal toxicity. Studies have shown that the cellular redox state has a role in cell death. In the brain, ethanol can produce oxidative stress by direct and indirect mechanisms and may cause the changes of antioxidant pathway such as GSH. We have previously shown that ethanol activates oxidative stress and apoptosis in developing hypothalamic neurons. Although NMDA and glutamic acid are known to play roles in neurodevelopment, it is not known whether these neurotransmitters control ethanol-induced oxidative stress and apoptosis in developing hypothalamic neurons. We show here that both NMDA and glutamic acid increase apoptotic cell death and the production of the cellular level of free oxygen. These treatments also decrease the ethanol-altered cellular level of glutathione. The receptor blocker MK-801 antagonized all effects of NMDA and glutamic acid. Furthermore, we provide evidence that the effects of NMDA and Glutamic acid in potentiating ethanol's neurotoxic action are partly mediated by microglia. This is the first demonstration that both NMDA and glutamic acid play roles in controlling ethanol's neurotoxicity, by increasing microglia-mediated oxidative status of developing neurons. (Supported by NIH grant R37 AA08757)

0453

ROLE OF INFLAMMATORY AND OXIDATIVE PROCESSES IN ETHANOL-INDUCED NEURONAL DEATH IN THE HYPOTHALAMUS DURING THE DEVELOPMENTAL PERIOD

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Fetal alcohol exposure has many detrimental effects on the developing fetus and has been known to cause many diseases and disorders such as fetal alcohol syndrome and fetal alcohol spectrum disorder. Ethanol has been shown to have a direct toxic effect on neurons; however glia cells have also been implicated in the damaging effect of ethanol in the CNS during neonatal ethanol exposure. Using the postnatal rat model, which is equivalent to the third human trimester, we have previously shown that ethanol causes apoptotic cell death of beta-endorphin neurons of the hypothalamus and this neurotoxic effect increases with prolonged ethanol exposure. In order to better understand the mechanism by which alcohol induces neuronal death, we studied the role of neuro-inflammation and oxidative process using the prenatal model of alcohol feeding. Newborn offspring was fed with ethanol containing milk formula (AF) and control milk formula (PF) during postnatal day 2 to 7. Arcuate tissue samples were obtained at 2 days interval between days 2 to 7. The levels of inflammatory cytokines and total antioxidant capacity were measured by ELISAs. Activated microglia were identified by immunofluorescence staining for IBA1. We show that ethanol exposure increases proinflammatory cytokines in the early days of exposure, which correlates with an increase in microglia activation. Prolonged ethanol exposure lead to increase in total microglia number and activation, and an imbalance between total antioxidant capacity and total ROS, suggesting that inflammatory environment induced caused by microglia activation may lead to abnormalities in oxidative status and cell death in the hypothalamus. This data suggest that inflammatory signals and oxidative process might mediate the neurotoxic action of ethanol in the arcuate nucleus. (Supported by NIH grant R37 AA08757).

0454

NRF2-MEDIATED ANTIOXIDANT RESPONSE IS A MAJOR DETERMINANT OF SUSCEPTIBILITY OF NEURAL CREST CELLS TO ETHANOL-INDUCED APOPTOSIS

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Nuclear factor erythroid 2-related factor (Nrf2) is a transcription factor that up-regulates a diverse array of antioxidant genes and protects cells from oxidative damage. Previous studies have shown that ethanol exposure induces apoptosis in neural crest cells (NCCs), an ethanol-sensitive cell population implicated in Fetal Alcohol Spectrum Disorders (FASD) and that Nrf2 signaling is involved in induction of an antioxidant response in ethanol-exposed NCCs and mouse embryos. The current study is designed to determine whether Nrf2-mediated antioxidant response is a major determinant of susceptibility to ethanol-induced apoptosis in NCCs. For this purpose, we tested whether down-regulation of Nrf2 increases the sensitivity of NCCs to ethanol-induced apoptosis and whether up-regulation of Nrf2 enhances the resistance of NCCs to ethanol-induced apoptosis. We found that the knockdown of Nrf2 by siRNA significantly decreased Nrf2 protein levels and the expression of antioxidant proteins, SOD1 and catalase, in control and ethanol-exposed NCCs, accompanying by an increased ROS generation and apoptosis in NCCs exposed to ethanol. In contrast, pretreatment with an Nrf2 inducer, D-L-Sulforaphane (SFN), significantly increased the Nrf2 protein levels and the expression and activities of antioxidant enzymes. SFN pretreatment also resulted in significant decreases in ROS generation and apoptosis in ethanol-exposed NCCs. Notably, SFN pretreatment provided no protection against ethanol-induced oxidative stress and apoptosis in ethanol-exposed NCCs in which Nrf2 was knocked down by siRNA, indicating that the protection of SFN against ethanol-induced oxidative stress and cell damage is mediated by Nrf2 signaling. These findings confirm the protective role of Nrf2 signaling in ethanol-induced oxidative damage in embryonic cells and demonstrate that Nrf2-mediated antioxidant response is a major determinant of susceptibility of NCCs to ethanol-induced oxidative stress and apoptosis.
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0455

MICROINJECTION OF MICRORNA-125B MIMIC INTO CULTURED MOUSE EMBRYOS PREVENTS ETHANOL-INDUCED APOPTOSIS AND EMBRYOTOXICITY

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MicroRNAs (miRNAs) are a recently discovered class of small non-coding RNA that has been implicated in regulation of a broad range of cellular and physiologic processes, including apoptosis. The objective of this study is to test the hypothesis that microRNA-125b (miR-125b) modulates ethanol-induced apoptosis in neural crest cells (NCCs) by the regulation of p53 and Bcl2 signaling pathways and that overexpression of miR-125b can prevent ethanol-induced embryotoxicity. We found that treatment with 50 or 100 mM ethanol for 24 hours resulted in a significant decrease in miR-125b expression in NCCs. Exposure of mouse embryos to ethanol *in vivo* or in whole embryo culture also significantly decreased miR-125b expression. In addition, we found that overexpression of miR-125b in NCCs by transfection with miR-125b mimic significantly reduced ethanol-induced caspase-3 activation and apoptosis, whereas miR-125b inhibitor increased caspase-3 activation and apoptosis in ethanol-exposed cells, indicating that miR-125b can diminish ethanol-induced apoptosis in NCCs. Using three algorithms for miRNA target prediction, we found that Bcl-2-modifying factor (Bmf), Bcl-2 antagonist killer 1 (Bak1) and p53-upregulated modulator of apoptosis (PUMA) are the direct targets of miR-125b. The binding of miR-125b to the 3'-UTRs of Bmf, Bak1 and PUMA mRNA has also been validated in NCCs using luciferase reporter assay. Notably, overexpression of miR-125b significantly reduced ethanol-induced increase in Bak1 protein expression in NCCs. To determine the role of miR-125b in preventing ethanol-induced apoptosis and embryotoxicity, miR-125b mimic was microinjected into cultured mouse embryos. Microinjection of miR-125b mimic resulted in a significant increase in miR-125b expression in mouse embryos. Overexpression of miR-125b resulted in a significant reduction in the Bak1 protein expression in ethanol-exposed mouse embryos. In addition, overexpression of miR-125b significantly reduced ethanol-induced caspase-3 activation and diminished ethanol-induced growth retardation in cultured mouse embryos. This is the first demonstration that miR-125b can prevent ethanol-induced apoptosis and that microinjection of miRNA mimic can prevent ethanol-induced embryotoxicity. These findings suggest an avenue for the development of novel strategy for the prevention of human Fetal Alcohol Spectrum Disorders (FASD) based on the regulation of miRNA.
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0456

UNDERSTANDING THE EFFECTS OF HYPOXIA IN COMBINATION WITH ETHANOL WITHDRAWAL *IN VITRO*

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Exposure to ethanol (ETOH) and oxygen deprivation during development can result in a variety of adverse outcomes for a fetus. Our lab has previously shown that hypoxia related cell death is enhanced in hippocampal slices that have been exposed to ETOH. The multiplicative damage observed following ethanol withdrawal (EWD) in combination hypoxia may be a result of the similar excitotoxic mechanisms that underlie these two insults. To better understand the characteristics of the cellular damage, two experiments were run using hippocampal slices taken from postnatal day (PND) 8 rat pups. The first experiment investigated the time course of damage over 24 hours following EWD and hypoxia (oxygen glucose deprivation (OGD)) and the 2nd experiment investigated the effects of these insults on neuronal survival using immunohistochemistry. Slices were exposed to 100mM ETOH or control culture media for 10 days. Slices then received OGD treatment or control (air) for 30 min. In Exp 1, propidium iodide (PI) uptake (a non-specific marker of cell damage) was analyzed every 4 hours for 24 hours following OGD treatment. In Exp 2, the neuronal nuclear protein (NeuN) was used to assess neuronal viability. EWD/OGD exposed slices showed a steady increase in PI uptake, relative to controls and EWD or OGD alone slices, from the 4 to 16 hour time point following treatment in the CA1. There was no interactive effect in the CA3; however, there was an increase in damage from the 4 to 20 hour time point in OGD treated slices. OGD slices had greater PI uptake compared to controls in the DG, but this effect did not change over time. Unlike damage observed with PI, NeuN staining revealed only a main effect of EWD such that slices exposed to ETOH had a decrease in neuronal content in the CA1, CA3, and DG regions compared to non-ETOH slices. Exposure to OGD during EWD did not reduce neuronal content beyond that of EWD alone. These results show that EWD/OGD related damage increases well after the initial insult, suggesting an importance in the timing and duration of possible protective interventions. The results also indicate that the interactive damage is not specific to neurons but may involve other cell types such as glia. Taken together, these findings highlight the need to further investigate the damaging mechanisms underlying ETOH and hypoxia exposure in order to discover effective treatments.
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0457

ETHANOL DISRUPTS PLURIPOTENCY STEM CELL MARKER EXPRESSION PROFILE IN CD24+ NEURAL STEM CELL SUBPOPULATION

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Ethanol exposure during pregnancy is a leading non-genetic cause of mental retardation and can lead to a spectrum of brain, craniofacial, cardiovascular and other developmental defects. Our laboratory has focused on the second trimester-equivalent period as a specific period of brain vulnerability to ethanol, because, during this critical developmental widow, stem cells of the fetal neuroepithelium give rise to most of the neurons of the adult brain. Previously, we showed that ethanol increased the proliferation of neuroepitelial cells while decreasing the expression of specific stem cell markers, suggesting that ethanol may promote maturation and premature loss of the neural stem cell niche. In these experiments, we used an ex vivo neurosphere culture model derived from gestational age 12.5 mouse dorsal telencephalon to assess ethanol's effects on two specific neuroepithelial cellular sub-populations; CD90+ population which constitutes presumptive early stem cells, and the CD24+ population which constitutes later progenitor cells that are committed to a neuronal lineage. Flow-cytometric analysis, showed that ethanol did not alter the proportion of CD90+ cells, but led to a dose-related and significant decrease in the proportion of CD24+ cells. We next used immunomagnetic cell separation protocols to isolate the CD24+ cell population from control and ethanol-treated neurosphere cultures. Real-time qPCR analysis showed that CD24+ cells express higher levels of mRNAs for early neuronal differentiation genes relative to CD24- cells (DCX; 21-fold higher, NeuroD1; 15.5-fold higher), whereas mRNA levels of PDGFra, a gene associated with oligodendrocyte lineage differentiation was more modestly over expressed (3.1-fold). These data suggest that CD24+ cells are selectively committed to the neuronal lineage. Our preliminary data also suggest that ethanol selectively prevents the increase in NeuroD1 and DCX in the CD24+ cells, suggesting that ethanol may divert this neuroepithelial cell population to a non-neuronal lineage. (Supported by a grant from NIAAA, AA013440 to RCM).

0458

ETHANOL-SENSITIVE MIR-153 CONTROLS NSC/NPC MATURATION BY TARGETING MULTIPLE CELL PROLIFERATION AND DIFFERENTIATION GENES

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Ethanol consumption during pregnancy can lead to a constellation of symptoms including mental retardation, brain, craniofacial and cardiovascular defects, collectively termed ''Fetal Alcohol Syndrome'' or FAS. Our laboratory ha focused on the second trimester as a specific period of fetal vulnerability because during this period, fetal neural stem cells (NSCs) give birth to most adult neurons of the brain. We previously showed that ethanol promoted NSC proliferation and maturation, and that these effects were in part mediated by the suppression of four miRNAs, including the miRNA, miR153. We know little about miR153 function and hypothesized that assessment of this miRNA may yield clues about ethanol teratology. Microarray analysis of miR-153 over-expression in a neurosphere model of fetal NSC/NPC (Benjamini and Hochberg False Discovery Rate corrected $p<0.1$, and 1.3 fold change cutoff) resulted in 38 candidate genes that were significantly down-regulated. Gene ontology analysis indicated that suppressed genes were primarily associated with signal transduction processes. We used RT-PCR to validate the expression of 7 miR153-targeted genes that are involved in stem cell proliferation or cell cycle progression such as VEGFa, Mapk3, AKT, HDAC8 and ones that regulate stem cell differentiation/ migration such as chemokines, CXCL1 and CCL2, and Matrilin2, an extracelluar matrix (ECM) protein. Regulation of these gene networks by miR153 is consistent with known ethanol effects on cell cycle progression and cell migration. This research work was supported by grant, NIH AA13440, to RCM..

0459

ALCOHOL MARKEDLY ALTERS METHYL BINDING PROTEINS DURING NEURAL DEVELOPMENT

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Alcohol use during pregnancy causes to Fetal Alcohol Spectrum Disorders (FASD), with varying degrees of neurodevelopment deficits. Proper DNA methylation which regulates gene repression is now known as a prerequisite for zygote differentiation, early development, tissue specification. We previously reported that DNA methylation is a program (DMP) which parallel to embryonic maturation during early neural tube development, and, alcohol exposure delayed this DMP along with retarded embryonic growth. To further understanding the methyl binding protein which connection between DNA methylation and gene expression in DMP, we studied the methyl CpG binding protein 2 (MeCP2) and methyl-CpG-binding domain protein 1 (MBD1). To mimic similar patterns of brain damage known to occur when pregnant women drink alcohol in chronic and in binge drinking pattern, we employed Liquid Diet [LD; 4% v/v alcohol on gestational (E) days 7 to E17; BAC 100–200mg/dL, analyzed at E17] and Vapor Chamber (VC, 6hrs of 300mg/dL beginning at E8 and harvest at E10) model of alcohol administration. Alcohol in LD paradigm, reduced the brain weights on E17, and markedly delayed the hippocampus development and a significant reduction in cortex thickness. In the VC model, alcohol caused embryonic growth retardation as indicated by Van Farber scoring system. Through immunostaining, we found that the MeCP2 and MBD1 exhibited reversed expression patterns. As compared to controls, a marked increase of immunointensity and number of MeCP2+ cells, while a significant decrease in immunointensity and number of MBD1+ cells were found in the developing hippocampal and migratory cortical areas. A similar finding was observed in VC binge model showing the marked increase of MeCP2 and decrease of MBD1 in the fore- and hindbrain regions of telencephalic wall, optic and otic vesicles, and first branchial arch in the alcohol treated E10 embryos. Through both chronic and binge models, we showed for the first time that alcohol-induced a contrast change of MeCP2 and MBD1 which correlated with neural developmental delay. This finding strongly supports our previous observation on alcohol disrupted DMP. Furthermore, since MeCP2 and MBD1 are functioning in mediate the DNA methylation to gene repression, the consequence of their alteration further signifies the altered DMP hypothesis on alcohol induced neurodevelopment deficit. AA016698 & P50AA07611 to FCZ & Fulbright Fellowship to NCÖ & BAP-SBEA (NCÖ) 2011-5DR to AHÖ.

0460

ETHANOL-ALTERED SINGLE-CELL DISTRIBUTION OF MOLECULAR PHENOTYPES DURING RETINOIC ACID DIFFERENTIATION OF MOUSE EMBRYONIC STEM CELLS

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The objective of this project is to determine the mechanism(s) of ethanol interference with the early developmental stages that underlie Fetal Alcohol Spectrum Disorders (FASD). We have previously characterized the effects of ethanol on the differentiation pathways of pluripotent mouse embryonic stem (ES) cells into neural cell types, using integrated experimental (multiparametric flow cytometry, single cell analysis, immunocytochemistry, high-throughput qPCR) and computational approaches. Evaluation of a set of 100 transcription factors (TFs) and signalling molecules that regulate the coordinated exit of cells from pluripotency, cell fate decisions and cell lineage determination, demonstrated that (i) the gene and protein expression of core TFs Sox2, Oct4 and Nanog decrease during differentiation for a period of 6 days, and (ii) exposure to ethanol differentially delays the downregulation of core TFs, (iii) resulting in an elevated Oct4 protein level, and thus (iv) altering significantly its relative abundance to Sox2. These finding support the hypothesis that ethanol-mediated changes in the Oct4/Sox2 ratio derail the differentiation program, favoring formation of mesoendoderm instead of neuroectoderm. The focus of the current study is on establishing an ethanol dose (25, 50, 100 mM) and duration of exposure (2, 3, 4, 6 days) threshold during retinoic acid (10 nM)-directed differentiation of ES cells towards neuroectodermal fate, and identifying ethanol-targeted cell populations. Our single cell measurements (of 50,000 individual cells) showed that the Sox2 and Oct4 expression during differentiation is regulated in opposite manner with increasing ethanol doses. The Sox2 level is decreased, while that of Oct4 is increased with ethanol resulting in an elevated Oct4/Sox2 ratio. Moreover, ethanol alters the cell distribution among the eight cell subpopulations (based on core TFs expression) in a dose-dependent manner (25–100 mM), resulting in an overall increase of Oct4-positive cells. Overall, these findings point to an early entry point of ethanol into the differentiation process of ES cells that results in aberrant distribution of molecular and morphological phenotypes that may be important in cell lineage decisions towards CNS development at the basis of FASD defects. Supported by grants from NIAAA T32 AA007563 and ABMRF, Thomas Jefferson University Pilot Research Award, Department of Pathology, Anatomy and Cell Biology Support Funds, and the Graham Fund.

0461

CHOLINE AND/OR GM1 GANGLIOSIDE REDUCES ETHANOL INHIBITION OF L1 MEDIATED PP60^{SRC} ACTIVATION

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Purpose: Our goal is to determine if choline and/or GM1 ganglioside, both constituents of lipid rafts, reduce the inhibitory effect of ethanol on L1 cell adhesion molecule (L1) activation of pp60^{src}. We have previously shown that choline and/or GM1 ganglioside reduces ethanol inhibition of L1 activation of ERK1/2 and L1 mediated neurite outgrowth. This study is to determine if the effect of choline occurs upstream of ERK1/2 activation.
Methods: Cerebellar granule neurons from postnatal day 6 rats are grown overnight in serum free media containing 40 mM choline and/or 40 mM GM1 ganglioside followed by treatment with 25 mM ethanol for 1 h. L1 is then activated by addition of an L1 clustering antibody. After 10 min, cell lysates are made. pp60^{src} is immunoprecipitated and detected by immunoblot with antibody to phospho-Src family 416 (T416). Blots are stripped and reprobed with an antibody to total pp60^{src} as a loading control. Blots from three separate experiments are quantified by densitometry. Data are analyzed using paired t-test.
Results: L1 activation of pp60^{src} is inhibited by pretreatment with ethanol, as we have previously shown. Choline and GM1 ganglioside in combination significantly reduce the inhibitory effect of ethanol on the activation of pp60^{src} by L1 ($P<0.01$, paired t-test). Choline or GM1 ganglioside alone also reduces the ethanol inhibition of pp60^{src} activation, but is less effective than the two combined ($P<0.05$, paired t-test).
Conclusion: The protective effects of choline and/or GM1 ganglioside occur at the proximate signaling partner of L1. Because pp60^{src} is a constitutive protein of lipid rafts, These results suggest that, in this simple system, agents which support lipid raft function ameliorate the inhibitory effects of ethanol on L1 cell adhesion molecule.

0462

HIGH-THROUGHPUT TRANSCRIPTOME SEQUENCING TO IDENTIFY GENETIC MODIFIERS OF ALCOHOL SENSITIVITY

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Ethanol-induced neuronal apoptosis contributes to the persistent behavioral deficits of Fetal Alcohol Spectrum Disorders. We possess a unique genetic resource: two closely related avian strains (W98S and W98D) that differ dramatically in their alcohol sensitivity. W98S neural progenitors have strong calcium transients and substantial apoptosis in response to 52 mM ethanol, whereas these responses are significantly blunted in the W98D strain. We used next-generation sequencing (NGS) to compare the transcriptome profile of these cells and identify genetic differences that account for their differential alcohol sensitivity. We utilized the Illumina II GX platform (75bp paired-end reads, two independent isolates/strain); data were analyzed using Genomics Workbench and open source software applications. We obtained 67.5 and 71.8 million high quality, paired-end reads for W98S and W98D, respectively, and 55% of reads could be mapped to the Ensembl annotation of the *Gallus gallus*-3 genome. There were no significant differences in expression (0/17,934 mapped genes; best p=0.47) between W98S and W98D and thus could not explain the differential sensitivity. Genetic comparison revealed 20 expressed genes containing complex SNPs that changed amino acid identity. Several genes could be linked directly or indirectly to the cell signaling pathway that mediates alcoholic neurodegeneration in this model. These include calsequestrin-1, the atypical CPCR/cadherin Celsr3, NKX1.1, and TRAIL-like protein. SNP analysis of the unannotated gene set is underway. Ongoing studies test which of these are expressed within developing neural crest and map the amino acid changes to each protein's functional domains. Our successful identification of significant SNP differences in candidate genes demonstrates the power of this approach to identify candidate effectors of alcohol sensitivity. The close genetic relationship and strikingly different ethanol responses of W98S and W98D make them powerful tools to discover novel genetic modifiers of alcohol's actions in the embryo and in other cell populations. [Supported by AA11085 and ARRA Suppl to SMS]

0463

PRIMARY AND SECONDARY FETAL HUMAN BRAIN-DERIVED NEURAL STEM CELLS RESPOND DIFFERENTLY TO ETHANOL

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Ethanol (ETOH) consumption can lead to Fetal Alcohol Spectrum Disorder. Several mechanisms have been proposed to explain the action of ETOH on the developing brain. While most *in vitro* studies are on primary murine and human cells, recently secondary cell lines (e.g., ReNcell VM) derived from fetal human brain have been developed. ReNcell VM is an immortalized human neural progenitor cell line derived from fetal human brain, which has the ability to differentiate into neurons and glial cells. We and others have shown that ETOH alters several pathways in differentiating primary human neural stem cells (NCS), including the Wnt signaling pathway. We have shown that proteins from wnt receptor complex (PLRP-6, DVL-2) and downstream wnt pathways (TYR- P-GSK-3 beta, SER-P-GSK3 beta, and beta-catenin) are altered by ETOH in differentiating primary NSC. For this study, we hypothesized that ETOH elicits a similar response in ReNcells, which are immortalized NSC isolated from the ventral mesencephalon of fetal human brain. The ReNcell line was purchased from Millipore Inc. and expanded in proliferation media containing 20ng/ml of EGF and b-FGF in a humidified chamber at 37°C. Cells from second passage were differentiated in the presence of 0, 20 or 100mM ETOH for 120h and lysed. Steady-state ETOH concentrations were maintained by using saturated chambers. Protein lysates from all conditions were used to perform westerns blots to probe for proteins of the Wnt signaling pathway. All experiments were performed in triplicate. Beta actin expression was used as a quantification control. Although ETOH significantly altered Wnt pathway protein expression in primary NSC, there was no significant change in wnt receptor complex protein (Dvl-2, PLR- P) expression nor in downstream wnt pathway proteins in ETOH treated RENcells at both 20 and 100mM concentrations. This observation suggests that immortalized cell lines, even when derived from primary normal tissues, may not respond to treatment as primary cells.

0464

ETHANOL-INDUCED DEFECTS IN NEURONAL CELL FATE DECISIONS IN CAENORHABDITIS ELEGANS

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Our goal is to understand the molecular mechanisms underlying the damage caused by fetal alcohol exposure, a severe form of which is fetal alcohol syndrome, the leading preventable cause of mental retardation in the Western world. We have taken a genetic approach to studying the effect of ethanol on a discrete cell fate decision made during embryogenesis in the nematode *C. elegans*. AWC cells are a pair of olfactory neurons that together allow *C. elegans* to detect and discriminate between several volatile attractive odorants. During embryogenesis, the AWC neurons compare basal activity and make an asymmetric cell identity decision. Consequently, specific groups of G protein-coupled receptors are asymmetrically expressed in the two AWC neurons. A GFP tagged receptor (STR-2::GFP; Troemel *et al.*, 1999) that is expressed in only one of the AWC neurons of wild-type animals allows us to monitor this cell fate decision. SLO-1, a voltage-gated potassium channel is expressed in these neurons, and activation of this channel can modify the normal AWC cell fate decision so that both AWCs adopt the same cell fate (which we identify as both cells expressing the GFP marker, or a 2 AWC^{ON} cell fate). Previous studies from our lab and others have shown that SLO-1 is a major molecular target of ethanol. We found that ethanol exposure during embryogenesis could alter the AWC cell fate, and that this effect of ethanol requires the SLO-1 channel. Notably, this effect on AWC cell fate occurs at a significantly lower ethanol concentration than is required to generate morphological effects in worms (Davis *et al.*, 2008). We have further demonstrated that by modifying the lipid composition of the cell membrane, we can render this cell fate decision resistant to the effects of ethanol. To determine if this change in AWC cell fate has functional consequences, we are testing the ability of adult animals that had been exposed to ethanol during embryogenesis to perform in chemotaxis and odorant discrimination assays, which require proper function of the AWCs. We predict that exposing embryonic worms to ethanol will cause persistent functional changes due to the altered AWC cell fate decision. We hypothesize that changing the lipids in the diet of ethanol-exposed mothers may be able to attenuate the effects of ethanol on cell fate decisions in the embryo. Our data have significant implications for the identification of molecular causes of fetal alcohol damage in humans.

7. DETERMINANTS OF ALCOHOL CONSUMPTION IN HUMANS

0465

DISCREPANCIES BETWEEN PARENT AND CHILD REPORTS OF PARENTAL MONITORING AND ADOLESCENT ALCOHOL-RELATED BEHAVIORS

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Parental monitoring refers to behaviors that parents carry out in order to track the activities of their children, and research has linked these behaviors with lower levels of youth alcohol use and related negative consequences. However, differential magnitudes of these associations have been observed across parent and child reporters, implying discrepancies in perceptions of monitoring. The current study seeks expand upon this work by looking at the extent to which these discrepancies are predictive of later child alcohol use. Models were performed where parent reports of monitoring and the discrepancy between child and parent reports were used as predictors. Given the known differences in alcohol use between (a) male and female adolescents and (b) older and younger students, child sex and year in school were included as covariates.

The sample was derived from the first three cohorts of participants in the iSAY project, funded by NIAAA. A total of 707 parent-child dyads were surveyed when children were in grades 6–8 and again one year later. Student demographic breakdown was as follows: 52% female; 74% White, 8% Black, 4% Asian; 15% ethnically Hispanic; and the mean age was 12.6 years. Students and parents each were surveyed on their perceptions of parental monitoring/knowledge, and students provided information on their lifetime alcohol-related behaviors (e.g., ever drank, ever been ''buzzed'', ever been drunk, maximum number of drinks in a sitting). Discrepancies between reporters were calculated by subtracting the child monitoring scale from the parent monitoring scale. Parents reported greater levels of monitoring than children, $t(616) = 12.39$, $p < .001$, leading to a positive mean discrepancy score ($M = .45$).

Results indicated that, when accounting for sex and grade, parental monitoring was associated with a decreased likelihood of ever having (a) drank alcohol, (b) been ''buzzed'', and (c) been drunk, in addition to lower levels of lifetime maximum drinks in a sitting. Discrepancies were also associated with these outcomes, but in the opposite direction, with greater discrepancy associated with increased likelihood of alcohol-related behavior. These findings have implications for parent-based programs aimed at preventing adolescent alcohol use. We also examined discrepancies in reports of parental control, solicitation, and child disclosure, and these analyses will be discussed in the poster, as will future directions and limitations.

0466

A COMPARISON OF PARENT AND TEEN REPORT OF MONITORING AND COMMUNICATIONAND THEIR RELATION TO TEEN ALCOHOL AND OTHER DRUG USE

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The current study had two goals: first, to compare parent and teen report of parenting strategies, e.g. monitoring and communication, and second, to examine the relation between these reports and adolescent drinking and marijuana use. A sample of 131 teens (mean age = 14.75) and their parents were recruited from a metropolitan area in the northeast (37% White, 55% males). The correlations between parent and teen report of parenting practices ranged from .27 to .45. Paired t-tests revealed that parents reported soliciting more information about their teen's whereabouts ($t = 5.59$, $p<.001$) and having more control over what their teens were allowed to do ($t = 4.84$, $p < .001$) than teens reported. In addition, parents also reported more problem solving discussions about general topics ($t = 2.51$, $p<.05$), fewer peer influences on teen substance use ($t= 9.98$, $p< .001$), and greater overall communication about substance use ($t = 4.73$, $p<.001$) than teens.

Adolescents in this sample were also categorized as: 1) not having used alcohol or marijuana; 2) having used either marijuana only or alcohol only in the prior 90 days, and 3) having used both marijuana and alcohol in the prior 90 days. An ANOVA controlling for age revealed that teens who used both marijuana and alcohol reported parents often not knowing what they did in their free time, not needing their parent's permission to stay out late, and not telling their parents where they were going when compared to teens who reported using only marijuana or alcohol or no substance use. On these same measures, however, there were no differences across teen groups when parents reported on their own parenting strategies.

As has been found in other studies, parents reported using more parenting strategies than their adolescents. In addition, teen perception of parenting strategies, such as monitoring and communication, were significantly related to adolescent substance use. If teens reported that their parents engaged in more parenting, they also reported less substance use. Interestingly, there were no differences in parent perception of their use of parenting strategies by level of teen substance use. Thus, studies need to assess both parents and teens with respect to these parenting behaviors and be cognizant of the fact that parents may not report accurately on their use of such strategies. Similarly, intervention programs should consider basing recommendations regarding parenting on teen rather than parent report.

0467

PARENTS' RULES ABOUT UNDERAGE DRINKING: A QUALITATIVE STUDY OF WHY PARENTS LET TEENS DRINK

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Studies have found that 33% of 6th graders reported getting alcohol from their parents (Hearst et al., 2007). However, little is known about why parents provide alcohol to their children. We conducted qualitative interviews with parents (n=44) of teens, ages 15–18 living in Northern California to learn more about parents' rules concerning underage drinking, and circumstances in which parents allow drinking. When parents were asked about whether they allowed their teen to drink, many parents' initial response was that they did not condone underage drinking. However, the in-depth interviews revealed many inconsistencies and exceptions. In many families, decisions about whether or not to allow underage drinking were made on a case by case basis and frequently depended on the drinking context. For example, many parents allowed drinking in the context of family celebrations. Parents also reported being pressured into allowing their teens to drink by other adults, often relatives. Reasons for letting teens drink alcohol were focused on the safety and education. Parents believed that letting teens drink at home was a way to reduce risky behavior such as drinking and driving. Parents also wanted to educate teens about drinking, including how to drink in moderation, how to minimize drunkenness, and how to appreciate alcohol. Some parents wanted to teach their teen how to drink appropriately before being exposed to outside influences such as peers or before going to college. Preserving family culture was another reason why some parents allowed their teen to drink alcohol. Lastly, underlying most parents' rules was a sense of helplessness that their teen would drink no matter what they did. This poster will detail why and under what circumstances parents allow their teens to drink alcohol. We will describe how these findings can inform prevention strategies designed to help parents enforce drinking rules in the home.

0468

FAMILY INVOLVEMENT AS A MODERATOR OF SUBSTANCE USE RISK FACTORS IN ADOLESCENTS WITH SEVERE EMOTIONAL AND BEHAVIORAL DISTURBANCES

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Previous research shows that adolescents with severe emotional and behavioral problems are at increased risk of problematic alcohol and other substance use. Research also suggests that family involvement can be a protective factor against risk for at-risk adolescents. To date, no studies have examined the protective influence of family involvement on substance use behaviors in a clinical sample of adolescents. Thus, the current study longitudinally examined the moderating effects of family involvement on the associations between internalizing and externalizing problems, respectively, and substance use (alcohol, marijuana, and tobacco) and problems in a sample of adolescents with severe emotional and behavioral problems. Adolescents and their parents were assessed at three waves over a one-year period as part of the SAMHSA funded Comprehensive Community Mental Health Services for Children and Their Families (CMHS) Program. Multilevel growth curve models were estimated using Hierarchical Linear Modeling (HLM). Results generally supported the hypothesis that family involvement is a protective factor in adolescent substance use by showing that the adverse effects of both internalizing and externalizing problems on substance use and problems were buffered by high family involvement. However, these effects differed depending on the substance use outcome. For alcohol use, family involvement buffered the negative effects of high externalizing problems. For tobacco use, family involvement buffered the negative effects of both internalizing and externalizing problems, respectively. For substance use problems, family involvement buffered the effects of only internalizing problems. Family involvement did not moderate effects of emotional and behavioral problems on marijuana use. Effects of family involvement remained after controlling for demographics, family history of substance abuse, and family structure. Taken together, these results suggest that the beneficial effects of family involvement on at-risk adolescents' substance use involvement are dependent on the type of emotional and behavioral problems the adolescent experiences as well as the type of substance the adolescent uses. Implications for family-based treatment of at-risk adolescents are discussed.

0469

SOCIAL INFLUENCES OF ALCOHOL AND DRUG USE AMONG YOUTH TREATED IN AN EMERGENCY DEPARTMENT

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Alcohol misuse among youth is a widespread public health concern that has been associated with physical health, mental health, social, and legal consequences. The Emergency Department (ED) provides an opportunity for screening, brief interventions, and treatment referrals for alcohol misuse. Additional data is needed regarding characteristics of alcohol misuse in order to refine ED-based interventions. This study examines the influences of parents, siblings, and peers simultaneously on youth substance use, while accounting for potential unique contributions of alcohol versus drug use. The sample included 482 patients (ages 14–20; 52% male; 79% Caucasian) who screened positive in an ED for alcohol misuse (AUDIT-C score >3 for youth 14–17; score>4 for youth 18–24). Participants completed computer screening and baseline questionnaires. Measures of parent, sibling, and peer drug and alcohol use, as well as alcohol related consequences were completed. Structural equation modeling was used to analyze how gender moderates social influences (parent, sibling, peer drug and alcohol use) on youth drug and alcohol use, and the relation to alcohol-related consequences (RAPI scores). Of those screened, 23% met criteria for alcohol misuse. Among those who qualified for the study, 20% received public assistance, 65% reported using marijuana, 14% reported using other illicit drugs, and 23% reported non-medical use of prescription medications. There were no significant sex differences in the models. Parent, sibling and peer alcohol and drug use were significantly correlated with each other. However, only peer alcohol and drug use was positively associated with youth alcohol use ($p=.001$ and $p<.001$, respectively). Peer alcohol use was negatively associated with youth drug use ($p<.01$) and peer drug use was positively related to youth drug use ($p<.001$). Youth alcohol and drug use was positively associated alcohol-related consequences ($p<.001$ for both). While social influences of alcohol and drug use were correlated (parent, sibling, peer alcohol/drug use), peer alcohol and drug use uniquely contributed to youth alcohol and drug use. Findings suggest that ED-based alcohol interventions for youth need to address the influences of peer alcohol and drug use. Also, future research is needed to understand ''alcohol-related consequences,'' as both drug and alcohol use were correlated with this variable. (Supported by NIAAA #018122 and NIDA T32 DA007267)

0470

HIGH SCHOOL PEER CROWD AFFILIATION AND PEER ALCOHOL USE IN PREDICTING PROBLEMATIC DRINKING IN COLLEGE

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Peer crowd affiliation (PCA) has been linked to engaging in various health-risk behaviors in adolescents, and these patterns of behavior tend to vary by crowd. However, a comprehensive examination of how peers influence college students' health risk behaviors, especially with regards to PCA, is lacking. One study that did examine PCA in young adults by Barber, Eccles, and Stone (2001) found that PCA significantly predicted substance use outcomes in adulthood. Nevertheless, this area of peer relations remains relatively understudied in a college population.

The current study seeks to replicate and extend findings from Barber et al. (2001) by examining whether high school PCA is associated with problematic alcohol use in a sample of college freshman. The current study will expand on this work by including friends' drinking as a mediator. Existing research has found that peers' behaviors influence one's own behavior, such as close friends' drinking predicting own drinking. Therefore, it would follow that this peer influence may be the mechanism by which PCA predicts alcohol use in college. Additionally, the present study uses a continuous measure of PCA, allowing for varying degrees of affiliation and overlap in crowds that is more consistent with how crowds appear in high school (e.g., affiliating with both populars and jocks to varying extents).

College students ($N = 449$) completed questionnaires assessing high school PCA, problematic drinking, and alcohol use habits among 3 close college friends. Hypotheses were tested using a hierarchical regression approach. Stronger affiliation with the Popular or Jock crowds in high school predicted more problematic levels of drinking in college, whereas stronger affiliation with the Brain crowd predicted less problem drinking. Furthermore, stronger affiliation with the Popular or Jock crowds predicted higher levels of friends' drinking, whereas stronger affiliation with the Brain crowd predicted lower levels of friends' drinking. Higher levels of friends' drinking, in turn, predicted more problematic drinking. Including this variable in the models considerably reduced the direct effects between PCA and problematic drinking, completely mediating the relation for Jocks. This study highlights the differing implications of high school PCA relating to problematic college drinking and suggests that crowds more susceptible to such outcomes may benefit more from early interventions that also address peer drinking.

0471

EXAMINING BREATH ALCOHOL CONCENTRATIONS THROUGH A SIMULATED DRINKING GAME PROCEDURE

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Drinking games (DG) are social activities with rules that dictate the rate of alcohol consumption and can lead to rapid intoxication. To date, research on DG has relied almost exclusively on retrospective self-reports. Thus, while participants have been asked to recall how much alcohol they consume during occasions on which they participate in a DG or the subsequent negative outcomes, very few published studies have reported efforts to systematically observe these behaviors during DG in a controlled laboratory setting. This presentation will discuss a series of studies designed to develop and assess a Simulated Drinking Game Procedure (SDGP). Two initial SDGP studies (n's = 52 & 92, respectively) focused on designing a safe, efficient, and alcohol-free laboratory protocol for studying DG behavior. Analyses focused on generating estimates of the liquid consumed during popular DG, and estimated blood alcohol concentration (BAC) were generated and examined as a function of gender and game parameters. In the most recent SDGP study, participants (n= 40) who were over the age of 21 were recruited to play a laboratory version of Beer Pong and randomly assigned to one of two beverage conditions: alcohol or water. Results from the SDGP studies suggest that playing DG leads to variable levels of alcohol consumption, and that the outcomes are influenced by both gaming conditions and individual differences within the participants. The findings also highlight the heightened risks for females who engage in DG, as they achieved higher BAC's despite drinking similar amount of alcohol as their male counterparts. Continued development of both an alcohol and an alcohol free version of the SDGP will allow researchers to conduct research on factors that influence risky drinking with underage and legal drinkers.

0472

USING EVENT-LEVEL DATA TO EXAMINE DRINKING GAME BEHAVIOR IN FIRST-YEAR COLLEGE STUDENT DRINKERS

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College students' participation in drinking games (DG) has been identified as an important risk variable related to greater alcohol use and use-related harm. Most studies in this domain have utilized global measures of behavior, assessing students' usual pattern of DG participation and its outcomes over an extended period of time. The use of an event-specific approach in which participants are asked to report their drinking behaviors on weekend drinking days may help to clarify both the circumstances and consequences of this behavior among college students. The current study utilized weekend diary data to examine event-specific (1) relationships between DG participation, alcohol use, and use-related consequences, (2) covariation between DG participation and other self-regulated drinking behaviors, and (3) contextual factors related to DG participation. The sample consisted of 358 first-year students (52% male) screened as drinkers. Participants were asked to complete a total of six web-based surveys that assessed DG participation and other self-regulated drinking behaviors, alcohol use, and related problems on weekend drinking events in fall 2010. Multilevel regression analysis of events when students reported alcohol use revealed that DG participation was associated with greater alcohol use ($p < .01$), which, in turn, was associated with more alcohol-related problems ($p < .01$). Significant, positive associations were observed between participation in DGs and other risky drinking behaviors, including pregaming and consumption of alcohol and energy drinks ($ps < .01$). DG participation was negatively associated with protective drinking behaviors, such as pacing one's drinks and determining in advance not to exceed a set number of drinks ($ps < .01$). Preliminary results suggested no evidence that salient events (e.g., home football games) were related to an elevated prevalence of DG participation. Results from this study reinforce the notion that DGs put students at risk for increased consumption and related harm. Analysis of event-specific data highlights that this is true for students regardless of their typical drinking pattern. Further, engagement in this popular, social drinking practice is associated with other risky drinking behaviors within those same drinking events.

0473

PARALLEL PROCESS GROWTH MODELS FOR ADOLESCENT AND PEER DRINKING IN INDIVIDUALS WITH AND WITHOUT CHILDHOOD ADHD

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Adolescent alcohol use may be influenced by exposure to peer drinking, adolescents may select drinking peers with whom to affiliate to support drinking behavior, and adolescent and peer alcohol use may be reciprocally influenced. ADHD is associated with long-term risk of alcohol-related problems; this risk could be associated with adolescent peer alcohol socialization that operates more strongly in individuals with than without ADHD. The current study conducted multiple-group parallel process latent growth curve models to examine associations between growth in adolescent drinking and growth in both peer alcohol use and peer alcohol tolerance and determined if these associations differed as a function of ADHD. 159 adolescents with childhood ADHD and 117 demographically-similar youth without ADHD were followed in the Pittsburgh ADHD Longitudinal Study. A cohort-sequential design collected up to 4 annual assessments from 14 to 17 year olds. Adolescents reported on the frequency of their own alcohol use in the prior 12 months, the number of peers who used alcohol regularly or occasionally (peer alcohol use), and how their close friends feel about regular or occasional drinking (peer alcohol tolerance). Parallel process models fit the data well. For the full sample, higher initial levels of adolescent alcohol use predicted slower growth in peer alcohol tolerance (b=−0.07, p<0.05). Multiple-group parallel process models also fit the data well and showed that increases in both peer alcohol use and tolerance were more strongly associated with increases in alcohol use for individuals with ADHD (peer use: b=0.48, p<0.001; peer tolerance: b=0.08, p<0.01) than without (peer use: b=0.12, p<0.01; peer tolerance: b=0.03, *ns*). These results suggest an important role for peer socialization to alcohol use in the etiology of AUDs for children with ADHD. Additional research would benefit from social network characterization to better understand whether peer alcohol socialization is stronger in adolescents with than without ADHD as a result of peer (i.e. increased deviance) or adolescent (i.e. misperception of peer alcohol use) characteristics. Further research on the persistence of differences in peer alcohol socialization in individuals with and without ADHD into early adulthood, the period of greatest risk for alcohol use problems, will be important to understand developmental manifestations of the increased propensity for individuals with ADHD to be at risk for AUDs.

0474

MODELING SOCIAL AND FUNCTIONAL NETWORK SUPPORTS FOR DRINKING AND READINESS FOR CHANGE AMONG RURAL AND URBAN AT-RISK PROBLEM DRINKERS

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Introduction: Individuals who are at-risk for drinking problems differ in their illness severity, perceptions of social and structural network support for drinking, and the need to change drinking habits.
Objective: We examined whether perceptions of social and structural network support for drinking motivation to change mediated the relationship between gender and baseline alcohol-severity with drinking outcome at 12-month follow-up in a longitudinal community sample.
Method: Data were from baseline and 12-month interviews from the Rural Alcohol Study, a probability sample of rural and urban at-risk drinkers (n=733) from six Southern states. At-risk drinkers were identified through a telephone-screening interview. Measures of motivation (problem recognition and taking action) were the resultant two factors derived from the Stages of Change Readiness and Treatment Eagerness Scale. Items on social consequences of drinking measured alcohol severity. Functional social support (tangible emotional support, physical support and informational support) were the resultant factors derived from the 19-item multidimensional social support survey developed for the Medical Outcomes Study. The proportion of individuals identified by the respondent as being in his/her who supported drinking measured structural social network support. Structural equation models examined relationships between baseline alcohol severity, functional support for drinking, structural support for drinking and motivation to change with number of drinks per drinking day at 12-months.
Results: We identified significant direct paths between functional social network support and alcohol severity with unstandardized estimate of (0.216, ($p < 0.05$)), between social network support and problem recognition (0.547, $p < 0.01$), structural network support and taking action (0.137, ($p<0.01$)). We also identified significant direct path between structural network support and alcohol consumption at 12-month follow-up (0.133, ($p <0.05$)).
Conclusions: The current study offers partial evidence for motivation to change as a viable mechanism through which structural and social network support for drinking and alcohol severity is associated with subsequent drinking outcomes. Additional research is needed to further explore the amenability of motivation to change on drinking outcomes over time.

0475

COMPARING THE EFFECT OF TWO TYPES OF SOCIAL SUPPORT ON CHANGES IN PROBLEMATIC ALCOHOL USE AMONG OFFENDERS BEGINNING DRUG COURT

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Research has repeatedly demonstrated that social support is important for recovery from problematic alcohol use. It is unclear, however, which aspect of social support is most important. The current research compares the effect of two types of support (providing direction versus unconditional acceptance) on problematic alcohol use in offenders enrolled in drug court. The data for this study were taken from the first assessment of a larger longitudinal study of drug court enrollees. Study participants (n = 55) were recruited within one month of enrolling in drug court. They completed a series of baseline questionnaires, including reports of alcohol use prior to their arrest, alcohol use after their arrest, and the Social Support Questionnaire (Sarason, Sarason, Shearin, & Pierce, 1987). The current analyses focus on the number of social network members who provide direction (Who can you really count on to tell you, in a thoughtful manner, when you need to improve in some way?), and the number of social network members who provide unconditional acceptance (Who accepts you totally, including both your worst and your best points?). Analyses examining changes in the frequency of alcohol use from pre- to post-arrest were conducted using block sequential regression analyses. Alcohol use prior to arrest was entered on the first block; providing direction and unconditional acceptance were entered simultaneously on the second block. The frequency of drinking prior to arrest was positively associated with the frequency of drinking after arrest. The stability of this association differed according to the type of support offered by social network members. When a greater number of social network members provided direction, the frequency of drinking increased from pre- to post-arrest. When a greater number of social network members offered unconditional acceptance, however, the frequency of drinking decreased from pre- to post-arrest. These results speak to the importance of considering different types of social support when examining recovery from problematic alcohol use. Although providing direction might seem conducive to recovery, this type of support had a negative impact on alcohol use in the current sample. Unconditional acceptance appeared beneficial for improvement in the current study.

0476

THE RELATIONSHIP BETWEEN SCHOOL CONNECTEDNESS AND ALCOHOL USE IN YOUNG ADOLESCENTS: A PROSPECTIVE STUDY

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It is well documented that the level of engagement or belonging to a school environment, otherwise known as ‘school connectedness’ is highly prognostic of many key markers of adolescent intellectual and social development, including psychopathology. However, little is known about the relationship between school connectedness and the development of alcohol use in early adolescence. Adolescence is a high risk period for alcohol initiation and the consequences of early use are well established. This study applied a prospective design to examine the role of school connectedness in predicting alcohol use in a cohort of young adolescents. One hundred and ninety-two students (mean age = 14 years) were administered questionnaires at baseline (Time 1) and at 12-month follow-up (Time 2), with a retention rate of 88.5%. Measures of alcohol use and the Psychological Sense of School Membership (PSSM) scale were completed at both testing sessions. Lower scores on nine of the 18 PSSM items administered at Time 1 were significantly associated with heavier Time 2 drinking. They clustered into constructs recently described in the literature as Caring Relationships and Individual Acceptance. After controlling for Time 1 alcohol consumption (15% of variance, $p < .001$), PSSM scores predicted 5% of unique variance to Time 2 alcohol consumption, which trended to significance ($p= 0.07$). In this study, level of alcohol consumption at Time 1 was the largest predictor of drinking 12 months post assessment. School connectedness offered novel but more modest contributions to drinking over the 12 month period. Attending to students’ engagement in the school community is an important factor in future alcohol use. School based programs that facilitate supportive school cultures are likely to have a positive impact on adolescent development, including alcohol use.

0477

EXAMINATION OF THE ASSOCIATIONS AMONG CHILDHOOD SEXUAL ABUSE, TRAUMA SYMPTOMS, AND EXPERIENCES OF DISCRIMINATION ON DRINKING BEHAVIORS

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Research has established that having a history of childhood sexual abuse (CSA) is associated with a variety of negative outcomes, including trauma symptoms and problematic substance use. Discrimination experiences are also related to psychological stress and mental health issues. However, the link between CSA, negative outcomes, and experiences of discrimination remains to be explored. The purpose of the study was to examine the interaction between CSA, trauma symptoms, and experiences of discrimination on drinking behaviors. Participants included 436 female heavy episodic drinkers (27% women of color) at high risk for sexually transmitted infections, age 21–30, recruited from the community. Sequential regressions were performed to examine whether (1) CSA, trauma symptoms, discrimination, and ethnicity each accounted for significant variance in drinking behavior beyond that accounted for by education level, and (2) the interaction among CSA, trauma symptoms, ethnicity, and discrimination accounted for significant variance in drinking behaviors beyond the main effects. Results revealed that women of color had greater frequency of peak drinking than Whites. Further, trauma symptoms were positively associated with the frequency of having a drink and of peak drinking. Results also revealed a significant interaction between trauma symptoms and discrimination, such that there was a stronger positive relationship between experiencing discrimination and the frequency of peak drinking for those who reported more trauma symptoms than those who reported fewer trauma symptoms. There were also significant interactions between CSA and discrimination on the frequency of having a drink and frequency of peak drinking, such that the relationship between discrimination and drinking frequency was positive for those who have experienced no CSA or CSA with non-oral-genital contact whereas the relationship was negative for those who have experienced CSA with oral-genital contact and CSA with penetration. Findings suggest a compound negative effect of having experienced CSA, having trauma symptoms, and having experienced discrimination on drinking behaviors.

0478

LONGITUDINAL ASSOCIATION OF ALCOHOL EXPECTANCIES AND ALCOHOL USE AND CONSEQUENCES DURING AND AFTER COLLEGE

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Research on alcohol expectancies has consistently documented the association of positive expectancies with alcohol use and alcohol-related consequences. However, longitudinal studies examining changes in expectancies and changes in their association with alcohol variables over time are scarce, and tend to focus on adolescence and young adulthood. The current study investigated the association between changes in three expectancy factors and four alcohol variables across college and post-college years using longitudinal data from 489 college students. Results showed that positive alcohol expectancies tended to decrease during college years and subsequently increase after college, whereas alcohol use and consequences decrease over both periods. Moreover, changes in expectancies were found to be associated with changes in alcohol use and consequences both during college and post-college years. These results suggest that, although mean changes in alcohol expectancies and alcohol use and consequences do not exhibit similar trajectories, they do correlate during young and middle adulthood.

0479

ALCOHOL EXPECTANCIES, PERCEIVED NORMS, AND DRINKING BEHAVIOR IN COLLEGE STUDENTS: EXAMINING THE RECIPROCAL DETERMINISM HYPOTHESIS

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Social learning mechanisms, such as perceptions about ''normal'' drinking behavior (norms) and positive alcohol expectancies (PAEs), play a major role in college alcohol use. According to the principle of *reciprocal determinism* (Bandura, 1977), norms and PAEs should have bidirectional, reciprocal associations with alcohol use. Yet, studies testing this premise have yielded mixed findings, and no prospective studies have examined norms and PAEs together in a single model of reciprocal influences. This study aimed to provide such an examination. Students (N=557; 65% female) completed online measures of norms, PAEs, and alcohol use in September of their first (T1), second (T2), and third (T3) years of college. Reciprocal paths were analyzed in an observed variable, cross-lagged panel design, with PAEs, norms, and alcohol quantity and frequency modeled at each time point. Gender was a covariate. As much college drinking is social in nature, we included only social enhancement PAEs. We hypothesized that alcohol use would show stronger reciprocal associations with norms than with PAEs; whereas PAEs form in childhood and become more stable with age, norms may be more malleable upon college entry as students encounter new peers and drinking contexts. Results showed that T1 PAEs had only unidirectional influences on T2 alcohol use (β=.13 for frequency, β=.11 for quantity, *ps*<.05). No other associations between PAEs and drinking were observed. We found reciprocal paths between norms and alcohol use for quantity but not frequency: drinking quantity at T1 predicted increased norms for quantity at T2 (β=.19, *p*<.001), which predicted increased drinking quantity at T3 (β=.08, p=.027). Also, T2 drinking quantity predicted increased quantity norms at T3 (β=.14, *p*=.006). The only significant indirect effect was a weak path from T1 PAEs to T3 drinking quantity via T2 norms (*B*=.06, 95% CI [.003, .171], β=.01). Findings support the reciprocal determinism hypothesis for norms but not for PAEs early in college; norms for quantity appear to relate reciprocally with drinking, whereas PAEs may be more robust to the influence of ongoing drinking experience. Findings are noteworthy given that we controlled for autoregressivity and used a two-year timeframe. By clarifying the dynamic nature of the norms-drinking association, these findings may inform norm-based interventions in college. This research was supported by NIDA grant R01DA018993 (J.P. Read).

0480

PARALLEL MEASURES OF EXPECTANCIES (ANTICIPATED EFFECTS OF ALCOHOL SCALE) AND SUBJECTIVE RESPONSE (SUBJECTIVE EFFECTS OF ALCOHOL SCALE) AND ALCOHOL USE

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Research on alcohol expectancies (AEs) and subjective response (SR) aims to explain how anticipated and actual alcohol effects relate to alcohol use behaviors. Social Learning Theory posits that AEs and SR are likely to be reciprocally related and complementary predictors of drinking behavior. Understanding the relationship between beliefs and experience is important as discrepancies between AEs and SR (e.g. underestimating alcohol-induced impairment) may confer risk for heavy drinking and related consequences. Unfortunately, AEs and SR have largely been examined in isolation due, in part, to the absence of a measurement tool permitting direct comparisons. The recent development of psychometrically sound, parallel measures of AEs and SR now permits an evaluation of the relationship between these constructs, and the role of discrepancies as predictors of drinking outcomes.
The Anticipated Effects of Alcohol Scale (AEAS) and the Subjective Effects of Alcohol Scale (SEAS) were administered to 215 participants in a placebo-controlled alcohol administration study. The AEAS and SEAS assess 13 overlapping effects that comprise four subscales: high arousal positive (e.g. funny), high arousal negative (e.g. rude), low arousal positive (e.g. calm), and low arousal negative (e.g. woozy). Participants reported AEs based on the NIAAA binge drinking criteria (4 drinks in 2 hours for women; 5 for men) which approximates the target peak alcohol level within this alcohol administration study (.08 g%). AEs and SR were also assessed for both the ascending and descending limb of the blood alcohol curve. Results indicated that all AEAS subscales were significantly correlated with their SEAS counterparts (e.g., High Arousal+ with High Arousal+). However, AEs accounted for an average of only 26% of the variance in SR, suggesting that AEs are an overlapping yet distinct construct from SR. AEs generally represented moderate overestimates of SR (Cohen's *d* = .14–2.71 in placebo; .13–.60 in alcohol), but AE *underestimates* relative to SR were more strongly associated with drinking outcomes. For example, within the alcohol condition, underestimates of low arousal negative effects on the ascending limb were associated with heavier drinking and engagement in drinking and driving. These preliminary results suggest that examining discrepancies between AEs and SR may have important implications for treatment and prevention efforts.

0481

DAILY VARIABILITY IN ALCOHOL EXPECTANCIES AND DRINKING AMONG COLLEGE STUDENTS

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Alcohol is the most prevalent psychoactive substance used by college students and is associated with a variety of short- and long-term negative consequences. Students who experience negative consequences may continue to drink at problematic levels. Although alcohol outcome expectancies, which are beliefs about the effects of alcohol on behavior, are typically measured as a trait-like construct, these beliefs are often theorized to vary by situation or context and may play a significant role in accounting for within-person variability in drinking. The present study aimed to explore the within- and between-persons variability in positive and negative alcohol outcome expectancies and to understand their relationship to drinking. Preliminary analyses of an ongoing study included 42 college students (50% women) participating in a longitudinal daily diary study examining daily alcohol expectancies, alcohol use, and alcohol-related positive and negative consequences. Participants completed three assessments daily via Interactive Voice Response on mobile telephones for a total of four weeks across two academic quarters. 79.7% of interviews were completed. Intraclass correlation coefficients (ICCs) were used to compare the between-person and within-person variability in expectancies (where ICC is the percentage of the total variability attributed to between-person variance). There was notable between- and within-person variability in both positive and negative expectancies (ICCs = .56 and .43) and the perceived desirability of those expectancies (ICCs = .60 and .46). Hierarchical generalized linear models (HGLM; Raudenbush & Bryk, 2002) were used to examine the between / within associations of expectancies and desirability with daily drinking. Within-person associations of both positive and negative expectancies of alcohol use as measured in the afternoon were significant and positively associated with drinking later that day (B = .44, $p < .01$; B = .51, $p < .01$), whereas between-person associations were smaller and non-significant (B = .13, $p = .58$; B = .25, $p = .22$). Discussion will focus on the influence of alcohol expectancies in relation to daily drinking and in the maintenance of high risk drinking and implications for prevention and intervention efforts on college campuses.

0482

ALCOHOL EXPECTANCIES AND DRINKING BEHAVIOR IN NATIVE AMERICAN AND NON-HISPANIC WHITE COLLEGE STUDENTS

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Positive alcohol expectancies are predictive of both recent drinking behaviors and the development of alcohol use disorders later in life (e.g. Patrick, Wray-Lake, Finlay, & Maggs, 2010). The relationship between positive alcohol expectancies and drinking behavior is particularly relevant to college students, as this population is at a high risk for unhealthy drinking practices, such as binge drinking (Knight et al., 2002). As part of a larger study examining various factors influencing drinking behaviors of Native American and non-Hispanic White college students, the present study analyzed the relationship between alcohol expectancies and scores on the Alcohol Use Disorders Identification Test (AUDIT; Saunders & Aasland, 1987). Native American (n = 85) and non-Hispanic White (n = 133) students at a large Southwestern university volunteered to complete the questionnaires. Based upon previous research (Garcia-Adrade, Wall, & Ehlers, 1996), we hypothesized that scores on the Alcohol Expectancy Questionnaire (AEQ-short form; Brown et al., 1980) would be positively correlated with scores on the AUDIT. In addition, an exploratory analysis was performed to test for differences between Native American and non-Hispanic White participants' scores on the AEQ total, as well as on each of the six AEQ subscales. Results of a Pearson correlation coefficient test indicated that, as expected, total AEQ score was positively correlated with total AUDIT score ($p < .01$). However, a one-way, two-factor ANOVA revealed no significant differences between the scores of Native American and White students on either the AEQ total or any of the six subscales. The two groups also did not differ on total AUDIT scores. This finding is consistent with previous research suggesting that Native American college students exhibit similar rates of drinking as compared to non-Native students, and that degree of Native American heritage does not account for a significant proportion of variability in alcohol expectancies. (Ward & Ridolfo, 2011; Garcia-Andrade et al., 1996). This study provides evidence to suggest that the AEQ is appropriate for use with a population of Native American college students.

0483

IMPLICIT ALCOHOL-COPE ASSOCIATIONS INCREASE IN RESPONSE TO STRESS

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Dual process models of alcohol use (e.g., Weirs & Stacy, 2006) stress the importance of both controlled (e.g., deliberative, reflective) and automatic (e.g., reflexive, spontaneous) processing in predicting alcohol use and/or problems. Research has demonstrated that implicit measures, which are hypothesized to capture processes that are relatively more automatic, predict unique variance in drinking behaviors (see meta-analyses by Reich et al., 2010, Roefs et al., 2011, Rook et al., 2008). However, the extent to which implicit measures are affected by context has received considerably less attention. Research by Lindgren et al., (2009) found that implicit alcohol associations were activated or increased following exposure to a written vignette that described an unsuccessful date. Although they speculated that negative affect or distress was responsible, they could not conclude this because their study did not measure affect, per se. The current study extends their work and investigates the effect of stress and gender on implicit alcohol-cope associations. A sample of 221 undergraduates (171 women, 33 men) was randomly assigned to read one of three vignettes about a day at college (neutral, academically stressful, or relationally stressful). Participants completed an Implicit Association Test measuring alcohol-cope associations both before and after reading the vignette. Measures of affect were completed following the vignette. Preliminary results are as follows. Participants reported greater negative affect after exposure to the stressful versus neutral day vignettes. After controlling for baseline alcohol-cope associations, results indicated a 2 (gender) x 3 (vignette interaction), $p < .05$. Analyses decomposing that interaction indicated that men had significantly stronger/higher alcohol-cope associations than women after exposure to the academically stressful vignette, $p < .05$. There was non-significant trend for women having stronger/higher alcohol-cope associations than men after exposure to the relationally stressful vignette ($p = .10$). There was no evidence of significant gender differences for the neutral day vignette. Results appear generally consistent with dual process models and models of negative affect-related drinking, both of which emphasize that specific cues, including negative affect, can become associated with substance use.

0484

LATENT PROFILE ANALYSIS OF NEGATIVE URGENCY AND SENSATION SEEKING ON ALCOHOL USE

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Negative urgency and sensation seeking are impulsivity-related traits and have been shown to be associated with alcohol use and related problems (Cyders & Smith, 2008; Cyders et al., 2009). To date, though, researchers have relied exclusively on variable-level analyses rather than person-level analyses to examine the relationship between these traits and alcohol-related outcomes. Person level-analyses allow researchers to categorize individuals into different groups based on shared characteristics of the variables in question, and then examine the degree to which the groups differ on outcomes of interest. Therefore, the purpose of the current study was to use Latent Profile Analysis (LPA) to examine how different profiles of negative urgency and sensation seeking were associated with alcohol use and related problems.

Participants were 437 college students (76% female, 56% White, 38% African-American) from a Southern US university. Results from the LPA supported the existence of four profiles that we labeled based on their negative trait urgency and sensation seeking scores, respectively: High-High, High-Low, Low-High, and Low-Low. After controlling for the effects of gender, the High-High profile had greater rates of binge drinking and peak alcohol consumption than any of the other three profiles ($p < .03$). There were also profile differences in alcohol-related problems, after controlling for the effects of gender and alcohol use. The High-High profile had more alcohol-related problems than the two profiles low in negative urgency ($p < .01$), but rates of alcohol-related problems between the High-High and High-Low profiles were similar ($p = .49$). The High-Low profile also reported more alcohol-related problems than the Low-High and Low-Low profiles ($p < .01$). These findings illustrate the benefits of using person-level analysis to examine the relationship between personality variables and alcohol-related outcomes.

0485

DIMENSIONS OF SELF-REGULATION MEDIATE THE EFFECTS OF PARENTING BEHAVIORS ON SUBSTANCE USE AND PROBLEMS AMONG COLLEGE STUDENTS

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The prevalence of substance use peaks during late adolescence (Steinberg, 2007), and poor self-regulation may underlie the development of substance use disorders during this developmental period (King & Chassin, 2004). Moreover, parenting may shape the development of self-regulation (Lengua, Honorado & Bush, 2006), and one prior study indicated that parenting styles are related to lowered risk for substance use via improved self-regulation (Patock-Peckham et al., 2006). The goal of the current study is to examine the mediating role of specific dimensions of self-regulation in the association between parenting and substance use.

Using data from 940 college students at a large Pacific Northwest university (54% female, 80% age 18 or 19, 31% Asian or Pacific Islander ethnicity) we tested the effects of three dimensions of perceived maternal and paternal parenting during childhood (emotional support, overprotection, knowledge) on four dimensions of self-regulation (premeditation, perseverance, sensation seeking, urgency), and then tested the mediated pathways from parenting to alcohol and drug use and problems using path analysis in Mplus (Muthén & Muthén, 2007). Results indicated that higher levels of maternal ($\beta = -.01$, $\underline{p} < .05$) and paternal ($\beta = -.01$, $p = .04$) knowledge were related to less alcohol use via greater premeditation. Additionally, maternal knowledge was related to less alcohol use via lower negative urgency ($\beta = -.01$, $p = .01$) and lower sensation seeking ($\beta = -.02$, $p = .03$). Maternal ($\beta = -.02$, $p = .01$) and paternal ($\beta = -.01$, $p = .02$) knowledge were also related to fewer alcohol consequences via increased premeditation, and maternal ($\beta = .02$, p = .004) and paternal ($\beta = .02$, p = .002) overprotection was related to more drug consequences via higher negative urgency. Moreover, maternal ($\beta = .02$, p = .001) and paternal ($\beta = .03$, p < .001) overprotection was related to more alcohol problems via higher negative urgency.

These findings suggest parenting may shape the development of self-regulation during childhood and adolescence via environmental characteristics that either facilitate or inhibit the development of effective self-regulation. It may also be that self-regulatory capacity and parenting develop as a joint, bidirectional system. The current study highlights the importance of jointly considering individual differences in self-regulation and parenting behaviors in the development of substance use among college students.

0486

CAN YOU SAY NO?: EXAMINING THE RELATIONSHIP BETWEEN DRINKING REFUSAL SELF-EFFICACY AND PROTECTIVE BEHAVIORAL STRATEGY USE ON ALCOHOL OUTCOMES

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Preliminary research has demonstrated reductions in alcohol-related harm associated with an increased use of protective behavioral strategies (PBS) and higher levels of drinking refusal self-efficacy (DRSE). To extend research that has evaluated these protective factors independently of one another, this study considered the interactive effects of PBS use and DRSE in predicting drinking patterns and negative alcohol-related consequences. Participants were 1084 college students who reported engaging in heavy episodic drinking (five/four or more drinks in one occasion for men/women in the past month) and who completed an online survey. The sample was 63% female. Two hierarchical linear regression models were conducted to examine differential impacts of the three components of DRSE (i.e., social pressure, emotional relief, opportunistic drinking) on alcohol consumption and resulting consequences. The first model revealed that social DRSE moderated the relationship between PBS use and typical drinks consumed per week, over and above covariates of gender and Greek status. The second model demonstrated that emotional DRSE moderated the relationship between PBS use and past month alcohol-related consequences over and above the amount of weekly drinking, sex, and Greek status. Opportunistic drinking predicted drinking consequences while controlling for drinking but did not moderate the relationship between PBS use and alcohol outcomes. Results indicate that participants who reported lower levels of PBS use and DRSE in the social pressure or emotional regulation dimensions were at greatest risk for heavy drinking and consequences respectively. The current study highlights that bolstering drinking refusal self-efficacy in a variety of contexts is a worthwhile goal for future alcohol harm reduction interventions. Results confirm the utility of PBS in reducing both collegiate drinking and associated consequences, and therefore support the increasing body of evidence highlighting the potential value of including PBS-skills-training components within alcohol-related harm reduction initiatives. To increase the likelihood that students may derive the greatest benefit from their use of PBS, incorporating an emphasis on building students' self-efficacy for refusing drinks in various contexts would be a valuable addition to these interventions.

0487

SELF-EFFICACY FOR AVOIDING HEAVY DRINKING AND DRINKING MOTIVES AS MEDIATORS IN THE SOCIAL ANXIETY-PROBLEMATIC DRINKING RISK PATHWAY

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Poor self-efficacy for avoiding drinking in risky situations is associated with heavy drinking and alcohol-related problems (Gilles et al., 2006). Social Anxiety (SA) predisposes individuals to experience anxiety or negative affect in social situations, making many situations particularly ''risky'' for these individuals. Indeed those high on SA report poor self-efficacy for avoiding heavy drinking in risky social situations and drink for coping-motivated reasons (Kashdan & Roberts, 2004). Both poor self-efficacy for avoiding drinking and coping-motivated drinking have been linked to heavy drinking and alcohol-related problems (Cooper, 1994; Burke & Stephens, 1997; Blume et al., 2003). The goal of the current study is to extend the SA risk model for alcohol use and related problems by simultaneously examining the roles of poor self-efficacy for avoiding heavy drinking and coping motives for drinking. We hypothesized that those high on SA will demonstrate poor self-efficacy for avoiding drinking and engage in coping and conformity-motivated drinking, which in turn will lead to elevated alcohol use and related problems. Undergraduates (N=654, 550 women) completed self-reports of SA, self-efficacy for avoiding heavy drinking, drinking motives (e.g., coping with anxiety, coping with depression, conformity) and retrospective alcohol use and alcohol-related problems. Path analysis was used to test the association between SA and alcohol use and problems, with self-efficacy for avoiding heavy drinking as the first mediator, and coping-motivated drinking as the second mediator. Bias-corrected bootstrap procedures supported an indirect link from SA to alcohol-related problems via poor self-efficacy for avoiding drinking and conformity and coping with depression motives. Further, poor self-efficacy for avoiding drinking and both motives mediated the association between SA and alcohol-related problems independently of alcohol use. This work contributes to the current literature by extending SA and problematic drinking risk models. Specifically, the findings suggest those high in SA are at risk for poor self-efficacy for avoiding drinking, which in turn puts them at risk for drinking to conform or to cope with depression, making them vulnerable for experiencing alcohol-related problems. Clinical interventions for individuals high on SA may benefit from incorporating self-efficacy skills training into treatments and targeting specific drinking motives.

0488

THE ROLE OF ACADEMIC MOTIVATION AND DRINKING MOTIVES IN COLLEGIATE DRINKING

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Motives to drink are important predictors of alcohol consumption for youth (Kuntsche et al., 2004), but the influence of other salient motives, such as those for academics, has garnered less research attention. In high school samples, academic performance predicted later drinking behavior (Hayatbakhsh et al., 2011), and intrinsic and extrinsic academic motivation differentially related to consumption patterns (Wormington, Anderson & Corpus, 2011). Although previous research examined how the amount of academic motivation influences drinking for college students (Vaughan, Corbin, & Fromme, 2009), research into the impact of specific academic motives is needed. In the present study, we examined the role of academic motivation and drinking motives on alcohol consumption and consequences for college students.

102 college students, aged18–25 (75% women; 83% Caucasian), reported on drinking behavior and motives for academic performance, alcohol use and abstention via online survey. Academic motivations were associated with motives to drink. External ($r = .23$, $p = .02$) and introjected regulation related to conformity motives ($r = .20$, $p = .04$). Academic, drinking and nondrinking motives predicted average drinks per week for students, but no individual variables emerged as significant, $F(14, 85) = 3.62$, $R^2 = .37$, $p = .0001$. Social drinking motives were associated with maximum drinks per week, $F(14, 85) = 3.05$, $R^2 = .33$, $p = .0008$, while coping and enhancement motives predicted greater drinking-related consequences among students, $F(14, 84) = 6.40$, $R^2 = .52$, $p < .0001$. Introjected academic motives and nondrinking motives due to personal or family history of alcohol abuse were associated with lower AUDIT scores,while coping motives predicted greater alcohol-related problems, $F(14, 85) = 10.19$, $R^2 = .63$, $p < .0001$.

These preliminary findings suggest that while the influence of academic motivation may be specific to hazardous alcohol use, they may also impact reasons college students choose to drink. As these relations differ from high school samples, questions arise as to whether changes in the academic environment (i.e., greater academic autonomy and choice for college students) and maturity influence the role of academic motivation on behavioral choices consequential for academic performance.

0489

PROS & CONS OF DRINKING: A QUALITATIVE ANALYSIS OF YOUNG ADULT MOTIVATIONS AND EXPECTANCIES

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The goal of this qualitative study was to examine young adult perceptions of and motivations for drinking through analysis of brief motivational interviews (BMI). BMIs often include a decisional balance component that examines the ''Pros and Cons'' of alcohol use, attempting to explore client ambivalence about drinking through a discussion of its good and ''not-so-good'' aspects. This discussion was analyzed for the purposes of this study. Participants were 28 young adult alcohol users involved in a large hospital-based clinical trial. All BMIs were recorded, transcribed, and the present sub-sample (20% random selection of 18–24 year olds) was analyzed using NVIVO 9.0 software. Responses to the ''Pros and Cons'' dialogue were coded and thematically organized with grounded theory methods. Participants' discussions about the pros and cons of drinking centered around prevailing motivations for drinking (reasons for drinking) along with expectancies regarding drinking (expected consequences of drinking), both positive and negative. Results showed that patterns of alcohol use were primarily driven by physiological, intrapersonal, and interpersonal motivations and expectancies. Physiological expectancies were primarily negative, including expected consequences such as getting sick and experiencing hangovers. Intrapersonal motivations included reasons such as mood management and boredom. Particularly salient reasons for drinking and expected consequences of drinking were interpersonal in nature (such as drinking due to peer influence and the belief that drinking will facilitate social interaction), illuminating the important role of social group membership in alcohol use. Patterns of alcohol use as influenced by social factors may depend on rejection sensitivity, suggesting that young people could especially benefit from an emphasis on social skills and abstinence-supportive relationships in trying to reduce alcohol use.

0490

CAN PREOCCUPATION WITH DRINKING OVER-RIDE THE PROTECTIVE PROPERTIES OF MINDFULNESS ON PROBLEMATIC DRINKING?

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Prior research indicates that drinking restraint in college students is a robust risk factor for alcohol dependence and problematic drinking. Recently, studies of heavy-drinking college students have shown that one characteristic in opposition to drinking restraint, mindful awareness, may be a protective factor that deters heavy alcohol consumption and related problems. However, little research has addressed whether the protective properties of mindfulness can be nullified by the presence of known alcohol-related risk factors, such as drinking restraint. The present study sought to assess the mediating role of drinking restraint, specifically preoccupation with urges to drink, on the relationship between mindfulness and alcohol consumption and related problems in a large sample of college student drinkers (N = 390; $\underline{M}$ = 19; *SD* = 1.23; 52% male; 58% white). Participants completed assessments of alcohol consumption (quantity and frequency in the prior 90-days), alcohol-related problems, and drinking restraint. The current sample consumed an average of 5.88 (*SD* = 3.95) standard drinks on weekend days, as well as 2.56 (*SD* = 2.74) standard drinks per day during the week. Results indicated that mindfulness was negatively associated with alcohol consumption ($\beta = -.11$, $p < .05$) and alcohol problems ($\beta = -.27$, $p < .001$), but that preoccupation with urges mediated these relationships (*consumption*: $\beta = .00$, $p > .05$; *problems*: $\beta = -.08$, $p < .05$). This study replicated previous findings documenting a negative association between mindful awareness and alcohol consumption and related problems in a young adult sample. Statistical mediation models suggest that preoccupation with drinking may be a risk factor that over-rides the health-promoting effects of mindfulness and should be a primary target in intervention programs aimed at reducing risky drinking and related consequences in this group of heavy drinkers.

0491

THE PSYCHOMETRIC PROPERTIES OF THE MINDFUL ATTENTION AND AWARENESS SCALE (MAAS) BASED ON A SAMPLE OF COLLEGE STUDENT DRINKERS

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Mindful awareness is an emerging construct that has recently been examined in relation to alcohol use and problems in college students. The Mindful Attention and Awareness Scale (MAAS) is a 15-item measure that was developed to assess for individual-level differences in the presence or absence of attention and awareness on present stimuli. Since its inception, the MAAS has become one of the most widely used measures of mindfulness awareness. Despite its widespread utility, psychometric evaluation of the MAAS has been lacking with few studies examining its reliability and validity in college student samples of current drinkers. Given this background, the present study sought to examine the psychometric properties of the MAAS in a sample of college students who are current drinkers. Participants (N = 393) were heavy-drinking college students (52% male), who consumed alcohol, on average, 17.24 (SD = 14.49) days in the prior 90. Each participant was assessed on measures of mindfulness (MAAS), self-control (SCS), alcohol consumption (prior 90-days), impulsivity (Barrat Impulsivity Scale) and alcohol-related problems (College Alcohol Problems Scale) via a self-report survey. A principal components factor analysis revealed a strong dominant single factor with factor loadings ranging from .471 to .784 accounting for 38.33% of the variance. The internal consistency reliability of the MAAS was adequate (Cronbach's alpha = .875) with the item to total scale correlations ranging from .289 to .712. The MAAS was moderately correlated with the self-control scale ($r = -.401$, $p < .01$), but had a lower correlation with impulsivity ($r = -.161$, $p < .01$). In addition, the correlations between the MAAS and frequency of drinking ($r = -.110$, $p < .05$) and quantity of alcohol consumption ($r = -.111$, $p < .05$) were low, but higher for alcohol-related problems ($r = -.299$, $p < .01$) and total number of DSM-IV AUD symptoms ($r = .221$, $p < .01$). Collectively, our findings indicate that the MAAS is a reliable and valid measure of mindfulness, but differentially predicts alcohol use and alcohol-related consequences in a sample of college students.

0492

A MEDIATIONAL MODEL OF PSYCHOPATHY & DRINKING CONTROL: THE INDIRECT EFFECT OF NEGATIVE URGENCY ON HEAVY EPISODIC DRINKING AND ALCOHOL PROBLEMS

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According to deviance proneness theory (Sher, 1991), alcohol problems are influenced by the interplay of environments and innate vulnerabilities such as a propensity toward impulsiveness, which is comprised of at least four distinct facets (i.e., negative urgency, premeditation, persistence, and sensation seeking; Whiteside & Lynam, 2001). Developmental literature suggests poor behavioral regulation may underlie deviance very early on (Gardner, Dishion, & Connell, 2008). As deviant behaviors are particularly likely among individuals higher on dimensions of primary psychopathy (i.e. looking out for oneself without any concern for others) we examined whether the four facets of impulsiveness were indirectly linked to drinking control, heavy episodic drinking, and alcohol-related problems through primary psychopathy as a potential mediating mechanism. To test this idea, a multiple group structural equation model with 452 college students (236 women, 216 men) was examined. Tests for structural invariance showed distinct differences among the gender groups. Moreover, two and three path mediation analyses were conducted for women and men, respectively. Two path mediation tests showed that for women, premeditation was indirectly linked to increased drinking control through lower levels of primary psychopathy. In addition, higher levels of premeditation were indirectly linked to fewer alcohol-related problems through lower levels of primary psychopathy. Three path mediation tests showed that for men, higher levels of negative urgency were indirectly linked to both increased heavy episodic drinking and alcohol-related problems through more primary psychopathy symptoms and reduced drinking control. Our key findings were congruent with both deviance proneness theory as well as developmental findings suggesting impulsiveness may underlie the development of antisocial behaviors. Our findings add to the literature showing that negative urgency is the facet of impulsiveness most likely to underlie this pathway among men, while premeditation may be protective against this pathway among women.

0493

ALCOHOL COGNITIONS AND COLLEGE STUDENT DRINKING: THE MODERATING EFFECT OF EXECUTIVE ABILITIES

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Heavy drinking and alcohol-related negative consequences continue to be significant public health issues among college students in the United States. Research informed by dual process models of addiction has shown implicit and explicit alcohol-related associations to be important determinants of alcohol use. However, the literature is limited with respect to examination of the cognitive abilities that may moderate these relationships across populations. This study examines relations among implicit and explicit alcohol-related associations, executive abilities of working memory and inhibition, and alcohol use in a sample of 271 undergraduate students. We hypothesized that individuals with weaker inhibition and working memory abilities would demonstrate stronger relations between implicit alcohol-related associations and use, while individuals with stronger inhibition and working memory abilities would demonstrate stronger relations between explicit alcohol-related associations and use. The average age of the sample was 19.1 years (*SD* = 1.2) and most participants were female (70.5%), white (79.6%), and non-Hispanic (87.1%). Of the sample, 54 participants (*n* = 19.9%) reported no alcohol use in the previous 30 days and were excluded from subsequent analyses. Drinkers reported consuming an average of 6.9 standard drinks per week (*SD* = 6.4) and an average of 3.4 (*SD* = 3.5) heavy drinking episodes in the previous 30 days. Separate structural equation models examining arousal and relaxation associations, inhibition, and working memory abilities were estimated. A latent factor of alcohol use was constructed with typical weekly number of drinks, peak number of drinks, and heavy drinking episodes as indicators. Exogenous manifest variables were covaried and included gender, implicit associations, explicit associations, executive ability (working memory or inhibition), and interactions among executive abilities and associations. Fit indices were acceptable across models (CFI = .94–.95 and RMSEA .11–.13). Alcohol use was predicted by sex ($p < .001$), working memory ($p < .05$), and explicit relaxation associations ($p < .05$). Hypothesized moderation of implicit and explicit associations by inhibition and working memory were not observed. Factors that may have contributed to these findings, such as the inclusion of a relatively high cognitively functioning sample, will be discussed and integrated with current research.

0494

PERSEVERATION IN ALCOHOL USE: EXECUTIVE COGNITIVE FUNCTIONING DEFICITS PREDICT SUSTAINED DRINKING IN THE FACE OF ALCOHOL-RELATED CONSEQUENCES

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Perseverative maladaptive behavior has been linked to deficits in executive cognitive functioning (ECF), and may occur when the brain fails to allocate the attention necessary for adjusting to new contingencies when confronted with an unexpected environmental event. It has been noted that a hallmark of alcohol abuse problems is persistent (perseverative) alcohol use despite serious negative consequences. Earlier research has shown linkages between ECF deficits and alcohol-related consequences, and we will extend this research by showing how these variables predict alcohol use over time. The present study hypothesized that, among those who experience more negative alcohol-related consequences, those with poorer ECF would sustain higher levels of drinking over time than those with better ECF. Data from 298 young adults were obtained over the course of a 5 year longitudinal study (average age at entry into study: ~18; average age at completion: ~23). Participants reported alcohol-related problems in the past three months and ECF was measured using the Wisconsin Card Sorting Test (WCST). A repeated measures ANOVA was used to examine change in drinking over the study period as a function of alcohol-related consequences and ECF. The results supported the hypothesis, showing that among those with high alcohol-related consequences, individuals with ECF deficits mature out of drinking more slowly than those with better ECF. These findings suggest that, compared to those with better ECF, individuals with ECF deficits fail to adjust behavior to avoid alcohol-related adverse consequences. This failure may contribute to the persistence of drinking despite these negative consequences.

0495

EXECUTIVE CONTROL MODERATES THE RELATIONSHIP BETWEEN ALCOHOL-RELATED INTERPRETIVE BIAS AND ALCOHOL USE

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Dual process models conceptualize (psychopathological) behavior as an imbalance between two distinct systems of information processing; a fast, impulsive, associative system and a regulatory executive system that can moderate the impact of the impulsive system. Alcohol (mis) use has been associated with several biases in the associative system, including an alcohol related interpretive bias; the tendency to associate ambiguous situations with alcohol use. The aim of the current study is to test a hypothesis derived from dual-process models that individuals with a relatively strong alcohol-related interpretive bias and weak executive control are most vulnerable for excessive drinking and drinking problems.
Participants were 93 students, who completed a new alcohol interpretive bias measure (alcohol Word Sentence Association Paradigm), an Operated Span task (measure of executive control), and the AUDIT and DMQ questionnaire.
Results revealed that, compared to individuals scoring low on those motives, individuals who drink to enhance their positive mood endorsed more alcohol interpretations in positive mood situations, and not in negative or neutral situations, while individuals who drink to cope with negative affect endorsed more alcohol interpretations in both negative and positive mood situations and not in neutral situations. Furthermore, alcohol-related interpretations were significantly correlated with AUDIT scores regarding drinking and drinking problems. Finally, as predicted, this relationship was moderated by executive control. As expected, alcohol-related interpretations predicted drinking and drinking problems more strongly in individuals with low executive control.
These findings are consistent with dual process models that argue that behavior can be conceptualized as the joint outcome of two processes. Alcohol use and associated problems were most strongly predicted by an alcohol-related interpretive bias, when not inhibited by executive control processes.

0496

CORRELATES OF USING ALCOHOL TO AID SLEEP IN ALCOHOL-DEPENDENT (AD) INDIVIDUALS

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Using alcohol as a sleep aid is common in the general population (6–13%), in people with insomnia (15–28%), and in AD individuals (40–60%). It has been suggested that such use is associated with relapse. We examined correlates of using alcohol as a sleep aid in 78 AD and 26 healthy control subjects (HCs) with no comorbid medical/psychiatric disorders, who were recruited from the community to participate in a sleep study. Among AD subjects, 42.3% reported using alcohol at least sometimes to aid sleep compared to no HCs ($p<.0005$), so analyses are limited to AD subjects. Using alcohol to aid sleep was associated with sleep disturbance (53% if Pittsburgh Sleep Quality Index [PSQI] >5 vs. 27%, $p=.02$), cigarette smoking (58% in smokers vs. 29%, $p=.008$), psychiatric severity ($p=.04$), adverse drinking consequences ($p<.0005$), severity of dependence ($p=.04$), craving for alcohol ($p=.001$), and diurnal preference (18% for a.m. preference vs. 52% for evening or intermediate types, $p=.007$). There were no differences in demographic variables, problem drinking duration, or age at onset of problem drinking between AD subjects who did and did not use alcohol to aid sleep. Stepwise logistic regression revealed that adverse drinking consequences, sleep disturbance, and craving remained as significant correlates. Of a subset of 47 AD subjects who completed follow-up interviews, nearly 60% returned to drinking within 12 weeks of completing their sleep studies. Paradoxically, abstainers were more likely than those who resumed drinking to have reported at baseline a history of using alcohol as a sleep aid (56% vs. 24%, $p=.035$). Study limitations include a low follow-up rate and a small sample of AD individuals who are not representative of treatment populations. In conclusion, AD individuals who do and do not use alcohol as a sleep aid can be distinguished in terms of sleep quality, drinking consequences, and craving. Further study is indicated to understand how clinical course is impacted. (Supported by R01AA016117.)

0497

DOES EXERCISE INCREASE ALCOHOL CONSUMPTION?

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Exercise and alcohol share many neurochemical effects. For example, the endogenous opioid system and the hypothalamic-pituitary-adrenal axis modulate a propensity for both alcohol intake and exercise. Similarly, the mesotelencephalic dopamine system mediates the rewarding/reinforcing properties of both alcohol intake and exercise. Thus, it is possible that exposure to exercise could alter neural or behavioral responses to alcohol. Consistent with this idea, exercise has been shown to reduce behavioral intoxication, raising the possibility that regular exercise may increase alcohol intake. Therefore, using a rodent model of voluntary alcohol consumption and a human analogue, we assessed the effect of exercise on alcohol intake.

For the animal model, adult female alcohol-preferring (P) rats either exercised in running wheels for 4 hours per day, 5 days per week, or remained sedentary. Following a one-hour break, half of the exercised rats and half of the sedentary rats were given access to alcohol for 17 h/day in a 2-bottle choice protocol (water or 15% ethanol v/v). Preliminary results indicate that exercised P rats consume more alcohol per day than sedentary controls. Potential underlying mechanisms, including exercise-induced changes in opioid receptor density and hippocampal neurogenesis are also being investigated.

In humans, we surveyed 205 undergraduate students and obtained self-reports of their drinking habits and exercise behavior. While drinking was unrelated to vigorous exercise, students who reported engaging in any moderate exercise reported drinking more on their peak drinking occasion in the past month. Frequency of moderate exercise (days per week) was also marginally associated with peak drinking. Finally, the average amount of time spent engaging in moderate exercise during exercise days was associated with consuming significantly more drinks per week and marginally more drinks per typical drinking occasion. Taken together this research provides preliminary support for a translational model of an association between exercise and alcohol consumption.

0498

TRANSITIONS IN AND OUT OF ATHLETIC INVOVLEMENT AND RISKY DRINKING

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Cross-sectional data suggests college athletes consume more alcohol and experience more general alcohol-related problems than those not participating in athletics (e.g., Nelson & Wechsler, 2001). To our knowledge, the current study is the first to use a longitudinal design to examine the extent to which the course of drinking and alcohol-related problems relates to involvement in intercollegiate athletics, including individuals who transitioned in and out of athletic involvement.

Participants were 3,720 college students from the Intensive Multivariate Prospective Alcohol College-Transitions Study who completed a survey every semester until their fourth year (see Sher & Rutledge, 2007). A series of repeated measures analyses were conducted to test for developmental differences among athletic groups on heavy drinking, frequency of intoxication, and alcohol-related problems.

Athletes vs. Non-athletes. Individuals with athletic involvement at either their freshmen or senior year were categorized as athletes; all other students were categorized as nonathletes. Individuals with athletic involvement at either time point showed sharper increases on all three outcomes between freshman and senior year than those with no athletic involvement ($p < .05$).

Starters vs. Stoppers. Individuals who were athletically involved at senior, but not freshman, year were classified as ''starters''; those who were athletically involved at freshman, but not senior, year were classified as ''stoppers''. Starters showed sharper increases on all three outcomes between freshman and senior year than stoppers ($p = .04$–$.06$).

Consistent Athletes vs. Inconsistent Athletes. Individuals who were athletically involved at both time points were classified as ''consistent athletes''; those who were athletically involved at only one time point were classified as ''inconsistent athletes''. Consistent athletes showed sharper increases on alcohol-related problems than inconsistent athletes ($p = .05$), but there were no differences on alcohol use variables.

These results indicate individuals who are more athletically involved tended to show sharper increases in problem drinking, and students who initiate participation in college athletics show sharper increases than those who cease participation. This project was supported by NIAAA Grants F31AA019596 to Andrew K. Littlefield, T32AA13526, R01AA13987, R37AA07231, KO5AA017242 to Kenneth J. Sher and P60 AA11998 to Andrew Heath.

0499

USING THE GENERAL UNIFIED THEORY TO PREDICT DRINKING BEHAVIOR AMONG NON-COLLEGE EMERGING ADULTS

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Nearly two-thirds of high school seniors transition to post-secondary experiences other than college; yet, a majority of the alcohol research and prevention initiatives targeting emerging adults focuses on the college population. Establishing a clearer understanding of the predictors, motives, and risk factors associated with alcohol use among this ''forgotten half'' of emerging adults is important, as these factors are the likely foci of future non-college-based alcohol prevention efforts. The General Unified Theory (GUT) is a helpful tool in gaining this understanding, as it provides an evidence-based conceptual framework for examining various psychosocial predictors of alcohol use (e.g., expectancies, norms, self-concept, intentions). The current study utilized the GUT to guide the examination of predictors of drinking behaviors and intentions among a nationally representative sample of non-college emerging adults. Participants were recruited from a pre-identified Internet panel (KnowledgePanel), which is designed to be representative of the general population of the United States, and maintained by the consumer information company Knowledge Networks (KN). To be eligible for the current study, panel members needed to be between 18 and 22 years old and have completed no more than a high school education. Forty percent of those who completed the screening survey met eligibility criteria and completed the web-based survey ($N = 264$), where they reported on factors related to alcohol use. A series of multiple regression analyses revealed that, individually, all five categories of predictors (expectancies, affect, norms, self-concept, and self-efficacy) had significant direct and indirect effects (through intentions) on alcohol use. Further exploratory factor analysis with these constructs revealed that a latent ''attitudes toward drinking'' factor, which included expectancies, affect, and injunctive norms, accounted for a majority of the variance in intentions to drink. The constructs measuring self-concept and self-efficacy were no longer significant when the resulting structural equation model was tested, as they only accounted for a small portion of the variance in drinking and intentions. Findings suggest that prevention initiatives designed for this population might benefit most from changing alcohol-related attitudes, especially positive alcohol expectancies, feeling favorable towards getting drunk, and perceived approval of drinking from peers.

0500

SUBJECTIVE RESPONSE TO THE FIRST DRINK IN SMOKERS AND NONSMOKERS: AN ECOLOGICAL MOMENTARY ASSESSMENT INVESTIGATION

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Alcohol and tobacco use are associated with one another, both within people and across moments. Investigators have used ecological momentary assessment to explore whether naturally-occurring co-use of both substances produces a unique profile of subjective effects. These studies have been limited to current smokers, and thus neglect potential differences in alcohol response between smokers and nonsmokers. The current study seeks to extend knowledge by comparing subjective responses to the first drink of alcohol in smokers and nonsmokers using data collected within users' natural environments. For three weeks, current smokers (n=259) and nonsmokers (n =145) completed real-time assessments of subjective state at random times across their waking hours and immediately after completing a first drink of alcohol in a drinking episode. First drink recordings also assessed explicit appraisals of alcohol reinforcement and punishment. Multilevel regression results revealed numerous statistically significant interactions between momentary drinking and smoking status. Specifically, smokers tended to show blunted changes in intoxication, positive affect, and drink craving in response to the first drink. These diminished responses were particularly evident in smokers who reported habitually consuming their first cigarette within 30 minutes of waking (an indicator of more severe tobacco dependence). Interestingly, analyses of drink appraisals revealed that smokers reported greater reinforcement and less punishment compared to nonsmokers. Results thus provide evidence for both diminished change in subjective states but enhanced valuation of alcohol effects among smokers. These processes may help to explain increased rates of alcohol use and abuse among smokers.

0501

EVENT-SPECIFIC RISK AND ECOLOGICAL FACTORS ASSOCIATED WITH PREPARTYING AMONG HEAVIER DRINKERS

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Preparty drinking is markedly different and can be more risk-enhancing than students' typical drinking patterns. Event-specific and ecological perspectives of prepartying can contribute to a richer understanding of the nuances and relative risks associated with the behavior. This research utilized a representative two-site sample of prepartiers who also reported a heavy episodic drinking event in the past month (n = 1,367). Specific objectives of this research were as follows: (1) compare event-specific Blood Alcohol Levels (BALs) and consequence outcomes as a function of the last drinking occasion where participants did not preparty and during their last prepartying event; (2) compare event-specific BAL and consequence outcomes within and between preparty and non-preparty occasions as a function of whether or not drinking games were also played during the event and as a function of the social context of the drinking environment (single sex / coed); and (3) examine the role of frequency of prepartying and BAL in predicting event-specific negative consequences. Results revealed that during a preparty event, participants drank significantly more, over a shorter duration, reached a higher BAL, and experienced significantly more negative consequences compared to the last occasion that they drank but did not preparty. Students who played drinking games when they prepartied had higher BALs and experienced more negative consequences than those who did not play games. Whether females prepartied in a single-sex or coed setting had little effect on their BALs. For males, however, their BALs were greater when they prepartied in a coed setting compared to a single sex setting. Moreover, participants reported more negative consequences when they prepartied in a coed setting than in a single-sex setting. Finally, regression analyses demonstrated that participants' BAL, frequency of prepartying and the interaction between BAL and frequency of prepartying all uniquely contributed to the prediction of alcohol-related negative consequences. As BAL increased, the number of negative consequences increased more sharply for those who prepartied infrequently, compared to those who prepartied frequently. All analyses were examined as a function of gender which revealed important gender effects and interactions. Interventions can be designed to intervene with high risk prepartiers by using BAL education emphasizing the impact of time-limited prepartying drinking.

0502

ALCOHOL AND NICOTINE: JOINT PHARMACOLOGICAL EFFECTS ON DRINKING AND SMOKING MOTIVATION

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Research has documented strong associations between alcohol and tobacco use, as well as high rates of comorbidity for alcohol and nicotine dependence. Despite the frequency with which these drugs are co-administered, little research has been conducted on the joint pharmacological effects of these substances on variables that may facilitate use. The present study examined the combined effects of these substances on craving to smoke and drink, as well as mood, among individuals with a wide range of alcohol and tobacco usage patterns. Participants (n = 87) completed four counter-balanced sessions. At each session, they consumed two beverages containing either a moderate dose of alcohol or equivalent placebo, and smoked a single nicotine or placebo cigarette, in a fully-crossed 2 x 2 design. Participants completed the Questionnaire on Smoking Urges – Brief, the Alcohol Urge Questionnaire, and the Mood Form immediately prior to and immediately following drug administration. Analyses revealed that nicotine significantly enhanced craving for alcohol immediately after drug administration, whereas alcohol had no effect. In contrast, nicotine and alcohol had opposing effects on craving to smoke for pleasurable effects, with nicotine suppressing craving and alcohol enhancing it. Similar trend-level effects were observed for craving to smoke to alleviate aversive effects, but were qualified by a significant alcohol by nicotine interaction revealing that nicotine did not reduce craving to smoke when combined with alcohol. Finally, nicotine was found to both enhance positive mood and decrease negative mood, but no effects for alcohol or alcohol by nicotine interactions were observed. Overall, these findings provide evidence for substantial cross-drug priming effects. The finding that nicotine enhanced craving to drink while alcohol had no effect provides some support for the idea that incorporating smoking cessation into alcohol treatment programs may have beneficial, rather than harmful effects on alcohol use outcomes. Furthermore, the lack of reduction in craving seen when nicotine was accompanied by alcohol may lead individuals to smoke more heavily while drinking, potentially enhancing dependence levels or fostering a progression to dependence in non-dependent smokers. Ongoing research into the combined effects of these substances may refine our understanding of how use and/or dependence on each drug is established and maintained.

0503

DAILY CRAVING REPORTS FROM DRINKERS NOT IN TREATMENT

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Aim: Craving is a central component in alcohol use disorders and most individuals who are dependent on alcohol experience craving (defined as a strong subjective drive to drink). Alcohol craving has been widely studied, although few studies have investigated how craving operates on a daily basis and no studies have investigated alcohol craving in non-treatment seeking participants. The purpose of this study was to describe the occurrence and key characteristics of craving in non-treatment seeking, heavy drinkers.
Methods: Ninety participants were recruited from primary care centers in Vermont and identified by primary care physicians as having at-risk drinking (based on NIAAA guidelines). Participants called an automated interactive voice response system (IVR) daily for 180 days and reported their alcohol use, craving, and life events and stressors. Participants rated craving on a scale of 0 to 9, with 0 being no urge to drink and 9 being the strongest urge ever.
Results: Participants called on a mean of 59% of days during the study and reported drinking alcohol on 72% of days. Participants reported experiencing craving on most (80%) call days. Participants reported craving on the majority (94%) of the days when they drank, compared to about half (46%) of days when they did not drink. Mean craving intensity was moderate (M=3.9) and the majority of craving ratings (89%) were low to moderate (1 to 6). There was a significant positive association (r=.421) between intensity of craving and the amount of alcohol drank on the same day, with higher levels of craving being associated with larger amounts of alcohol consumed (p<.01, n=9535).
Discussion: Daily process data from heavy drinkers in a primary care sample indicate that craving occurs nearly every day, and that craving intensity is associated with amount of same-day alcohol use. These data address a gap in the literature and describe the occurrence of daily craving in a non-treatment seeking, heavy drinking participant group. Further research examining the drinking-craving relationship would further improve our understanding of the natural course of craving.

0504

PHOSPHATIDYLETHANOL LEVELS IN SOCIAL AND BINGE DRINKING ADULTS BEFORE AND AFTER ALCOHOL ADMINISTRATION

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Phosphatidylethanol (PEth) is a direct metabolite of ethanol that accumulates in red blood cells and is a proposed biological marker for moderate to heavy alcohol consumption. The half life of PEth is reported to be 4 days. The purpose of this study of social and binge drinkers was to compare (1) PEth levels versus total drinks during the prior 1–8 days and (2) PEth levels before and after oral administration of a 1 g/kg dose of ethanol in a simulated binge in a human lab experiment. Participants were required to visit the lab several times during the study to receive either placebo or alcoholic drinks during the middle 2 hour period of a 6 hour session. Participants were required to have zero breath alcohol content at the beginning of each session and blood was drawn either before and after or only after each session. Uncoagulated blood samples were stored at −80 C until the day of assay. A time line follow back assessment of daily drinking during the prior several days was administered. PEth was quantified using HPLC with evaporative light scattering detection. PEth levels correlated with total drinks during either the prior 2, 3, 4, 5, 6, 7, or 8 days in a statistically significant manner ($p < 0.05$), but not with total drinks on the previous day. The highest correlation was observed for total drinks during the prior 5 days ($r = 0.52$; $N = 51$). During the human lab experiment, PEth levels increased by 461 ± 326 (SD) ng/mL at 2 hours after receipt of a 1 g/kg oral dose of ethanol. PEth levels did not change during the sessions when the placebo drink was administered (N = 3). These preliminary results support the use of PEth as a biochemical marker for ethanol consumption and suggest that PEth levels increase during ethanol consumption. (This study was supported by a grant from NIAAA to NH-K)

0505

WITNESSING DOMESTIC VIOLENCE AND TRAUMA-MEDIATED PATHWAYS TO ALCOHOL USE AND THE PERPETRATION OF DATING VIOLENCE IN ADOLESCENCE

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Limited research has examined a link between alcohol use and dating violence within adolescent samples despite high rates of heavy drinking and dating violence perpetration (DV-P) among individuals between the ages of 15 and 24. Moreover, although both problem drinking and DV-P have been linked to a history of childhood maltreatment (CM; physical, sexual, or emotional abuse, physical or emotional neglect, or witnessing physical or emotional domestic violence), few studies have examined the potential mechanisms of a relationship between these variables. The purpose of the current study was to extend past research by assessing the predictive role of childhood maltreatment in adolescent alcohol use and DV-P, as well as the temporal co-occurrence of these behaviours. It was hypothesized that trauma symptomatology would play a mediating role in these relationships. Data was collected from the longitudinal Maltreatment and Adolescent Pathways (MAP) study (N = 556, ages 14–17 at initial testing), which examines CM outcomes among adolescents recruited from child welfare in a major Canadian urban centre. Maltreatment history was assessed at the initial time point (T1), trauma symptomatology at 1.5-year follow-up (T2), and alcohol use and problem drinking as well as DV-P at 2-year follow-up (T3). Bivariate analyses demonstrated significant associations between several types of maltreatment and both alcohol use and problem drinking (r=.17, p<.01 to r=.40, p<.01) as well as between maltreatment and DV-P (r=.18, p<.05 to r=.30, p<.01); alcohol use variables and DV-P were also significantly correlated (r=.19, p<.05 to r=.28, p<.01). In addition, several subtypes of trauma symptomatology were found to be significantly associated with all three of these variables. Witnessing emotional domestic violence was the only maltreatment variable that was significantly correlated with both trauma symptomatology (depression, anger, and dissociation) and the co-occurrence at T3 of alcohol use (r=.38, p<.01) or problem drinking (r=.30, p<.01) and DV-P. Binary logistic regression identified witnessing emotional domestic violence as a significant predictor of the co-occurrence of both alcohol use and DV-P (B=.61, p<.01) and problem drinking and DV-P (B=.41, P<.01), even after controlling for trauma symptomatology. Results highlight exposure to domestic violence as an important risk factor in the development of maladaptive and dynamically related adolescent behaviours.

0506

WHAT IS STRESSFUL FOR HIV-INFECTED WOMEN? CHRONIC GLOBAL STRESS AND TRAUMA-RELATED STRESS AMONG HAZARDOUS/HEAVY DRINKERS IN HIV PRIMARY CARE

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Purpose: Global stress and specific trauma-related stress may independently influence alcohol consumption and alcohol-related problems among HIV-infected women. We examined the effects of both types of stress and their combined relationship to hazardous/heavy drinking and drinking related consequences.
Methods: Women were recruited from an urban HIV primary care clinic as part of a randomized trial of a brief alcohol intervention. We used the Perceived Stress Scale (PSS), a global measure of stress appraisal and the Impact of Events Scale-Revised (IESR), a measure of symptoms of posttraumatic stress disorder related to their most severe problem. AUDIT-C and Short Index of Problems (SIP) were used as alcohol outcomes. All logistic regressions were adjusted for age, education, race, employment status, living arrangements and drug use, including marijuana, opioids, cocaine, and benzodiazepines.
Results: HIV-infected women (n=387) were: median age 46 years, single 50%, 86% African American, 83% unemployed, 40% hazardous/heavy drinkers and 51% using drugs. Women with higher PSS scores were more likely to screen positive screen (≥3) on the AUDIT-C (OR=1.04; 95%CI, 1.01–1.07, p=.01); whereas no association between IESR scores and hazardous drinking was detected. Among hazardous/ heavy drinkers (n=153), IESR scores were associated with higher SIP scores (OR=1.04; 95%CI, 1.01–1.07, p=.006), whereas no association was found between PSS and SIP scores. In multivariable regression, higher IESR scores were associated with higher SIP scores (OR=1.11; 95%CI, 1.0–1.24, p=.05); neither the PSS nor the interaction between PSS and IESR was significant.
Conclusions: Different types of stress mediate alcohol use and alcohol-related problems among HIV-infected women. Chronic stress is associated with hazardous/heavy alcohol use among HIV-infected women. Trauma-induced stress does not appear to directly affect alcohol consumption. Among hazardous/heavy alcohol users, however, trauma specific stress, but not global stress, is associated with reporting alcohol-related problems.

0507

PREDICTORS OF RECENT DRINKING BEHAVIOR IN HEALTHY VOLUNTEERS AND ALCOHOL DEPENDENT POPULATIONS

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Previous research suggests that people with more years of education are more likely to be current drinkers (having had one or more alcoholic beverages in the past 90 days). The relationship between education and recent drinking behavior may be dependent upon multiple factors. The objective of this study was to examine the hypothesis that people with more years of education are drinking more within the 90 days preceding their admission into the study.
This study collected data from healthy social drinkers (N=92) and alcohol dependent patients (N=213) during their screening visits for alcohol studies at the NIAAA. Recent drinking history was assessed using the 90-day Time Line Follow Back (TLFB). Drinking days (DD), total drinks (TD), drinks per drinking day (DPD) and heavy drinking days (HD) were measured. Years of education, IQ measured by the Weschler Abbreviated Intelligence Scale, household income, age and gender were also recorded.
There were significant correlations between TLFB measures and our predictor variables of age, gender, IQ and years of education. For social drinkers, age was positively correlated with TD, DPD, DD, and HD (all p<.05). IQ and years of education were negatively correlated with TD, DPD, DD and HD (all p<0.05, except years of education which was p<0.05). For alcoholics, years of education was negatively correlated with TD and DPD. Age was positively correlated with HD and DD, while IQ was negatively correlated with HD and DD. Multiple regression analyses revealed that in the social drinkers, DD was negatively associated with IQ, with age and gender as significant covariates. TD and PD were negatively associated with IQ, with gender as a significant covariate. HD was negatively associated with IQ, with no significant covariates. In the alcoholics, TD and DPD were both associated with gender but not any covariates. HD was related to age, but not with any other covariates.
Results indicate that different factors influence the recent drinking behavior of healthy social drinkers and alcohol dependent participants. In social drinkers, IQ was negatively associated with all drinking measures. Alcoholics did not display an association between IQ and TLFB measures, however, gender and age were significantly associated with TLFB measures. The results of this study were contrary to our hypothesis but indicate that predictors of recent drinking may be different depending on the population being studied.

0508

EFFECT OF INTRAVENOUS ETHANOL ON HYPOTHALAMIC-PITUITARY-ADRENAL (HPA) AXIS HORMONES AND BETA-ENDORPHIN IN HEALTHY MALES

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The endogenous opioid system and HPA axis hormones have been implicated in alcohol consumption. Specifically, β-endorphin is involved in reward and reinforcement, and ACTH and cortisol are implicated in the anxiolytic properties of alcohol. Plasma level changes of these hormones in response to ethanol administration could serve as identifiable phenotypes for susceptibility to alcohol use disorders. The objective of this study was to examine the effect of IV ethanol on HPA axis hormones and β-endorphin and the influence of a functional mu-opioid receptor polymorphism (OPRM1 A118G) on this effect in healthy males. Healthy male social drinkers were screened to obtain two groups: (1) subjects homozygous for the major 118A allele (n=18); and (2) subjects carrying 1 or 2 copies of the variant 118G allele (n=13). Subjects were challenged in separate sessions with IV ethanol to a target breath alcohol level of 0.08% and placebo, and plasma levels of ACTH (adrenocorticotropic hormone), β-endorphin and cortisol were measured at four timepoints. Repeated measures ANOVA was conducted to examine the effect of treatment, time, genotype, and baseline levels on change in hormone levels. There was a significant main effect of treatment and time for change in ACTH, with a greater decrease in ACTH following alcohol compared to placebo. There was a treatment by baseline level interaction for ACTH, suggesting that baseline ACTH level is an important determinant of the ACTH-lowering effect of alcohol. There was a treatment by baseline interaction for change in β endorphin, suggesting that baseline β-endorphin level is an important determinant of the β endorphin-lowering effect of alcohol. Alcohol had no effect on change in cortisol, although there was a significant effect of baseline levels. OPRM1 A118G genotype was not a significant predictor of change in ACTH, β endorphin, or cortisol. The greater decrease in ACTH following alcohol is consistent with the stress-lowering effects of alcohol. However the greater decrease in β-endorphin following alcohol is inconsistent with the hedonic effects of alcohol. Given the strong baseline effects for ACTH and β-endorphin, this study highlights the importance of basal ACTH hormone and β-endorphin levels in regards to alcohol consumption and possibly vulnerability to alcohol use disorders.

0509

ASSOCIATION OF INTRAVENOUS (IV) ETHANOL SELF-ADMINISTRATION WITH HAZARDOUS AND HARMFUL USE AMONG HEAVY DRINKERS

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Nicotine dependence is highly prevalent among people with heavy drinking and/or alcohol use disorders and the amount of smoking directly correlates with level of alcohol consumption and the severity of alcohol problems. This study aims to evaluate IV ethanol self-administration behavior in smoking and non-smoking heavy drinkers. 37 male and female, smoking and non-smoking, heavy drinkers, aged 21–58 years, underwent a baseline Computer-Assisted Self-infusion of Ethanol (CASE) session as part of a medication study. Following protocol screening and medical evaluation, eligible participants underwent an initial IV ethanol self-administration session. The session consisted of an initial 25-min priming phase followed by a 125-min *ad-lib* phase, where subjects could press a button for short standardized ethanol infusions. Self-administration measures included peak breath ethanol level (BrTH), average BrTH (AvgBrTH) and number of button presses. Alcohol use disorder identification test (AUDIT) score was used to index hazardous and harmful alcohol use. Baseline plasma hepatic biochemical measures, γ-glutamyltransferase (GGT), alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), and bilirubin levels were also evaluated. There was a significant correlation among self-administration measures in this sample. MANOVA analysis indicated a significant effect of AUDIT score on self-administration measures. There was no effect of sex or smoking history; however there was a trend for association of peak BrTH with the Fagerström measure of smoking dependence and breath carbon monoxide (BrCOC) levels in smokers. AvgBrTH showed significant association with BrCOC. Drinking history and hepatic biochemical measures were not significantly associated with self-administration measures in this sample. Heavy drinkers demonstrated robust IV ethanol self-administration that was associated with hazardous and harmful alcohol use. There were no differences in self-administration measures between smokers and non-smokers in this sample. Future analysis will examine medication effects on self-administration measures and associated pathological consequences of heavy drinking.

0510

DIFFERENTIAL EXPOSURE AND DIFFERENTIAL VULNERABILITY FOR RACIAL/ETHNIC MINORITIES

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Purpose: The current study examined whether race/ethnicity a) was related to the likelihood of exposure to economic loss in the 2008–9 recession, and b) influenced associations between economic loss and heavy drinking and alcohol problems.
Methods: Data were from the 2009–10 National Alcohol Survey (*N*=5,382). Surveys assessed a range of moderate and severe economic losses. Drinking outcomes included total annual volume, monthly drunkenness, 2+ drinking consequences, and DSM-IV alcohol dependence. Analyses included linear and logistic regressions.
Results: Blacks and Hispanics were significantly more likely than Whites to report both job loss and trouble paying the rent or mortgage as a consequence of the 2008–9 recession. Housing loss showed a similar pattern, though effects for race/ethnicity were nonsignificant. Conversely, Whites were more likely than Blacks and Hispanics to report loss of retirement savings. All effects were robust in multivariate analyses, except that the differential risks for Hispanics were found to be at least partially attributable to state-level variation in unemployment. Further, interaction tests suggested that associations between exposure to severe recession-related loss (i.e., job and/or housing loss) and both drinking consequences and alcohol dependence were stronger among Blacks than Whites: Given severe loss, Blacks reported over twice the rates of 2+ consequences and dependence compared to Whites, whereas rates of alcohol problems were nonsignificantly *lower* among Blacks than Whites given moderate or no loss. Relationships between economic loss and all drinking outcomes were equivalent among Hispanics and Whites.
Conclusions: Results suggest greater exposure to economic loss for both Blacks and Hispanics (vs. Whites), and that the Black population may be particularly vulnerable to some of the negative effects of economic hardship on drinking problems. Findings are a signal to policy makers and service providers that racial/ethnic minorities may be at special risk for both financial and health problems during the recession.

0511

POTENTIAL ASSOCIATIONS OF OFFSPRING DRINKING PATTERNS TO MATERNAL ALCOHOL INTAKE DURING PREGNANCY

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Purpose: The adverse impact on offspring from heavy drinking during pregnancy has been well established. However, less is known about the effects of more modest maternal quantities and frequencies of drinking on future drinking patterns of offspring.
Methods: Data were gathered about maternal drinking and offspring alcohol outcomes using SSAGA interviews from 1104 maternal/offspring dyads (1.6 offspring/mom) from the COGA study. The mothers were asked to retrospectively report their substance intake during the relevant pregnancy, and for the 342 dyads where mothers drank during that pregnancy, her alcohol quantities and frequencies.
Results: The drinking mothers consumed alcohol an average of 2 times per month, with 2–4 drinks/occasion. During the relevant pregnancy, 10.0% had consumed an illicit drug, and 34.1% ever smoked a cigarette. The offspring, who weighed 911.0 (114.3) oz at birth, currently reported drinking 6.1 (3.77) usual drinks and 9.5 (4.88) max drinks/occasion, 60.2% had experienced 1+ alcohol problems, and 63.9% had a parent with an AUD. Maternal drinking (+/−) during a pregnancy did not relate to offspring max drinks (.03, p=.28), but correlated positively with offspring alcohol problems (.08, p<.01), as did maternal smoking (.09, p<.01) and the FH of an AUD (.10, p<.01). When those 3 variables were entered into a backward elimination regression, only FH significantly predicted offspring alcohol problems (β=.10, p=.001). Among the 342 drinking mother/offspring dyads, her max drinks (−.19, p<.001) and drinking frequency (−.20, p<.001) during pregnancy correlated negatively with offspring max drinks, as did maternal drug use (−.08, p<.05), along with FH (.10, p<.001) and offspring birth weight (.11, p<.001). When all 5 variables were evaluated in a regression predicting offspring max drinks, mother's max drinks (β= −.15, p=.02), her drug use (β= −.13, p=.04), and offspring birth weight (β=.14, p=.02) were significant.
Conclusions: While the presence of maternal drinking correlated positively with offspring alcohol problems, this may have reflected the FH of AUDs. Among those mothers who did drink during pregnancy, the more she drank, the lower the offspring's quantity per occasion. These results require further evaluation before definitive conclusions can be drawn.

0512

ADDICTION ETIOLOGY ACCORDING TO CURRENT ADDICTION SCIENTISTS

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Howard Kushner recently accused addiction scientists of paying ''scant attention'' to the wider cultural and environmental frames of addiction. To explore this, we interviewed 20 biological scientists engaged in addiction research on their current views regarding the etiology of addiction, including alcoholism, using qualitative methods to analyze the transcripts. Most respondents acknowledged that cultural and environmental components, such as: family/peer influence, glamorization in the media, and access to the substance, were nearly impossible to disentangle from biological factors. Though many desired the discovery of a discrete molecular mechanism, most expressed doubt that any one central pathway could be found. Several scientists expressed a sense of futility over the debate about the extent to which addiction is environmental vs. genetic. There was excitement about the new epigenetic understanding of addiction; one scientist termed the epigenetic lens as 100% environment and 100% genetic, rather than 50/50.
Furthermore, most of the conversations dealt with the tricky semantics of whether addiction should be termed a disease. In our sample, 40% agreed that addiction should be considered a disease, and 60% did not. Those that thought addiction was a disease felt that categorizing it as such would increase the number of future scientists willing to study it, would expand the scope of potential funding sources, and might ameliorate moral stigma and other barriers that prevent substance abusers and alcoholics from seeking treatment. Among the majority that did not think it a disease, the arguments against claimed: addiction is better termed a ''syndrome'' because disease implies concrete, measurable etiology, and there is none yet; the focus on ''disease'' may be a problem for treatment because it puts blinders on clinicians, prevents them from looking at their patients holistically, and tempts them to seek a magic pill as a ''cure''; and, addiction is a behavior that causes diseases (cancer, hepatitis, etc), it is not itself a disease.
Our findings reveal that addiction scientists, including those who focus on alcoholism, do indeed pay attention to the frames used by the soft sciences. Though situated within their own academic communities and limited by the lenses through which they view their data, addiction scientists' views are perhaps wider, less positivist and less reductionist than those they have been said to hold.

8. CONSEQUENCES OF ALCOHOL CONSUMPTION IN HUMANS

0513

DATING VIOLENCE, ALCOHOL, AND OTHER DRUG USE AMONG ADOLESCENTS AND YOUNG ADULTS

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One in ten U.S. high school students report being the victim of dating violence (DV). An emergency department (ED) visit provides an opportunity to screen adolescents and young adults for DV and provide interventions once identified. This paper describes DV (physical victimization and aggression) prevalence and correlates among adolescents and young adults screened in an ED. This paper also assesses DV risk and promotive factors among adolescents and young adults with alcohol misuse. Descriptive statistics for DV prevalence and correlates among baseline sample, and bivariate and multivariate analyses for DV risk and promotive factors among alcohol misuse subsample, were conducted. During the ED visit, 2156 patients ages 14–20 years (56.4% female, 71.6% Caucasian) presenting to a suburban ED were screened. Rates of past year DV were 16.0% (5.8% moderate DV; 10.2% severe DV). Examination of the overlap in past year DV aggression and victimization by sex showed that most females reported both aggression and victimization (44.9%) or aggression only (40.9%), with 14.2% reporting victimization only. In contrast, males were most likely to report victimization only (61.7%), with 34.2% reporting both and 4.2% reporting aggression only. DV markers were female sex, receiving public assistance, using substances (including cigarettes, alcohol, marijuana, other illicit drugs, and non-medical prescription drug use), and higher AUDIT and ASSIST marijuana scores. Among subsample of participants who screened positive for alcohol misuse (n=405; 18.8%; AUDIT-C >3 ages 14–17 and >4 ages 18–20), bivariate analyses showed that DV risk factors included negative peer influences and depressive symptoms, while promotive factors included positive peer influences, parent support, and community and school activities. Multivariate analyses showed salient DV markers were female sex (Adjusted odds ratio [A.O.R.] 1.82, 95% Confidence interval [C.I.] 1.04–3.18), greater AUDIT score (A.O.R. 1.05, 95% C.I. 1.00–1.11), and negative (A.O.R. 1.06, 95% C.I. 1.00–1.13) and positive peer influences (A.O.R. 0.88, 95% C.I. 0.78–0.98). Based on findings from a suburban ED, DV intervention approaches for adolescents and young adults should address alcohol misuse in particular, but also other drug use, as well as peer influences. (Supported by NIAAA #018122)

0514

HIGH-RISK DRINKING IN FIRST-YEAR COLLEGE STUDENTS: PATTERNS OF ALCOHOL AND ENERGY DRINK COCKTAIL CONSUMPTION

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A growing body of literature has highlighted the risky drinking practice of consuming alcohol and energy drink cocktails (AECs), a phenomenon popular among college student populations. Consumption of AECs has been linked to increased binge drinking and alcohol-related consequences. However, little is known about patterns of AEC consumption among first-year students, a population that tends to be at higher risk to dangerous drinking practices. Thus, the aim of the current study was to examine patterns of AEC consumption in a sample of first-year college students during their first semester. The sample consisted of 332 first-year students (53% male) screened as drinkers at a large, public university in the Northeastern U.S. Participants were asked to complete four web-based surveys that assessed AEC use and other stylistic drinking behaviors, alcohol use, and alcohol-related consequences on weekend drinking events (i.e. Friday and Saturday) in fall 2010, yielding up to eight drinking occasions per student. Results revealed approximately one-third (35.8%; n=119) of first-year students reported AEC use on at least one drinking occasion, with approximately 42% of AEC users reporting AEC consumption on two or more occasions. No gender differences in patterns of use were observed. AEC users reported drinking nearly two and a half drinks more than non AEC users, on average, and experienced significantly more consequences than non AEC users after controlling for typical alcohol use (ps < .001). Further, AEC users were more likely to engage in other stylistic drinking behaviors that serve to increase alcohol consumption and related harm (e.g., pregaming) and were less likely to engage in protective actions that serve to reduce alcohol use and related harm (e.g., pacing drinks, setting drink limits), all ps < .05. This study extends current research on AEC use by highlighting patterns of this risky drinking behavior among first-year students as well as through documenting the associations between AEC use and other stylistic drinking behaviors. Notably, the prevalence rate of AEC use found in the current study is higher than found in other college samples, which suggests first-year students are at elevated risk for this behavior. This is especially concerning given AEC use was found to be linked to increased consumption, more alcohol-related consequences, greater use of other alcohol-related risk behaviors, and less frequent use of protective drinking behaviors.

0515

THE SUBJECTIVE PHYSIOLOGICAL, PSYCHOLOGICAL, AND BEHAVIOURAL RISK-TAKING CONSEQUENCES OF ALCOHOL AND ENERGY DRINK CO-INGESTION

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The increasingly popular practice amongst adolescents and young adults of consuming alcohol mixed with energy drinks (AmED) has raised concern regarding potential increases in maladaptive drinking practices, negative psychological and physiological intoxication side-effects, and risky behavioural outcomes. Comparison of user types has revealed that AmED users report engaging in greater risk-taking behaviour relative to alcohol users. However, the comparative likelihood of risk-taking according to session type (i.e., AmED versus alcohol session) remains relatively unknown. Thus, the current study was designed with the aim of establishing the subjective physiological, psychological, and behavioural risk-taking outcomes of AmED consumption relative to alcohol consumption for AmED users drawn from the general population. Between May and June 2011, 403 Australians aged 18–35 who had consumed AmED and alcohol only in the preceding six months completed a 10–30 minute online survey about their use of these substances. Despite participants consuming a significantly greater quantity of alcohol in AmED sessions compared to alcohol sessions, the odds of participants experiencing disinhibition and engaging in 26 risk behaviours were significantly lower during AmED sessions relative to alcohol sessions. Similarly, the odds of experiencing several physiological (i.e., speech and walking difficulties, nausea, and slurred speech) and psychological (i.e., confusion, exhaustion, sadness) sedation outcomes were less during AmED sessions compared to alcohol sessions. However, the odds of enduring physiological (i.e., heart palpitations, sleep difficulties, agitation, tremors, jolt and crash episodes, and increased speech speed) and psychological (i.e., irritability, tension) outcomes potentially related to over-stimulation were significantly greater during AmED sessions than alcohol sessions. Thus, co-ingestion may provide a double-edged effect. The increased stimulation from energy drinks may negate some intoxication-related sedation side-effects by increasing alertness. However, it could also lead to negative physiological side-effects associated with over-stimulation. Notwithstanding any stimulatory effects of energy drinks, risk and negative effects of excessive alcohol consumption were present in both session types. Objective measurement of behavioural risk-taking via laboratory-based measures could confirm the causal relationship between AmED and risk-taking.

0516

ENHANCED ACUTE TOLERANCE TO SUBJECTIVE EFFECTS WHEN ALCOHOL IS COMBINED WITH ENERGY DRINKS

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Acute Tolerance (AT) refers to the observation that alcohol-induced impairment is greater on the rising limb of the blood alcohol curve, compared to the declining limb, even when BACs are similar. AT does not develop to all effects of alcohol but reliably occurs for subjective feelings of intoxication, one variable that may lead to impaired driving (Marczinski & Fillmore, 2009). There is a new trend of mixing energy drinks with alcohol. Alcohol energy drink (AED) consumers have high rates of impaired driving and experience increased rates of accidents and injuries compared to alcohol alone consumers (Arria et al., 2010). AED beverages enhance feelings of stimulation in users, compared to alcohol alone (Marczinski et al., 2011, 2012). Therefore, AED beverages appear to alter subjective state and these changes might alter the development of AT. Therefore, the purpose of this study was to determine if AED beverages enhance the development of AT to alcohol compared to alcohol alone. Using a within-subjects design, 12 social drinkers were recruited to participate in this study where participants received alcohol (0.65 g/kg), energy drink (3.57 ml/kg), AED, or placebo in random order. Dose administration was double-blind. Following each dose administration, participants completed a behavioral control task (cued go/no-go task) and subjective measures on both the ascending and descending limbs of the BAC curve. The subjective measures included various assessments including ratings of sedation/stimulation and willingness to drive. Mean BACs during testing were .07g% for the ascending and descending limb tests for both the alcohol and AED conditions. The results revealed that alcohol impaired task performance equally on both limbs. For the subjective measures, development of AT was quite pronounced for the AED condition, compared to the alcohol condition. For the AED condition, participants reported feeling less sedated and more willing to drive, compared to the alcohol alone condition, particularly on the declining limb test. The results of this study suggest that AEDs may increase the development of AT to alcohol. Given that AT to alcohol is thought of a risk factor for future alcohol dependence problems, this study suggests that AEDs may be enhancing the abuse potential of alcohol. Research supported by NIAAA grant R15 AA019795.

0517

PATTERNS OF ALCOHOL USE AND EXPECTANCIES PREDICT SEXUAL RISK TAKING IN A COMMUNITY SAMPLE OF SOCIAL DRINKING WOMEN

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Although alcohol and sexual risk taking are associated (Brown & Vanable, 2007; Theall et al., 2007), not everyone who drinks alcohol engages in such behavior. A more nuanced assessment of the specific patterns of drinking behavior and alcohol expectancies is needed to understand who is at greatest risk of sexual risk taking to guide future interventions. The purposes of the present study were to (1) identify patterns of alcohol use behaviors and expectancies in a community sample of women, and (2) determine how these patterns are associated with indices of sexual risk. Background data was analyzed from 758 female social drinkers, aged 21–35, who were not abstainers or problem drinkers. Measures included typical alcohol consumption, alcohol expectancies, sexual behaviors, and attitudes toward casual sex and condom use. Latent profile analysis was used to determine underlying latent groups based on alcohol use behaviors (i.e., quantity, frequency, number of heavy episodic drinking episodes) and expectancies (i.e., social/physical pleasure, social expressiveness, sexual enhancement, cognitive/physical impairment, careless unconcern). Four patterns emerged: light drinkers/low expectancies (Class 1; $n = 110$), moderate drinkers/average expectancies (Class 2; $n = 227$), light drinkers/negative expectancies (Class 3; $n = 388$), and heavy drinkers/positive expectancies (Class 4; $n = 33$). ANOVAs using the Tukey-Kramer procedure for pairwise comparisons were conducted to examine differences in sexual risk among these classes. Classes 2 and 3 had the least positive beliefs about condom use whereas Classes 2 and 4 had the most positive attitudes toward casual sex. Class 4 had the most sex partners in the previous year and drank more often before sex. Classes 3 and 4 reported greatest subjective intoxication prior to sex. There were no differences among classes on frequency of sex, proportion of times a condom was used in the past 3 months, or lifetime number of sex partners. Results suggest that distinct classes of social drinking women differ with respect to sexual risk taking. Interventions could be improved if they target women's specific drinking and associated sexual risk behavior patterns.

0518

LONGITUDINAL ASSOCIATIONS BETWEEN PROBLEMATIC ALCOHOL USE AND RISKY SEXUAL BEHAVIOR FROM ADOLESCENCE TO ADULTHOOD

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The relationship between alcohol use and risky sexual behaviors is complex and may vary based on gender and race. The goal of this longitudinal study was to examine the influence of early alcohol use and sexual behavior on trajectories of risky sex and problematic use into adulthood; interactions with gender and race were also analyzed. Data came from 1,867 adolescents living in the Buffalo, NY area (50% female; 47% African American, 53% European American), surveyed up to 5 times between ages 13 and 30.
Results indicated that alcohol use and risky sex are reciprocally linked, but these relations are moderated by both gender and race. Controlling for age of sexual debut, baseline use predicted higher initial levels of sexual partners, sex with a stranger, and one-night stands. Growth patterns showed that initial differences in sexual partners dissipated over time, whereas differences in sex with a stranger increased through the mid-20s before abating. Men's use predicted sexual risk during adolescence, whereas women's use emerged as a risk factor later in adulthood. Whites' use positively predicted risky sex across time, whereas Blacks' use predicted more risky sex mainly during adolescence. At the same time, baseline sexual behavior predicted higher initial levels of typical use, heavy use, and drinking problems, controlling for age of heavy drinking initiation. Again, these differences attenuated into adulthood, but did not disappear completely. Only race moderated these effects: Sexual behavior positively predicted use among Whites, but for Blacks, having more partners showed evidence of being protective against problematic use.
Outcomes revealed a reciprocal pattern of association between alcohol use and sexual behavior that diminished across development, but was still evident at 30 years old. Use was a stronger predictor of risky sex for men in adolescence, but for women in adulthood, suggesting that the relationship between these behaviors differs over time for men and women. Furthermore, use and sexual behavior were positively related among Whites, but showed a complex pattern among Blacks. Most notable is the finding that more sexual partners were associated with less use among Blacks, suggesting that sexual opportunity may inhibit Blacks' use. These results indicate that prevention efforts for both alcohol use and risky sex should account for the other behavior to be most successful, as well as consider the moderating influences of gender and race.

0519

THE EFFECT OF HEAVY ALCOHOL USE ON HIV VIREMIA DETECTABILITY AND CD4 COUNT AMONG A CLINICAL COHORT OF HIV-INFECTED MEN WHO HAVE SEX WITH MEN (MSM)

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A. Heavy alcohol use among HIV-infected MSM has been associated with increased sexual risk, immunodeficiency, and suboptimal antiretroviral adherence. Lack of virologic suppression among those engaging in unprotected sex can result in HIV transmission. The implications of intermittent or chronic heavy alcohol use among this group are unclear.
B. 201 HIV-infected MSM were recruited from a community health center in Boston, and completed assessments at baseline, 3, 6, 9, and 12-months. Only participants taking antiretroviral therapy (ART) at 12-months were included in the current analysis (n=173). The primary dependent variable was plasma HIV viremia detectability [viral load (VL); dichotomized at ≤75 or >75] and the secondary dependent variable was CD4 count (continuous), both at 12-month follow-up. Heavy alcohol use was defined as consuming 5 or more drinks/day at least once a week in the past 3 months. The primary independent variable, chronicity of heavy alcohol use, was categorized as (1) no heavy alcohol use, (2) intermittent use (between 1 and 3 study time points), or chronic use (during at least 4 study time points). Analyses were conducted using logistic regression (VL) and linear regression (CD4 count) with multiple imputation.
C. The multivariable models for both outcomes each controlled for past four-day ART adherence at 12-month follow-up, depression, age, and intervention status. For VL, in the model that also controlled for VL at baseline, those reporting chronic heavy alcohol use (compared to those with no use) had an increased odds of having a detectable VL (OR: 5.93; CI: 1.28–27.55). However, in the final model, which also controlled for length of time on ART, the effect was not significant (OR: 3.37; CI: 0.50–22.77). For CD4 count, in the final regression model which also adjusted for length of time on ART and CD4 count at baseline, those reporting intermittent heavy alcohol use (compared to those with no use), on average, had a significantly lower CD4 count at 12-months (β: −81.20; CI: −152.82, −9.58).
D. Findings indicate that intermittent heavy alcohol use may affect HIV-infected MSM's CD4 counts. Although unmeasured confounding (e.g., changes in ART regimens, prior non-adherence, etc.) could partially explain this finding, and it is not clear if this is primarily due to alcohol-mediated non-adherence or a direct biological effect, interventions should consider focusing on the length of time and volume of alcohol use among HIV-infected MSM.

0520

ALCOHOL CONSUMPTION AND UNPROTECTED SEXUAL INTERCOURSE IN YOUNG ADULT FEMALE EMERGENCY DEPARTMENT PATIENTS

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We examined the relation between alcohol consumption and unprotected sexual intercourse among young adult AUDIT-C positive female Emergency Department (ED) patients. Using a structured, web-based timeline followback procedure, 26 participants reported their alcohol and sexual events over a 28-day period. A median (IQR) of 5 (2–6) drinks were consumed over a median of 3 (1–5) days, with a median of 2 (1–2) drinks per drinking episodes. A median of 4 (1–10) sexual intercourse episodes were reported, with a median of 2 (0–6) without condom use. Among individual participants, 42% always using condoms, 50% never used condoms, and 8% used condoms some of the time. There was no association between total sexual encounters or risky sexual behavior and alcohol consumption variables using global and event-level analysis. Consistent with prior studies of other populations, alcohol consumption does not seem to be directly associated with unprotected sexual intercourse in a population of hazardous drinking female ED patients. We will examine baseline demographic and cognitive-behavioral factors associated with risky sex.

0521

ALCOHOL USE AND WOMEN'S SEXUAL BEHAVIORS; RETHINKING HIV RISK FACTORS IN AN EMERGENCY DEPARTMENT AT THE US/MEXICO

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Objectives: For women, unsafe heterosexual sex is the leading cause of HIV transmission. Screening for sexual behaviors that increase HIV risk informs prevention programs aimed at reducing HIV risk. This study was designed to determine risk factors for HIV among sexually active women patients in the Emergency Department and to explore relationships between risk factors.
Methods: After IRB approval, medical students obtained consent and interviewed all available sexually active female patients (18–64 years old) during hours 5–9 PM (June-August 2010) using a composite of questions from 3 previously published HIV risk questionnaires, concerning HIV risk factors and perception of HIV risk. Data were double entered and all discrepancies were resolved. Statistical analyses utilized logistic regression to estimate odds ratios for each exposure variable.
Results: Complete questionnaires were completed on 65 women; average age 34, 18% in Spanish. Injection drug use was reported as an HIV risk behavior by only one participant. Unsafe heterosexual sex was reported by the majority of women. 'At risk' alcohol use (above NIAAA guideline) was found to be the single factor predicting unsafe heterosexual sex. Age was not an independent factor predicting unsafe heterosexual sex. Of those who reported "at risk' alcohol use, 61.1% reported sexual encounters with high risk persons and/or in high risk situations, 55.6% had sexual encounters in risky locations, and 94.4% had sex after alcohol or substance use. Of those who reported not using alcohol "at risk" 27.7% (OR= 5.59, P=0.005), 15.2% (OR= 7.29, P=0.002) and 25.0% (OR= 52.7, P= < .001) reported sex with risky person/situations, in risky locations or after alcohol/drug. Concern about HIV risk was equal between those drinking at risk and those not drinking at risk, 48.8% vs. 50.0% respectively (OR=0.95, P=0.931). While there was a trend toward more condom use among 'at risk' alcohol users, a minority in each group reported always using condoms (13.6% vs. 27.8%) (OR =2.76, P=0.152).
Conclusion: In an ED at the US-Mexico border, survey of sexually active female patients confirmed unsafe sex as a major HIV risk factor and showed that 'at risk' drinking is associated with increased unsafe heterosexual behavior. This survey suggests that at the US-Mexico border alcohol reduction and HIV prevention programs should focus on addressing the link between alcohol use and unsafe sex and aim at reducing both.

0522

THE ROLE OF HAZARDOUS DRINKING AND CRACKCOCAINE USE IN EXCHANGING SEX AMONG INNER-CITY WOMEN

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Individuals who drink alcohol may also use other drugs that enhance the risk of HIV infection. There is dearth of research on of the interactive influence of crack cocaine and alcohol use on high-risk sexual behaviors, such as exchanging sex. Women who exchange sex are particularly at higher risks of HIV infection. The present study examines the role of hazardous drinking and crack cocaine use in exchanging sex among inner-city women.
This was a cross-sectional analysis of 567 female participants recruited through street outreach, posted advertisements and network referral in Baltimore, MD, USA for an HIV prevention study. The primary outcome was exchanging sex, which was defined as having a sex partner that participant had sex with in exchange for drugs, money, shelter, or food in the last 3 months. Hazardous drinking was assessed through the Alcohol Use Disorders Identification Test (AUDIT) using score>=8 as cut-off point. Crack cocaine use during the past 3 months was also assessed. A 4-level categorical variable of hazardous drinking and crack cocaine use was "no hazardous drinking and no crack cocaine use," "crack cocaine use only," "hazardous drinking only" and "hazardous drinking and crack cocaine use." Logistic regression models were conducted to assess the associations between hazardous drinking and crack cocaine use and exchanging sex.
Over one quarter of the participants (25.8%) reported exchanging sex in the last 3 months. Almost two-thirds (32.5%) used crack cocaine but did not report hazardous drinking, 8.8% only engaged in hazardous alcohol use, and 22.4% reported hazardous alcohol use and crack cocaine use. Among crack cocaine users, 40.8% engaged in hazardous drinking. The prevalence of crack cocaine use among hazardous drinkers was 71.8%. Results from the multivariate logistic regression model indicated that after adjusting for sociodemographic background, exchanging sex was significantly associated with crack cocaine use only (AOR: 2.94, 95%CI: 1.76,4.89) and concurrent hazardous drinking and crack cocaine use (AOR: 2.57, 95%CI:1.49, 4.44). The exchanging sex was marginally significantly associated with hazardous alcohol use only (AOR: 2.01, 95%CI: 0.98,4.14).
Results of this study suggest exchanging sex among inner-city women is associated with both crack cocaine use and hazardous drinking. Results of this study highlight the importance interventions on sexual risks and alcohol and crack cocaine use in the context of commercial sex.

0523

EXPLORING THE RELATIONSHIP BETWEEN ALCOHOL CONSUMPTION, BMI AND RESTRAINED EATING ATTITUDES: IMPLICATIONS FOR DIABETES RISK

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Diabetes is a leading cause of death and significant public health concern in the U.S. Interestingly, moderate alcohol use may confer a beneficial effect on diabetes relative to abstinence or heavy consumption (Rehm et al., 2003). This U-shaped relationship stands in contrast to the linear association between alcohol and a key risk factor for diabetes: obesity. Specifically, alcohol use may contribute to weight gain through failure to offset alcohol calories in total daily caloric intake (Hetherington et al., 2001) as well as acute disinhibition (increased eating while/after drinking; Caton et al., 2004). However, findings regarding the alcohol-obesity relationship are inconsistent, perhaps due to other factors such as restrained eating attitudes. Such attitudes are known to promote a cyclical pattern of dieting and over-consumption, which may contribute to obesity (Polivy & Herman, 1985). Given the significant harm related to diabetes, the purpose of this study was to explore the relationship between three factors associated with diabetes risk—alcohol consumption, body mass index (BMI) and restrained eating attitudes. It was hypothesized that abstainers and heavy drinkers would report higher restrained eating attitudes, which would in turn be associated with higher BMIs.
Undergraduate students were invited via email over the fall and winter quarter to complete a web-based survey as part of a larger study on daily associations between alcohol use, expectancies and consequences. Of the 1409 individuals who consented, 1335 provided data relevant to the current study (62% Female, Age: M=19.53, SD=1.18). As predicted, a curvilinear relationship was found between total drinks consumed per week and restrained eating attitudes, $F(2, 1303)=4.20$, $p=.001$; however, subsequent analyses revealed that heavy drinkers were driving this effect and a linear model more accurately described the data, $r=.06$, $p=.04$. Consistent with hypotheses, a positive linear association was found between restrained eating attitudes and BMI, $r=.12$, $p<.001$, and between alcohol consumption and BMI, $r=.07$, $p=.02$.
Consistent with prior research, greater restrained eating attitudes and higher levels of alcohol consumption were associated with higher BMIs. In this sample, heavier alcohol use was also associated with higher restrained eating attitudes. Alcohol interventions that target decreasing these attitudes along with heavy alcohol use may help decrease diabetes risk among emerging adults.

0524

A LATENT CLASS APPROACH TO CHARACTERIZING ADOLESCENTS WHO PLAY DRINKING GAMES: ARE ALL GAMERS ALIKE?

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Heavy alcohol use and its associated negative consequences continue to be an important health issue among adolescents. Of particular concern is participation in risky drinking practices such as drinking games. While retrospective accounts indicate that participation in drinking games is common among high school students, very little is known about the characteristics of drinking game participation in this population. Thus, utilizing data from a sample of high school students who reported current drinking game participation (N=178), we used latent class analysis to investigate the negative consequences directly resulting from playing drinking games. Subsequently, we examined the underlying demographic and alcohol-related behavioral characteristics of gamers as a function of these classes. A three-class model (aBIC=970.8) was chosen which consisted of the following: (a) a "low-risk" group (n=121) who had a lower probability of endorsing negative consequences compared to the other groups, (b) an "over-consumption" group (n=34) who reported they experienced hangovers, became rude, obnoxious, or insulting, got physically sick, and experienced difficulties limiting their drinking as a result of playing drinking games, and (c) a "sexual regret" group (n=21) who reported that they engaged in unplanned sexual activity that they later regretted and were unable to recall large stretches of time resulting from playing drinking games. Comparisons among the three groups revealed that compared to girls, a higher proportion of boys were in the "over-consumption" and "sexual regret" classes, while the inverse emerged for the "low-risk" class. Results also indicated that the "low-risk" group consumed less drinks in a typical drinking game session compared to the other two groups. Additionally, the proportion of gamers who reported that they pregamed at least once in the past month was higher in the "over-consumption" class, compared to the "low-risk" and "sexual regret" classes. The present findings suggest that students who participate in drinking games are a heterogeneous group. They differ in terms of their participation on other risk behaviors, and the negative consequences they experience as a result of playing drinking games. Additional research is needed to determine if they also differ in terms of their response to prevention or intervention efforts.

0525

ALCOHOL USE AND PSYCHOSOCIAL FACTORS ASSOCIATED WITH DEPRESSION SEVERITY IN PREGNANT ADOLESCENTS

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While national rates of teenage pregnancies have declined in recent years, rates of depression are twice as high among pregnant adolescents when compared to pregnant adults. Adolescent depression during pregnancy is associated with increased morbidity for the teen and her infant as well as costs to society. Despite these higher rates of depression, there is little understanding of identifiable factors that contribute to depression in this vulnerable population. Alcohol and drug use have been implicated in adolescent pregnancy and shown to contribute to compromised psychological well-being during pregnancy. This cross-sectional study examined the correlates of depression severity among a pregnant adolescent population, specifically, exploring the relationship of reported history of alcohol use, history of drug use, history of depression, and history of abuse (physical or sexual) on depression severity in 116 pregnant adolescents (56% Hispanic; mean age = 16; mean gestational age = 20 months) who attended an inner-city prenatal clinic. Participants completed the Children's Depression Rating Scale (CDRS) as a measure of depression severity. Items assessing history of substance use (e.g., ''Have you ever had an alcoholic drink?'') and history of physical/sexual abuse (e.g., ''Has someone forced you to have a sexual experience in your lifetime?'') were correlated with scores of depression severity (CDRS). Multivariable linear regression was used to estimate slopes for CDRS-T scores. Ever having had an alcoholic drink was a significant predictor of higher CDRS scores in the bivariate analysis, β = 3.3 (0.8, 5.7); p < 0.05. History of abuse was associated with a significant 4.3 point higher mean CDRS score in the bivariate analysis, β = 4.3 (1.8, 6.7); p < 0.001, and remained a statistically significant predictor of more severe depressive symptoms (higher CDRS score) after adjustment for history of alcohol use, history of drug use and history of depression. This study identified that a history of physical or sexual abuse is a significant factor related to the severity of depressive symptoms in pregnant adolescents, independent of a history of substance use or depression. Efforts to identify adolescents at-risk for antenatal depression should include an assessment of history of alcohol use as well as abuse history. Identification of risk factors during this already vulnerable time for this group could better inform assessment and prevention efforts.

0526

CRITICAL INFLUENCE OF PREVIOUS ALCOHOL CONSUMPTION ON ISCHEMIC STROKE AND THROMBOLYSIS

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Although alcohol consumption is a risk factor for stroke, the impact of alcohol consumption on the progression of ischemic lesions remains barely investigated. Besides, the effects of alcohol consumption on thrombolysis (the only approved acute treatment for ischemic stroke which consists in the injection of recombinant tissue plasminogen activator, tPA, to dissolve the blood clot) have not been studied to date.

Here, we have evaluated the influence of different patterns [uninterrupted (''chronic'') or intermittent (''cycles'') drinking] of chronic alcohol consumption (p.o., alcohol 10% diluted in drinking water during 6 weeks) on (i) the progression of brain lesions after stroke, and (ii) thrombolysis. Mice were subjected to thromboembolic ischemia through direct injection of thrombin into the middle cerebral artery. Twenty min after the stroke onset, a subgroup of mice was thrombolysed (i.v. tPA), and another one was injected with saline.

Alcohol-exposed mice (both uninterrupted and intermittent exposures) showed higher final lesion volumes than control animals (78% and 44% increase respectively). As expected, thrombolysis reduced final lesion volumes in control animals (65% reduction *versus* control-saline mice). However, thrombolysis lost its beneficial effect after both types of alcohol consumption.

We detected changes in several coagulation factors (prothrombin ratio, factor V, factor VIII and platelet number) in alcohol-exposed mice, suggesting liver damages induced by these alcohol exposure protocols. By contrast, we did observe neither changes in endogenous tPA levels nor changes in the capacity to form/dissolve clots after alcohol exposure. We detected decreased levels of low-density lipoprotein receptor-related protein (LRP-1) and the inhibitor of tPA, PAI-1 (both implicated in tPA clearance) in the liver of alcoholised mice (both kinds of alcohol exposure). We thus hypothesize that alcohol could reduce the liver clearance of tPA and in case of thrombolysis, tPA would thus remain longer in the blood, which could be deleterious for the brain parenchyma.

In conclusion, here we show that previous alcohol consumption has a deep impact on the progression and the final extent of ischemic lesions, as well as on the efficiency of thrombolysis. Here we report the first evidence showing that alcohol misusers represent specific sub-populations of stroke patients, for whom acute treatment must be adjusted accordingly.

0527

A MODEL OF TRAIT-BASED AFFECTIVE PROCESSES IN ALCOHOL-INVOLVED RISK BEHAVIOR AMONG COLLEGE STUDENTS

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Alcohol use is associated with alcohol-related problems, but consumption accounts for only a portion of the variance of such problems. Affect dysregulation plays a role in both alcohol use and related problems. Several studies have shown trait positive affect (PA) is related to use, and negative affect (NA) is related to problems after controlling for use. Positive (PU) and negative urgency (NU) are also independently associated with substance-related problems over and above use, and may moderate relationships between affect and alcohol variables. Individuals low in distress tolerance may also seek rapid methods for alleviating emotions and thus use more alcohol. This study examined relationships between trait affect, distress tolerance, and urgency traits on ''typical'' alcohol use, high-level, single occasion drinking, and risk behavior. Participants were 545 college students. We tested a SEM with three alcohol variables: ''Typical'' alcohol use, ''blackout'' drinking,'' and risk behavior. The full model fit the data well, χ^2 = 766.38, p < .001, RMSEA = 0.032 (CI: 0.028 – 0.037), CFI = 0.96, WRMR = 0.97. NA was positively associated with both negative and positive urgency, while PA was inversely associated with both urgency constructs. Distress tolerance was negatively associated with NU.NU exhibited a direct, positive association with risk behavior and mediated the associations between both NA and distress tolerance and risk behavior.PA and PU both directly predicted ''typical'' alcohol use and exhibited indirect associations with risk behavior via the effects on drinking level. Conclusions: High trait negative affect and low tolerance for affective distress contribute to difficulty controlling behavior when negatively aroused and this is directly associated with increased risk behavior when drinking. In contrast, associations between positive urgency and risk behaviors are indirect via increased alcohol consumption. Positive associations between positive affectivity and the drinking outcomes were offset by inverse associations via urgency, resulting in an insignificant total effect. These findings contribute important information about the distinct pathways between affect, alcohol use, and alcohol-involved risk behavior among college students.

0528

ALCOHOL MEDIATION ROLE IN THE RELATIONSHIP BETWEEN PERSONALITY AND INTERNET USE

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Previous research has shown that Internet addiction and problematic alcohol use are related, and that both these behaviors are related to the BAS fun-seeking subscale (Yen et al., 2009; Ko et al.; 2008). Although these behaviors are related and likely share a common underlying personality risk factor, no research has yet to determine which personality traits are most likely to be uniquely related to both these behaviors, nor has research addressed how alcohol use might mediate the relationship between personality and Internet use. The goal of this project is to (1) determine which impulsivity factors are predictive of both Internet use and alcohol use, using the UPPS-P Impulsive Behavior Scale (Lynam et al., 2009), (2) determine which personality factors predict both Internet use and alcohol use, using the Five Factor Model (via the NEO Personality Inventory – Revised, Costa & McCrae, 1992), and (3) investigate how alcohol use might mediate the relationship between personality and Internet use, as consistent with other risk research (see Dir & Cyders, 2010). Six hundred eleven college students at a public mid-western university participated in the study (78% female, 22% male). They were all sampled through online survey during the school year of 2010 to 2011; their age ranged from 18 to 51 (mean = 21.2, SD = 5.403) and most participants were Caucasian (77%). We conducted a series of hierarchical regressions, as well as a product of coefficients test of mediation to test study hypotheses. Results showed that positive urgency, the tendency to act rashly in response to a positive emotional state, Extraversion, and Conscientious were common predictors of both Internet Use and Alcohol use. Mediation tests indicate partial mediation of the relationships between these personality traits and Internet use by problematic alcohol use: Indirect effect of PUR through alcohol use (z = 2.31 p=.02), of Extraversion through alcohol use (z = 2.48, p = .01), and Conscientiousness through alcohol use (z= –2.57, p = .01). Although cross-sectional in nature, the data is consistent with the theory that multiple behaviors of risk are predicted by common personality factors, and that, at least in part, alcohol could be increasing the risk for potentially problematic Internet use.

0529

INTERACTIVE EFFECTS OF AGING AND ALCOHOL CONSUMPTION ON SIMULATED DRIVING

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Introduction. Protective effects of a moderate drinking lifestyle are frequently reported, particularly for older adults. Critically, the potential deleterious effects of acute moderate alcohol doses on performance and how they may change with aging are understudied. This report from an ongoing study extends previous findings of impairing effects of alcohol on simulated driving performance through the use of more moderate doses and recruitment of both older (55–70 years of age) and younger adults (25–35 years of age).
Methods. Healthy older (n=13; 5 women) and younger (n=28; 10 women) adults were recruited. Following medical and psychiatric screening, subjects completed an ~8 minute simulated drive consisting of a curvy two-lane road with no pedestrians. Subjects returned for an additional session and were received a placebo beverage or a dose of alcohol targeted to a BAC of 40 mg/dl or 65 mg/dl (Watson et al., 1981). On the descending limb of the BAC curve, subjects repeated the ~8 minute drive. Variables of interest related to the driver's ability to maintain constant speed and lane position and avoid sudden corrections (i.e., high steering rates). For this early report, active doses were collapsed. BrAC was assessed immediately before and after driving.
Results. As expected, repeated measures ANOVA (2 [pre/post] X 2 [placebo/alcohol] X 2 [older/younger]) revealed main effects of age for both lane position standard deviation ($F_{1,37}$=6.29, p=.02) and average steering rate ($F_{1,37}$=11.59, p=.002) with older subjects performing more poorly than younger subjects. A significant interaction of time point and age group was observed for steering rate; older but not younger subjects improved between lab sessions ($F_{1,37}$=4.22, p=.05; t_{12}=2.38, p=.03). A significant age group by dose group interaction was detected for variability in speed ($F_{1,37}$=6.41, p=.02). Post-hoc tests showed that older subjects given an active dose performed more poorly than those given placebo (t_{11}=2.62, p=.06), an effect not seen in younger subjects.
Conclusions. These preliminary results reveal general aging effects on simulated driving and suggest effects of moderate alcohol administration in older adults may not be general. Rather, we detected negative effects only on the ability to maintain a constant speed. This interaction between age group and alcohol effects suggests continued study of the effects of acute low to moderate alcohol use in middle aged and older adults is needed.

0530

COMPARATIVE ANALYSIS OF GAIT AND BALANCE IN INDIVIDUALS WITH AN ALCOHOL USE DISORDER AND HEALTHY CONTROLS

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Impairment of gait and balance is a problem commonly associated with an alcohol use disorder (AUD). Several studies have shown impaired gait and balance cross-sectionally in this population, but in limited sample sizes. In addition, the few studies that have compared AUD with controls across time have shown no significant differences for AUD. It is critical to understand recovery rates of gait and balance longitudinally to develop a clearer picture of general health following abstinence from alcohol.
Treatment seeking AUD (time point [TP] 1, n=53 [30 smokers]; TP2 n=29 [16 smokers] approximately 8 months later) along with light drinking (LD) healthy controls (TP1 n=34 [7 smokers]; TP2 n=12 [1 smoker]) were assessed using the Fregly Ataxia battery testing balance and gait. Groups were not significantly different on age (AUD 50 ± 10 years; LD 46 ± 10). Four trials were administered to each group: (1) Standing Eyes Open; (2) Standing Eyes Closed; (3) Walk-a-Line Eyes Open; and (4) Walk-a-Line Eyes Closed. Analyses were restricted to the Fregly Ataxia Standing Eyes Closed (FAEC) task due to ceiling and floor effects of the other ataxia tasks. Groups were compared at each TP, and longitudinally using general linear mixed modeling (GLM) controlled for age and smoking status.
Results show that AUD perform worse at baseline (p=.00) and after 8 months (p=.05) of sobriety when compared to LD. Findings also show a trend (p=.06) for improvement on the FAEC in the AUD population across time while the LD remain stable (p=.30). Additionally, a higher number of lifetime years drinking was significantly correlated with poorer performance on the FAEC (r=−.33, p=.017).
These results suggest that there are trends for improvement of gait and balance in AUD during abstinence. However, a return to normal functioning is not achieved at 8 months of sobriety. The results also show that performance relates to lifetime drinking history. Although the findings in this analysis broaden our understanding of gait and balance, there is still a need for further study with a larger sample size and possibly over a longer period of time to determine if complete recovery is possible.

0531

GAIT AND BALANCE DEFICITS IN CHRONIC ALCOHOLICS: NO EVIDENCE OF IMPROVEMENT AT 9 MONTHS ABSTINENCE

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Background: Disturbed gait and balance are among the most consistent and salient sequelae of chronic alcoholism. Previous research has suggested that some of these deficits in gait and balance diminish with extended abstinence. However, questions remain regarding the degree of recovery in gait and balance as a function of abstinence duration.
Methods: We performed a follow-up study 6–9 months after of a cross-sectional assessment of gait and balance in 37 Short-Term (6–15 weeks) Abstinent Alcoholic's (STAA), 25 of whom maintained abstinence throughout the follow-up period and 12 who relapsed prior to follow-up assessment. Fourteen Non-Alcoholic Controls were also brought back for a follow-up assessment to examine practice effects.
Results: Our findings were 1) alcoholics showed no improvement in gait and balance measures over the follow-up period, 2) there was no difference on gait and balance measures at baseline between STAA who remained abstinent through the follow-up period and those who relapsed, 3) At follow-up, NSAC had marginal improvement on the Walk on Floor Eyes Closed measure.
Conclusions: Results suggest that gait and balance deficits in alcoholics show no clear evidence of recovery over 6–9 months. Moreover, gait and balance measures at baseline showed no relationship to later relapse. Additionally, NSAC showed improvement on Walk on Floor with Eyes Open at retest (STA did not), suggesting that cross-sectional comparisons may underestimate the magnitude of the alcohol related deficiency on this measure.

0532

RELATIONSHIP BETWEEN SUBJECTIVE RESPONSE TO ALCOHOL AND RESPONSE INHIBITION IN ALCOHOL DEPENDENT INDIVIDUALS

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The Stop Signal Task (SST) is a widely used measure of response inhibition, a component of impulsivity that has been linked to increased risk for alcohol problems. Acute alcohol administration has shown mixed results in changing performance on this task and few studies have tested the acute effects of alcohol on SST among alcohol dependent populations. Additionally, little is known about how subjective responses to alcohol are associated with the effects of alcohol on response inhibition. Thus, the aims of this study were to assess: 1) the effects of alcohol vs. placebo on SST performance in a sample of alcohol dependent participants and 2) for moderating effects of subjective intoxication on SST performance. Forty-three (11 female) alcohol dependent participants completed three laboratory visits consisting of a baseline assessment, and counterbalanced alcohol-placebo infusions. The SST was administered at the baseline visit, at peak BrAC (0.06 g/dl) during the alcohol infusion, and at the equivalent time point (75 mins) during the placebo infusion. Subjective intoxication was assessed at during the infusion using the Biphasic Alcohol Effects Scale (BAES) and the Subjective High Assessment Scale (SHAS). SST variables analyzed were mean go reaction time (MGRT), Stop Signal Reaction Time at 50% probability to inhibit (SSRT50), stimulus discrimination errors, and mean stop signal delay (MSSD). Analysis revealed a main effect of alcohol vs. placebo on SSRT50 and MGRT. For SSRT50, both infusion visits (alcohol and saline) had significantly lower reaction time values than baseline, likely showing a practice effect. For MGRT, reaction time significantly decreased during the placebo infusion visit compared to baseline and alcohol infusion ($ps < 0.05$), indicating that alcohol may counteract any practice effect performance gains. Significant interactions were observed between measures of subjective intoxication and stop signal performance across infusion visits in several indices of SST performance. In general, those with higher stimulation BAES scores had larger MSSD values than those with lower values under alcohol vs. placebo. Participants reporting higher BAES sedation scores or SHAS scores made more discrimination errors under alcohol vs. placebo than less sedated participants. Taken together these results indicate that including subjective intoxication in analysis of SST performance may enhance predictions of the effect of an acute alcohol challenge.

0533

DIFFERENTIAL EFFECTS OF ALCOHOL ON CONTRAST PROCESSING MEDIATED BY THE MAGNOCELLULAR AND PARVOCELLULAR PATHWAYS

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The majority of sensory information that reaches the central nervous system in humans comes through the eyes, therefore, visual impairment caused by alcohol drinking has a large impact on alcohol-related injury or accidents. The processing of stimulus contrast, which indicates the relative variation in luminance of a visual stimulus relative to its background, is fundamental for object detection, recognition and perceptual decision-making for the visual system. Further, the magnocellular (MC-) and parvocellular (PC-) pathways, the two primary early neural pathways transferring different aspects of visual information from the eye to the brain, have very different contrast response characteristics. As there has been little research on alcohol's acute effects on contrast processing in these two pathways, we examined such effects in a sample of social drinkers before and after alcohol and placebo consumption in the laboratory.

Participants were 16 (9 men) young healthy non-alcoholic social drinkers (age: 27.1±5.6 years). Each subject completed two randomized sessions (0.8 g/kg alcohol, or a placebo) that consisted of contrast processing measurements at baseline (Pre) and at 45 minutes after the beverage consumption (Post), using three psychophysical paradigms designed by to separately evaluate contrast sensitivity and gain in the MC- and PC- pathways (Pokorny & Smith, 1997). The difference in estimated MC- and PC-contrast sensitivity and gain parameters at the two time points within a session (Post-Pre) was used to quantify the beverage effect.

The results showed that compared to placebo, alcohol significantly reduced MC- contrast sensitivity (alcohol vs placebo: -0.12 ± 0.03 vs -0.05 ± 0.01, $p = 0.01$) and PC- contrast gain (-0.47 ± 0.18 vs 0.20 ± 0.10, $p = 0.01$), but did not affect MC- contrast gain (0.005 ± 0.02 vs -0.002 ± 0.02, $p = 0.81$) or PC- contrast sensitivity (-0.04 ± 0.03 vs 0.02 ± 0.02, $p = 0.11$). The results suggested that alcohol affects contrast processing in the MC- and PC- pathways differently. The findings may provide further insights on the mechanisms underlying other higher order visual functional losses after acute alcohol consumption.

0534

COMORBID ALCOHOL ABUSE AND AFFECTIVE DISORDERS: INDEPENDENT AND CUMULATIVE IMPACT ON VIRAL LOADS AND VIRAL SUPPRESSION IN HIV-POSITIVE OUTPATIENTS

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This pilot study prospectively examined the independent and cumulative impact of alcohol abuse and affective disorders on viral loads and viral suppression in a cohort of HIV-positive patients receiving outpatient medical care.

Based on confidential self-report of symptoms of alcohol abuse, assessed using the CAGE screen, and major depression and generalized anxiety, diagnosed using DSM-IV criteria, participants (n=73, 31.3% female) were categorized as "no diagnosis" (50.0%), "affective disorder(s) only" (29.0%), "alcohol abuse only" (6.5%), and "comorbid alcohol abuse and affective disorder(s)" (14.5%). Self-report was linked to viral load data, accessed via chart review at the time of survey completion (baseline), and 6- and 12-month follow-up. Outcomes of interest were 1. the impact of alcohol abuse and affective disorders on changes in viral loads over time, and 2. the proportion of patients in each group who achieved viral suppression, defined as a viral load of less than 500 copies/ml, at each of the three time points.

Results revealed a significant multivariate main effect of alcohol abuse on HIV RNA viral loads [Wilk's λ=.88, F(3,52)=4.17, p=.01, η_p^2=.19], with no significant main effect of affective disorders, and no interaction. Post-hoc analyses showed significantly higher HIV RNA viral loads in patients with alcohol abuse at 6- and 12-month follow-up (all p<.05), with no significant differences at baseline. Examining the likelihood of viral suppression, at baseline, there were no significant between-group differences. At 6- and 12-month follow-up, differences were significant (χ^2=13.91, p=.003 and χ^2=10.77, p=.01). Post-hoc analyses indicated that a significantly smaller proportion of alcohol abusing patients achieved viral suppression at both time points (both p<.05), compared to patients without alcohol abuse, with no significant differences between those with and without affective disorders.

Results from this preliminary study support previous findings of a marked negative impact of alcohol abuse on HIV viral loads and likelihood of viral suppression, with no evidence for a significant additive effect of major depressive and/or generalized anxiety disorders. In the absence of evidence for a direct or cumulative impact on HIV disease progression, the possibility that affective symptoms play a role in increasing the risk of problem drinking in HIV-positive patients should be explored in future studies. Supported by T32AA007577.

0535

BLOOD ALCOHOL LEVEL, ALCOHOL USE DISORDER, AND POISONING SEVERITY IN DELIBERATE SELF-POISONING CASES

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Background: Alcohol Use Disorders (AUDs) and acute use of alcohol increase the risk of self-deliberate self-poisoning (DSP) however it is not clear how AUDs, or the acute use of alcohol, influences the medical severity of an act of DSP.

Methods: Retrospective descriptive case review of Toxicology bedside consult case records initially performed by one of the authors (TJW) over a one year period (1/1/2011–12/31/2011) with analysis of socio-demographic and clinical variables including age, sex, history of self-injury, and probable or known history of AUD, drug use disorder (DUD), and other mental disorder based on clinical record and bedside interview, and blood alcohol level (BAL). Primary outcome was medical severity of DSP based on Poisoning Severity Score (PSS), a validated measure with range 0 (none) to 4 (fatal). Secondary outcome was total number of 12 specific organs/systems affected by DSP, an alternative indicator of severity.

Results: 534 unique patient encounters were seen by the Toxicology Consult service during the study period including 315 acts of DSP, of which 69 (22%) were judged to involve acute use of alcohol during the consultation. Analyses of these 69 cases showed mean age of 36.7 years (SD 12.0), 46.7% were male, with PSS scores showing a normal distribution including 29.3% mild, 37.9%moderate, and 29.3% severe, along with one fatality. BAL was positive in 46 (66.7%) cases with mean level of 86.45 mg/dL (STD 95.19 mg/dL). 70% had a previous history of DSP and 76.7% AUD history. In univariate tests PSS was associated with AUD (p=0.026) and history of self-injury (p=0.019). Tests of number of organ systems affected showed similar results.

Discussion: AUD and history of DSP were shown to correlate with measures of medical severity of DSP in cases judged to directly involve alcohol. Other variables, including BAL, did not correlate with medical severity of DSP. The nonsignificant BAL result is interpreted with caution because BAL does not accurately reflect the amount of alcohol consumed in some cases of DSP due to its rapid metabolism (15 mg/dL/hour in average individuals) and delays presenting to the hospital in some acts of DSP. Further analyses of the role of acute alcohol use and AUD in the entire case series of DSP (N=315) will be performed to overcome the restriction of range that may affect results in analyses of cases perceived to directly involve alcohol alone.

0536

UGANDA, RUSSIA, BOSTON ALCOHOL NETWORK FOR ALCOHOL RESEARCH COLLABORATION ON HIV/AIDS (URBAN ARCH) CONSORTIUM

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In the fourth decade of the HIV epidemic, many questions remain about how alcohol use affects HIV clinical manifestations and how treatments beyond ART might mitigate alcohol-related harms. Such questions about the complex relationship between HIV and alcohol need to be addressed in order to accelerate the development of more effective treatments. The Uganda Russia Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS (URBAN ARCH) Consortium was funded by NIAAA in September 2011 to carry out cohort and intervention studies to address gaps in our understanding about HIV and alcohol. The central goal of the URBAN ARCH Consortium is to examine the consequences of alcohol on HIV disease and to mitigate its harmful effects. To realize this goal, the URBAN ARCH Consortium incorporates the expertise of researchers in epidemiology, internal medicine, addiction medicine, HIV/AIDS, psychiatry and biostatistics. The Consortium studies build upon three existing HIV-infected cohorts from Boston, Uganda, and Russia with distinctive strengths and well-characterized alcohol consumption patterns. The Boston Cohort (PI: Saitz) incorporates an intervention study and is designed to answer two research questions: is heavy alcohol use associated with osteopenia in HIV-infected adults and does buprenorphine reduce heavy alcohol use? The Uganda Cohort (PI: Hahn) is examining the effects of heavy alcohol use on HIV disease progression pre-ART. The Russian Cohort (PI: Samet) is designed to address the question of whether heavy alcohol use is associated with elevated inflammatory markers in ART naïve HIV-infected individuals. The two international cohorts allow study of clinical issues that would not be possible in the United States, yet have important implications for US HIV-infected populations. The three cohorts are integrated in terms of characteristics and common measures, which will allow evolution of cross-cohort studies. Moreover, samples collected from all three cohorts are stored in a centralized repository for future use. The URBAN ARCH Consortium will conduct and disseminate interdisciplinary alcohol/HIV research aimed at understanding the consequences of alcohol on HIV disease and advancing clinical approaches to mitigate its harm in the United States and globally. Hence, we will provide insights about the relationship of alcohol and HIV infection and improve clinical and public health outcomes.

0537

FLORIDA CONSORTIUM FOR HIV/AIDS AND ALCOHOL-RELATED RESEARCH TRIALS: FOCUS ON WOMEN, IMMUNOLOGY, AND TREATMENT INTERVENTIONS

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Alcohol consumption is associated with significant behavioral and biological outcomes in persons with HIV infection. However, few strategies to help persons reduce their drinking have been evaluated in persons with HIV/AIDS, and questions remain about the direct causal impact of alcohol on both behavioral and biological outcomes. Moreover, few studies involving alcohol and HIV have been sufficiently powered to make gender-specific conclusions in women. To address these research gaps, we will conduct a series of three projects, funded by the National Institute of Alcohol Abuse and Alcoholism, that are inter-related and that will share specimens and resources. A clinical trial project, ''Pharmacotherapy for alcohol consumption in HIV-infected women: randomized trial'' (R.L. Cook, PI), is a double-blind, placebo-controlled, randomized trial designed to determine whether the medication naltrexone can reduce drinking and improve HIV-related health outcomes in women with HIV infection. A longitudinal cohort project, ''Platelets Mediating Alcohol and HIV Damage'' (M.J. Miguez, PI), is currently recruiting 550 persons with and without HIV infection into a longitudinal study to better understand alcohol's impact on immunologic parameters, cardiovascular risk markers, and other short-term and long-term health outcomes in persons with HIV. An immunologic project, ''Immune dys-regulation in HIV-infected women with alcohol consumption'' (S. Desai, PI) will test hypotheses regarding the direct impact of alcohol consumption on immune activation and senescence among HIV-infected and –uninfected women. The majority of study participants will be recruited in Florida, the state with the 2nd highest number of women living with HIV infection in the US. Our immunologic studies will also involve samples from participants in the ongoing Women's Interagency HIV Study (WIHS). An additional goal of the Florida Consortium is to establish the research infrastructure and recruit sufficient numbers of participants that will support joint research projects that involve other HIV-alcohol consortia. Taken together, this series of projects will not only accurately characterize outcomes related to HIV and alcohol consumption, but also will provide needed evidence regarding the clinical effectiveness of interventions to improve the overall health of women with HIV who consume alcohol.

0538

CONSORTIUM TO IMPROVE OUTCOMES IN HIV/AIDS, ALCOHOL, AGING & MULTI-SUBSTANCE USE (COMPAAAS)

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The Consortium to improve OutcoMes in HIV/Aids, Alcohol, Aging, and multi-Substance use (COMpAAAS) (PI: Justice) will coalesce findings from observational research, intervention and operations research. It includes the Veterans Aging Cohort Study (VACS), the largest HIV cohort in the North America (40,594 HIV+ matched 2:1 to 81,188 HIV-) and a nested, consented 8 site sample of 3,660 HIV infected (HIV+) patients demographically matched to 3652 uninfected patients (HIV-) which has longitudinal data spanning nearly 10 years on alcohol, substance use, and health and behavioral outcomes. The COMpAAAS observational study (PI:Justice) compares longitudinal patterns and consequences of alcohol and multi-Substance use (MSU) in HIV+/–, collect TLFB in HIV+/– initiating care to study longitudinal associations of alcohol, tobacco, opioids, and cocaine, with outcomes and develop an interactive Web-Based laboratory. The COMpAAAS intervention (PI: Fiellin) compares onsite Integrated Stepped Care treatment (ISC) to treatment as usual (TAU) in three, linked, 6-month randomized clinical trails in 642 HIV+ patients with unhealthy alcohol use. Patients with 1) at-risk drinking, 2) alcohol abuse or dependence or 3) moderate alcohol consumption and liver disease will be randomized to ISC or TAU. The primary outcome will be change in alcohol consumption. Secondary outcomes include change in the VACS Index, ART adherence, and sexual risk behaviors. The COMpAAAS operations research study (PI: Braithwaite) compares the effectiveness of different interventions and alternative portfolios of interventions, and places particular emphasis on alcohol because it is a common modifiable risk factor for HIV transmission and progression. Because unhealthy alcohol use often occurs together with MSU and depression, because they often act on similar pathways to impact HIV transmission, the proposal considers portfolios of interventions that address these behaviors simultaneously or in a sequenced, prioritized progression. We also consider interventions that can be tailored to patient characteristics such as age and comorbidity. We seek to implement this operations research within an interactive web-based laboratory to improve research methods by encouraging greater ''cross-talk'' between modeling, observational data analysis, and trial design; and by identify patient groups that may particularly benefit from interventions, or tailoring results to the needs of particular stakeholders.

0539

SUBJECTIVE INTOXICATION IS BETTER PREDICTED BY DEFICITS IN MOTOR THAN BY COGNITIVE PERFORMANCE MEASURED IN A FIELD SETTING

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Subjective experiences/interpretations of the effects of alcohol are often associated with different outcomes. For example, decreased subjective rating of intoxication has been identified as a risk factor for development of alcohol use disorders (Schuckit et al, 2010), whereas increased subjective stimulation in response to alcohol is associated with greater proximal physiological consequences of alcohol use (i.e., hangover and blackout; Wetherill & Fromme, 2009). A parallel line of research has focused on predictors of subjective intoxication ratings. However, this research has been largely conducted in laboratory settings (e.g., alcohol challenges) or based on retrospective self-report. The aim of the current investigation was to evaluate individual factors contributing to subjective intoxication ratings *during* an acute drinking episode. To this end, we administered a survey and objective testing battery to young adults (i.e., age 18 to 25) within a naturally occurring environment. Participants (N = 213; 37% female) gave subjective ratings of current intoxication using a single likert scale item, reported their total drinks consumed during the current episode, and rated their typical level of alcohol-related risk using the Alcohol Use Disorders Identification Test (AUDIT). Participants also provided a Breath Alcohol Concentration (BrAC) sample and completed the Trail Making and Finger Tapping tests as objective measures of cognitive and motor performance, respectively. First-order correlational analyses demonstrated that subjective intoxication ratings were significantly associated with total drinks consumed, current BrAC, AUDIT total score, and cognitive (as indexed by the Trail Making composite score) and motor performance deficits. When multiple regression analyses were used to assess the unique predictive power of these variables of interest, BrAC was the strongest predictor of subjective intoxication, as expected. After accounting for the unique variance predicted by BrAC, of the factors examined, only motor performance remained as a significant predictor of subjective intoxication. This finding is particularly exciting, as it lends ecologically valid support to the suggestion that subjective intoxication is better predicted by motor than by cognitive performance deficits associated with alcohol use.

0540

COMPARISON OF SELF-REPORTED AND OBJECTIVE MEASURES OF SLEEP QUALITY AND DURATION IN AN INPATIENT ALCOHOLISM TREATMENT PROGRAM

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Purpose: Insomnia and other sleep disturbances are common among alcohol-dependent individuals and can increase risk of relapse. Objective measures of sleep are difficult to obtain in this population and it is unclear whether self-reported sleep measures are reliable given the immense physical and psychological burden associated with alcoholism. The purpose of this analysis was to compare self-reported, subjective sleep quality and duration to objective measures and to describe the prevalence of baseline sleep disturbances in an inpatient population of alcoholics during their first week of treatment.
Methods: Participants enrolled in an inpatient alcohol treatment completed the self-reported Epworth Sleepiness Scale (ESS) on day 5, Pittsburgh Sleep Quality Index (PSQI) on day 2, and daily sleep diaries. Participants agreed to wear an actigraph watch tracking ambient light and motion as an objective measure to assess sleep and wake times.
Results: The sample (n=22) was 50% male and ranged in age from 22 to 53 years (mean 40.14, SD ± 9.34). The mean Day 5 ESS score was 7.45 (SD ± 5.19) indicating no excessive daytime sleepiness at baseline in our sample. The mean baseline PSQI score of 12.57 (SD ± 4.38) indicated a prevalence of sleep disturbances over the month prior to admission. Objective measures provided through actigraphy during the first seven days of treatment indicated that the average sleep onset latency was 15.26 minutes and average sleep efficiency was 75.89%. Sleep efficiency scores were significantly correlated with self-rated sleep efficiency (p=.05). Sleep duration as calculated by the actigraph watches was significantly correlated with self-reported sleep duration (p=.03).
Conclusions: Based on these preliminary results, this sample of inpatient alcohol treatment patients experiences poor sleep efficiency on average and significant sleep disturbances in the month before entering treatment. Self-reports of sleep quality and duration correlate with objective measures. Ongoing analysis of sleep prevalence data may be a valuable tool for informing the development of customized sleep hygeine interventions in a similar future sample. Validating the correlation between self-reported sleep measures and corresponding objective measures, including actigraphy and clinician progress notes, may provide a more complete and accurate quantification of sleep quality and efficiency among alcoholics.

0541

CONCURRENT EATING DISORDERS & SUBSTANCE USE: THE ASSOCIATION BETWEEN ALCOHOL USE, EATING DISORDER SYMPTOMS AND SYMPTOM SEVERITY

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Several previous studies have documented that individuals with concurrent disorders (i.e. substance use and another mental health disorder) are at a heightened risk for negative consequences compared to those with a substance use disorder (SUD) alone. Individuals with a concurrent SUD and an eating disorder (ED) experience more severe substance abuse problems, poorer health and more disturbed cognitive functioning (i.e. memory lapses and disorientation) compared to those with a single diagnosis (Courbasson, Smith, & Cleland, 2005). The present study examines the relationship between alcohol use, eating disorder symptoms and symptom severity among individuals with concurrent SUD and ED. The goal of the current study is to further elucidate some of the differences between individuals with concurrent SUD and ED and those with an ED alone. Participants were 72 clients (91.7% female) between the ages of 18–56 (M=31.5) who were receiving residential treatment for an ED and a concurrent SUD (n=40) or were receiving treatment for an ED alone (n=32). Participants completed baseline measures (i.e. pre-treatment) of alcohol use frequency, nicotine dependence (the Fagerstrom Test of Nicotine Dependence), severity of mental health symptoms and difficulties in functioning (the Behavioral and Symptom Identification Scale; BASIS-32), and disordered eating (the Eating Attitudes Test; EAT-26). The results indicate that individuals with a concurrent ED and SUD had significantly higher symptom severity on the BASIS-32, $t(70)= -2.53$, p=.02 and greater nicotine dependence, $t(69)= -3.84$, p=.02, compared to those with an ED alone. Contrary to our hypothesis, frequency of alcohol use, total drinking and severity of disordered eating were not significantly different among the two groups; however, both groups had a high frequency of weekly alcohol use over the past 6 months (i.e. 47.2% reported drinking at least 2–3 times/week). In addition, among those with a concurrent ED and SUD, the frequency of alcohol use was highly correlated with eating disorder symptoms. These results suggest that individuals with a concurrent SUD and ED diagnosis experience greater difficulty on several dimensions, but that individual's with an ED alone may also demonstrate high rates of alcohol use. These results provide valuable information for clinicians and treatment providers to inform treatment and suggest an integrated treatment approach which addresses correlates specific to this population.

0542

IMPULSIVITY: A CAUSE OR CONSEQUENCE OF ALCOHOL USE?

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Impulsivity has been found to be a robust predictor of substance use. Recent findings suggest a bidirectional relationship between impulsive personality and substance use, with impulsive personality predicting later substance use, and substance use predicting later impulsive personality (Horvath et al., 2004; Quinn, Stappenbeck, & Fromme, 2011). Recent models of impulsivity suggest that, rather than being a unitary construct, impulsive personality can be better understood as consisting of several distinct traits that can serve as pathways to rash action. Negative urgency, understood as the tendency to act rashly while experiencing negative affect (Whiteside & Lynam, 2001), seems to be an important addition to our understanding of impulsive personality, and has been found to predict problematic substance use across a number of studies. Although previous studies have demonstrated that substance use predicts later sensation seeking (Horvath et al., 2004; Quinn et al., 2011) and prototypical impulsivity (Quinn et al., 2011), no known studies have examined whether substance use predicts later negative urgency. The present study sought to expand our understanding of the impact of substance use on impulsive personality by examining the impact of alcohol use on later negative urgency.The current study examined the bidirectional relations between alcohol use and impulsive personality traits, specifically sensation seeking and negative urgency, in a longitudinal sample of college students (N = 153). Participants completed questionnaires assessing personality and drinking behavior during their first year of college (Time 1), and completed the same measures at a follow-up session one year later (Time 2). Hypotheses were tested using regression models. Consistent with previous findings, both Time 1 sensation seeking and Time 1 negative urgency predicted Time 2 average weekly alcohol use. Time 1 average weekly alcohol use predicted Time 2 sensation seeking, even when controlling for Time 1 sensation seeking. Similarly, Time 1 average weekly alcohol use predicted Time 2 negative urgency, even when controlling for Time 1 negative urgency. These results are consistent with previous findings indicating bidirectional effects between impulsive personality and substance use. Additionally, the finding that Time 1 drinking predicted Time 2 negative urgency contributes to our understanding of how alcohol consumption can impact later personality.

0543

PROSPECTIVE INFLUENCES OF POSITIVE DRINKING CONSEQUENCES ON HEAVY DRINKING

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A range of theories of drinking assert that drinking behavior is determined by not only the person's cognition but also consequences obtained from the environment. In contrast to the extensive literature documenting the effect of positive outcome expectancies (anticipation of positive outcomes from drinking) on drinking, however, few studies have examined the association between drinking behavior and self-reported positive outcomes experienced from drinking (positive drinking consequences). Moreover, prospective influences of positive drinking consequences on subsequent drinking behavior have yet to be characterized. Using structural equation modeling based on 2-wave prospective data obtained from 256 college students (60% female, 69% White, and 43% 18 years old), we demonstrated that higher levels of positive drinking consequences at baseline were significantly associated with higher frequencies of heavy drinking at follow-up, after controlling for baseline heavy drinking, positive alcohol outcome expectancy and demographics. This result held even when negative drinking consequences were added to the model. In addition, greater importance of the positive 'Fun-Social' consequences was associated with higher frequencies of heavy drinking at follow-up, whereas greater importance of positive 'Image' consequences was associated with lower frequencies of heavy drinking at follow-up.
These findings suggest that actual experiences of positive outcomes from heavy drinking facilitate further heavy drinking, over and above the influences of cognitive anticipation of positive outcomes. Implications of the findings were discussed in terms of the role of positive drinking consequences within the nomological network of correlates and determinants of drinking behavior.

0544

THE USE OF PROTECTIVE BEHAVIORAL STRATEGIES WHILE DRINKING AMONG STUDENTS ACCESSING COLLEGE COUNSELLING SERVICES: THE MODERATING ROLE OF ANXIETY

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Protective behavioral strategies (PBS) are skills for reducing the negative consequences of alcohol. Recent data suggest that students with poorer mental health may be less likely to use PBS, but when they do, they may have the most to gain from their protective benefits. It is not currently clear whether some types of PBS (e.g., selective avoidance strategies, strategies used while drinking or alternatives to drinking) may be more beneficial than others for students facing mental health challenges. The current study aimed to extend past research by examining the use of three different types of PBS in a sample of students at high risk for alcohol problems (i.e., heavy episodic drinkers accessing mental health services), and to test whether anxiety moderates the relationship between PBS and alcohol-related negative consequences. Participants (N = 97) were students recruited from a West Coast private university counseling center. Participants reported high levels of alcohol consumption (M = 17.5 drinks per week) and negative consequences. Nearly a third of the students had passed out from drinking (28.9%) and found it difficult to limit their drinking (29.9%) in the past 30 days. Participants reported using the majority of the PBS they were asked about at least once in the past month, but utilized selective avoidance strategies less frequently than the other types of PBS. A three-step hierarchical multiple regression model examined the role of anxiety and protective strategies in predicting alcohol-related negative consequences. Results revealed that the number of drinks consumed per week (β= .38, p < .001), anxiety (β = –.21, p =.023), and Strategies While Drinking × Anxiety (β = –.26, p = .02) all uniquely contributed to predicting consequences. Simple slopes analyzes revealed that among students with high anxiety, increasing use of strategies while drinking was associated with fewer alcohol-related drinking consequences. Among those with lower anxiety, there was no relationship between use of strategies while drinking and experiences of negative consequences. For those with high anxiety, employing strategies while drinking reduced the number of alcohol-related negative consequences by half. The results suggest that these simple risk-reduction strategies employed in drinking situations may be intuitive to students with poorer mental health and particularly useful for those who are highly anxious.

0545

BINGE DRINKING AND HOOKUP FREQUENCY AS PROSPECTIVE PREDICTORS OF SUBSTANCE-FACILLITATED RAPE IN COLLEGE WOMEN

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Drinking behavior and sexual behavior are risk factors for sexual assault. Numerous studies describe an association between alcohol consumption, particularly heavy episodic (binge) drinking, and sexual victimization. Hookup behavior has also gained attention as a potential risk factor for unwanted sex. Heavy drinking and hooking up seem to be associated, and when combined into a factor for ''risk behaviors'' have been shown to mediate the relationship between adolescent and college sexual assault. The purpose of the current research is to examine the extent to which drinking behavior and sexual behavior (frequency of hooking up) independently and interactively predict subsequent sexual assault. The relationship between hooking up and sexual assault may be due in part to the correlation between hooking up and heavy drinking. It is also possible that binge drinking and hooking up interact, such that women who regularly engage in BOTH behaviors are at especially high risk of being victimized.

College women (*N*=424) provided preliminary background data (T1) and then provided weekly data on sexual behavior (including hookups) and drinking behavior (T2–T10). One year later (T11), participants completed a follow-up survey (80% retention) that included questions about past-year sexual victimization.

Independent variables for the current study included the percentage of weeks (during T2–T10) for which participants indicated engaging in at least one instance of binge drinking (4+ drinks), and the percentage of weeks for which participants engaged in at least one hookup.

Dependent variables included reporting any instance of unwanted oral, anal, or vaginal sex (regardless of method of coercion) at T11 (*n*=171), and experiencing substance-facilitated (SF) rape specifically (incapacitated unwanted oral, anal, or vaginal sex; *n*=14).

Logistic regressions analyzed each dependent variable: binge frequency and hookup frequency were entered on the first step; an interaction term combining binge frequency and hookup frequency was entered on the second step. The model predicting general sexual assault was not significant. Binge frequency (*B*=2.3, *OR*=10.1, *p*<.05) and hookup frequency (*B*=2.5, *OR*=11.6, *p*<.05) independently predicted SF rape; the interaction term was not significant (*B*=1, *OR*=2.8, *p*=.7). Future models of sexual victimization, especially those examining SF victimization, should consider drinking and sexual behavior as separate predictors.

0546

CORTISOL AWAKENING RESPONSE DURING DETOXIFICATION DIFFERS IN PATIENTS WITH PSYCHIATRIC COMORBIDITY

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Raised cortisol with loss of circadian fluctuation is well-described in alcohol detoxification and is hypothesised to contribute to dysphoria and risk of relapse. Raised cortisol is also described in a variety of psychiatric disorders. Here we present preliminary data from salivary cortisol samples, indexing biologically available cortisol. We measured the cortisol awakening response (CAR), the best naturalistic measure of physiological HPA axis response, during medically managed alcohol detoxification in alcohol dependent patients.

Methods: 10 (45±11; M=6) in-patients undergoing in-patient alcohol detoxification were recruited. Six had at least one previous diagnosis of psychiatric disorder: depression (n=4), psychosis (n=1), borderline personality disorder (n=1) and anorexia nervosa (n=1). Five were treated with antidepressants, one with haloperidol. Other treatments, such as benzodiazepines, acamprosate, thiamine did not differ between groups. Four salivary cortisol samples were collected during the first 45 minutes of waking by patients in early (day 1–3), mid (day 4–6) and late (day 7–10) detoxification. Withdrawal severity was rated using the Clinical Institute Alcohol Withdrawal Assessment. Visual analogue scale (VAS) ratings of depression and anxiety were collected. Cortisol levels were analysed using a standardised ELISA kit. Statistical analysis of data was carried out using GraphPad Prism.

Results: CAR was blunted (rise of <9nmol/l between waking and peak) throughout detoxification in both groups (early: 6.38008±7.250614; mid: 1.115592±4.554683; late: 4.93166±8.85979). The CAR area under the curve (AUC) of patients with psychiatric co-morbidity (840.2 ± 84.02) greatly exceeded that of those without psychiatric comorbidity (341.8±52.84; p=0.0003). Those with co-morbid psychiatric diagnoses had a slightly higher VAS depression score at each time point which did not reach significance. There was no statistically significant relationship between CAR and withdrawal severity or mood symptoms.

Conclusion: Patients with psychiatric comorbidity have a higher CAR AUC during alcohol detoxification than those without psychiatric comorbidity. This may represent one of the mechanisms whereby this group of patients suffers worse outcomes in terms of relapse. We are continuing to collect data and hope to replicate this finding in the complete sample of 50.

9. PREVENTION

0547

DAILY VARIATIONS IN COLLEGE STUDENT SPRING BREAK TRIP CONTEXTS AND ALCOHOL AND SEXUAL BEHAVIORS

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There are known risks of alcohol use and sexual behavior for college students on Spring Break, and particularly for students on Spring Break trips. However, little is known regarding whether it is the choice to go on a Spring Break trip that increases risk behaviors, or whether the context of the Spring Break trip may have an effect. This study was designed to document the behaviors and correlates associated with being on a Spring Break trip on a given day, controlling for average time spent on a Spring Break trip during the 10 days of Spring Break. Participants were undergraduate students ($N = 261$; 55% women) who reported that they planned to go on a Spring Break trip. Web-based survey responses prior to and after Spring Break documented perceived norms, intentions, and actual behavior on each of the 10 days of Spring Break using timeline follow-back. Multilevel models were used to document that students who went on longer Spring Break trips, who previously engaged in more frequent heavy episodic drinking, or who had greater pre-Spring Break intentions to drink reported greater alcohol use during Spring Break. Similarly, students with greater pre-Spring Break intentions to have sex, greater perceived norms for sex, or more previous sexual partners had greater odds of having sex. On days students were on trips, they had a greater likelihood of having sex, drinking to higher estimated blood alcohol content (BAC), consuming more drinks, and reporting perceived drunkenness than on non-trip days, especially if they had intentions to have sex and drink alcohol (and, to a lesser extent, had greater perceived norms for drinking). Students engaged in more risk behaviors when on Spring Break trips. In addition, the context of being on a trip on a given day was associated with increased risk. Further research is needed to describe the contexts of Spring Break trips and how to intervene effectively.

0548

TAILGATING AS A SUB-TYPE OF PREGAMING IN A SAMPLE OF MANDATED COLLEGE STUDENTS

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The objective of this study is to better understand two potentially similar high-risk drinking behaviors, pregaming (i.e., drinking before going to a social event) and tailgating (i.e., drinking before a concert or sporting event). These two behaviors are conceptually similar, yet limited research exists that compares these behaviors. As tens of thousands of college students receive campus alcohol violations and mandatory alcohol interventions each year, it is important to better understand these risky drinking behaviors. In this study, we investigated characteristics associated with pregaming and tailgating in a sample of college students ($N = 354$) who were mandated to receive an alcohol intervention following a campus alcohol policy violation, arrest for driving while intoxicated, and/or alcohol-related medical complication. Specifically, we compared students who engaged in pregaming and tailgating to those who do not engage in these behaviors on a variety of constructs, including demographics, other drinking behaviors, estimated typical and peak blood alcohol concentration (BAC), alcohol-related cognitions, and personality variables. Results indicated that individuals who reported pregaming also reported higher levels of alcohol use relative to students who do not pregame or tailgate ($ps < 0.001$). In addition, participants who engaged in both tailgating and pregaming reported drinking more alcohol than students who pregame only ($ps < 0.001$). However, peak estimated BAC (eBAC) from pregaming ($M = 0.099$, $SD = 0.071$) was significantly higher than estimated peak eBAC from tailgating ($M = 0.081$, $SD = 0.077$; $t[132] = 2.30$, $p \leq 0.05$) for the subset of participants who reported both pregaming and tailgating. On average, participants who reported both pregaming and tailgating reported higher alcohol normative estimates of peer drinking and endorsed more positive alcohol beliefs than those who engaged in pregaming only. However, students who engaged in those behaviors did not differ on different personality variables (i.e., impulsivity, sensation seeking, anxiety sensitivity, and hopelessness). Overall tailgating appears to be a subtype of pregaming and individuals who engage in both tailgating and pregaming are a higher-risk population than students who pregame without tailgating. These results highlight the importance of both brief and event-specific interventions for heavy drinking.

0549

WHERE YOU LIVE MATTERS. THE IMPORTANCE OF LIVING ARRANGEMENTS ON SELF-ESTEEM AND HAZARDOUS DRINKING BEHAVIORS

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College students are at increased risk for problematic substance use, and identifying factors that increase risk of hazardous alcohol use among college students is a research priority. Past research has determined self-esteem to be a strong predictor for alcohol use, with low self-esteem being indicated as a risk factor for risky drinking behaviors among college students. Furthermore, differences in levels of alcohol consumption have been found across different living arrangements. Although the link between self-esteem and hazardous drinking has been repeatedly supported, little research has examined whether the predictive value of self-esteem differs according to different living arrangements. In the present study, we examined the consistency of the association between self-esteem and hazardous drinking across different living arrangements. An online survey was used to measure self-esteem and a structured interview was conducted to determine drinking behaviors. Participants were 101 (60 female, 41 male) undergraduate university students. The influence of self-esteem on drinking behavior was found to be moderated by living arrangement such that self-esteem predicted binge drinking B=−.43, R^2=.18, p<.05 and scores on the RAPI B=−.45, R^2=.20, p<.05 among participants living with parents, but not among students living on campus, all R^2 > 05. These findings highlight the importance of considering living arrangements when examining risk for hazardous drinking among college students, and suggest that the pathway to problematic alcohol consumption may be different for students who live at home compared to students living on campus.

0550

THE ROLE OF RESIDENCE HALL CHARACTERISTICS AND POLICIES IN HIGH-RISK DRINKING BY COLLEGE STUDENTS

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It is estimated that almost 3 million college students (about 20% of the total) live in residence halls or other on-campus settings. Yet relatively little is known about the ways in which residence hall characteristics and policies affect high-risk drinking and alcohol-related consequences. As part of a group-randomized trial (the Study to Prevent Alcohol Related Consequences), we conducted biannual surveys of resident advisors (RAs) at the 8 universities participating in the study. The survey included questions about characteristics of the dorm and the particular unit supervised by the RA, as well as a log of alcohol-related behaviors and incidents that the RA could observe in her or his unit over 7 consecutive days. The data reported here are from the fall 2010 survey, and include responses from 646 RAs representing 102 dorms across the 8 schools in the study (response rate = 81%). We created three scales reflecting alcohol-related behavior and consequences in the unit the RA supervised: ''Consequences'' (number of students sick or injured due to alcohol, vomiting, sleep or study disturbances, property damage), 2) ''Environment'' (number of students suspected or seen drinking, number of parties/pre-parties), and 3) ''Activity'' (number of party ads posted or received by email). Multivariate logistic regression using GLIMMIX, which controlled for clustering of the data by residence hall and by university, was used to examine the relationship between housing unit and RA characteristics and these outcomes. Items on the Consequences scale were significantly more likely to be reported for all-male units, freshman-only units, units with larger numbers of residents, and units where a major event (i.e., campus-wide or local sporting event, Greek event, or campus event) took place during the week. Items on the Environment scale were significantly more likely to be reported for all-male units, units that were affiliated with the Greek system, and units where an event took place during the week. Items on the Activities scale were significantly more likely to be reported for units where an event took place during the week. These results suggest that (1) RA surveys may be a useful complement to student-self reports as an indicator of the level of alcohol-related problems on campus, and (2) the college housing environment may be a useful target for educational and structural interventions to reduce the incidence of high-risk drinking and consequences.

0551

A BEHAVIORAL ECONOMIC ANALYSIS OF THE EFFECT OF NEXT-DAY RESPONSIBILITIES ON DRINKING

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Existing research suggests that increasing drink price and next-day morning academic responsibilities reduces hypothetical alcohol consumption measured with behavioral economic demand curve measures (Skidmore & Murphy, 2010). The purpose of this study is to extend this research further by exploring the impact of ten different next-day responsibilities on hypothetical alcohol consumption in heavy drinking college students. Participants were 82 heavy drinking college students, who reported engaging in at least one binge drinking episode (i.e., 4/5 alcoholic beverages for women/men on one occasion). The sample was 50% female and reported a mean of 17.4 drinks per week in a typical week over the past 30 days. Participants were asked to report how many standard drinks they would consume in an evening preceding each of ten hypothetical next-day responsibilities (e.g., no next-day responsibilities, a college class at 9:00 a.m., class at 11:00 a.m., an internship at 9:00 a.m., paid employment at 9:00 a.m.). Paired sample t-tests were used to compare the mean drinks reported for each of the 9 responsibility conditions to the no-responsibility condition. Participants reported that they would drink 9.68 (SD = 5.472) drinks during an evening prior to having no next-day responsibilities. The mean alcohol consumption estimates for all 9 next-day responsibility conditions were significantly lower than the no responsibility condition (all ps < .001). Internship duties at 9:00 a.m. resulted in the greatest reduction in drinking (7.46 standard drinks from the no responsibility condition) compared to all other conditions (in all nine pairs, p < .001). Interestingly, volunteer work at 9:00 a.m. and paid employment responsibilities at 9:00 a.m. reduced drinking significantly more than college classes (ps < .02). The effect of classes at 9:00 a.m and classes at 10:00 a.m in reducing drinking in this sample was not significantly different; classes at 12:00 p.m. generated the smallest reduction in drinking. Though these findings are preliminary, they provide support for the role of next-day responsibilities for promoting more moderate drinking patterns. This study is the first to provide specific support for the role of Friday morning employment and internship responsibilities in reducing drinking.

0552

ALCOHOL INEBRIATION, DRUG USE AND RELATED WORK PROBLEMS AMONG RESTAURANT EMPLOYEES

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International and U.S. surveys analyzing occupational variables related to substance abuse consistently demonstrate that among all major occupations, restaurant and bar workers have the highest rate of elevated risk for misuse of alcohol and drugs during and after work. In this poster, we investigate the frequency of self-reported drug use and the frequency of alcohol intoxication in relation to problems experienced at work among young adults employed in chain bar-restaurants. The data are drawn from 1,286 completed telephone surveys with randomly selected employees, 18–30 years of age with response rate of 68%. A series of questions examined problems experienced at work, including having conflicts with supervisors, arguments with coworkers and being injured on the job. Questions addressed the frequency of self-reported drug use for five categories: marijuana, amphetamines, cocaine, ecstasy, and prescription drugs without a doctors' prescription. Drinking questions concerned the frequency of alcohol consumption in the hour prior to work, during work hours, and after work, and the frequency of drinking alcohol to the point of intoxication. Among current drinkers (n=1,093), multivariable linear regression analysis found that both frequency of self-reported drug use and frequency of self-reported alcohol inebriation were positively associated with frequency of experiencing problems at work. Being a current smoker and working the day shift compared to night shift were also significantly correlated with work problems. Implications for prevention of drug- and alcohol-related problems at work include training managers to be alert to signs and symptoms of impairment and granting food service workers access to employee assistance programs. Another reasonable outcome of this study would be to create consciousness-raising communications within the food service workforce regarding this study's findings of an association between impairment (whether on or off the job) and work-related problems.

0553

FEASIBILITY OF USING INTERACTIVE VOICE RESPONSE TO STUDY DAILY PROCESSES IN ALCOHOLIC FAMILIES

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Aims. Test the feasibility of using Interactive Voice Response (IVR) to collect daily process data from alcoholic families.
Methods. As part of the Family and Daily Life Study, 10 alcoholic probands (5 females, 5 males), their spouses, and one of their pre-teen or adolescent children (3 females, 7 males) ages 10–16 years were recruited from a local addiction treatment center and from the local community. Alcoholic probands, their spouses, and the target child separately called in to an automated interactive voice response (IVR) system every night for 14 consecutive nights and answered 80 questions about daily moods, family interactions, daily routines, and alcohol use. Participants also rated their satisfaction with using the IVR system, from 0 = "not at all satisfied" to 4 = "very satisfied." Mean (SD) ages for probands, their spouses and the target child were 47.1 (2.6), 49.2 (5.2), and 14.4 (1.9) years old, respectively.
Results. Participants completed 388 of a possible 420 ($10 \times 3 \times 14$) daily process reports, for an overall compliance rate of 92.4%. Probands, their spouses, and the target child had compliance rates of 89.3%, 92.1%, and 95.7%, respectively. Average time taken to complete the daily reports was about 11 minutes for probands ($M = 11.3$), spouses ($M = 10.9$), and adolescents ($M = 10.8$). Mean (SD) satisfaction ratings for probands, their spouses, and the target child were relatively high at 3.3 (0.8), 3.7 (0.5), and 3.4 (0.5), respectively. Four of the 10 target children (40%, ages 10.2 to 16.6 years old) reported drinking at least one alcoholic beverage on at least one night during the study (range: 1 to 11 drinks). For probands and spouses, 9.0% of all IVR surveys required more than one call; among adolescents, the rate was 19.4%.
Conclusions. To our knowledge, this is the first study to demonstrate feasibility of using IVR to collect daily process data from alcoholics, their spouses, and their 10–16 year old children. Results indicated that IVR compliance rates were good even among children from high-risk families, and substantial amounts of data can be collected in relatively brief calls. Participants reported relatively high satisfaction with the IVR system. However, children of these ages might benefit from shorter surveys to avoid multiple calls per day.
This project was supported by Award Number UL1-RR024986 from the National Center for Research Resources to the Michigan Institute for Clinical and Health Research (MICHR).

0554

DRINKING CONTEXT AND INTIMATE PARTNER VIOLENCE: EVIDENCE FROM THE CALIFORNIA COMMUNITY HEALTH STUDY OF COUPLES

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Objective: Couples in which one or both partners is a heavy or problem drinker are at elevated risk for intimate partner violence (IPV), yet little is known about the extent to which the context of each partner's drinking (volume per setting in bars, parties, at home, or in public places) contributes to the likelihood that partner aggression will occur. The purpose of this study is to analyze the associations between each partner's drinking context and IPV among couples in the general household population.
Methods: The Community Health Study of Couples obtained a geographic sample of married or cohabiting couples residing in 50 medium-to-large California cities. Cross sectional survey data were collected via confidential telephone interviews (n=1,585 couples; 60% response rate). Couples provided information about the occurrence of past-12 month IPV, drinking contexts, frequency of intoxication, impulsivity, adverse childhood experiences, and demographic factors. We developed separate multivariate logistic regression models to analyze each couple's drinking contexts in relation to risk for male-to-female IPV and female-to-male IPV.
Results: After adjusting for other covariates, the male partner's volume per setting in bars (Odds Ratio [OR]=1.41; 95% Confidence Interval [CI] 1.20, 1.65); at parties at another's home (OR=1.20; 95% CI 1.01, 1.43); while having friends over at one's own home (OR=1.17; 95% CI 1.02, 1.33); and in parks and public places (OR=1.36; 95% CI 1.16, 1.60) were associated with elevated risk for male-to-female IPV. For female-to-male IPV, the male partner's volume per setting in bars (OR=1.20; 95% CI 1.05, 1.37); during a quiet evening at home (OR=1.09; 95% CI 1.01, 1.18); and in parks and public places (OR=1.21; 95% CI 1.05, 1.40) were significantly associated with the outcome. The female partner's drinking contexts were not associated with either outcome.
Conclusions: Among couples in the general population, the male partner's drinking in specific contexts (e.g., bars, public places) is an independent risk factor for the occurrence of partner aggression. These findings could be incorporated into IPV screening, treatment, and prevention programs. Longitudinal research is needed to further explore the mechanisms through which drinking context contribute to the likelihood of IPV among married/cohabiting couples.

0555

INTIMATE PARTNER VIOLENCE AMONG CALIFORNIA COUPLES: ALCOHOL OUTLETS, DRINKING, AND PARTNER CHARACTERISTICS

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Objective: This study assessed the extent that alcohol outlet density, drinking, and partner characteristics (demographic and psychosocial factors) contribute to risk for intimate partner violence (IPV) among married/cohabiting couples in California.
Method: A geographic sample of 18–50 year old heterosexual couples (n=1775; response rate 60%) residing in 50 medium-to-large California cities was contacted by telephone. Cross-sectional survey data were collected via confidential interviews with both partners in the dyad. Alcohol outlet densities (off-premise outlets, bars/pubs, and restaurants licensed to sell alcohol) were appended to the survey data at the block-group level. Past-year prevalence of male-to-female partner violence (MFPV) and female-to-male partner violence (FMPV) were estimated based on uncorroborated reports from each partner concerning their own and their partner's aggression and victimization. Multilevel logistic regression models were developed to analyze the role of alcohol outlets, drinking, and partner characteristics in relation to MFPV and FMPV risk.
Results: Approximately 6.6% of couples reported MFPV, and 9.8% reported FMPV. The male partner's impulsivity and each partner's adverse childhood experiences were significantly associated with MFPV risk. Risk factors for FMPV were the male partner's impulsivity and frequency of intoxication, and the female partner's adverse childhood experiences. Alcohol outlet densities were not associated with either outcome.
Conclusions: The absence of significant associations between outlet densities and IPV in this study, in contrast to previous studies that have found outlets to be associated with more severe types of IPV (i.e., aggression that results in police calls or Emergency Department visits), may indicate that outlets do not have an impact on the types of moderate aggression (e.g., pushing, shoving, grabbing) typically seen in population-based studies of IPV. Instead, individual/couple characteristics appear to be the most salient IPV risk factors. The findings suggest that the male partner's heavy drinking may lead to negative partner/spousal interactions that result in FMPV. The male partner's impulsivity, and each partner's adverse childhood experiences, may potentiate couple conflict and result in aggression. Interventions that target prevention of family dysfunction during childhood may help reduce interpersonal violence in adulthood.

0556

DO PSYCHOSOCIAL CHARACTERISTICS AND INTOXICATION FREQUENCY MEDIATE THE RELATIONSHIP BETWEEN ADVERSE CHILDHOOD EXPERIENCES AND INTIMATE PARTNER VIOLENCE?

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There is mounting evidence that exposure in early life to adverse childhood experiences (ACE) is associated with an increased likelihood of intimate partner violence (IPV) in adulthood. Psychosocial factors, such as depression, anxiety, and impulsivity, and alcohol consumption are potential mediating factors between ACE and IPV. The purpose of this study was to explore the associations between ACE and IPV and determine the importance of psychosocial factors and intoxication frequency as mediators of this relationship. We used couple-level data from the Community Health Study of Couples, a cross-sectional geographic sample of married or cohabiting couples residing in 50 medium-to-large California cities (n=1,803 couples). We examined hypothesized associations depicted in a conceptual model with intoxication frequency, depression, impulsivity, and anxiety in the pathways between male and female ACE and male-to-female partner violence (MFPV) and female-to-male partner violence (FMPV) with structural equation path models (SEMs) using Mplus 4.21. We first tested the significance of the individual direct paths in the hypothesized models and then, based on the significance of direct pathways, tested the indirect associations of ACE and current unemployment with MFPV and FMPV, as mediated by depression (for both male and female partners), anxiety, and impulsivity (male partners only). Significant, positive direct associations were found between ACE and depression, anxiety, and impulsivity for male and female partners. Impulsivity was positively related to intoxication frequency for male and female partners. Male partners' anxiety and impulsivity, and female partners' depression, were positively related to MFPV. Male partners' depression and intoxication frequency, and female partners' depression, were positively related to FMPV. The indirect association between male partner's ACE and MPFV via male partner's depression was positive and significant ($p = 0.02$). Indirect associations between male partner's ACE and FMPV via male's partner's anxiety and impulsivity were also positive and significant ($p = 0.05$ and $p = 0.01$, respectively). The indirect associations between female partner's ACE and both MPFV and FMPV via depression were positive and significant ($p = 0.01$, both pathways). It appears that ACE impact IPV in part through psychosocial characteristics. Interventions targeted at reducing ACE and subsequent psychosocial outcomes may help reduce adult IPV.

0557

HOT SPOTS FOR VIOLENCE, ALCOHOL OUTLETS AND DRUG ARRESTS IN BOSTON
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Objectives: The spatial relationship between alcohol outlets, drug markets and violence in the city of Boston, 2006 is explored, hot spots are identified.
Methods: Data from the Boston Police Department, the census, survey data and Massachusetts state data on alcohol outlet type and location are used. Geographically weighted regression is employed at the block group level (n=544), maps of hot spots for violence, alcohol outlets and drug markets are produced.
Results: Positive relationships were found for increased minority presence, increased percentages of: poor families, vacant housing, and renters. Restaurants selling any type of alcohol, liquor stores and drug distribution arrests were positively related to violence. Violent hot spots had higher percentages of: population younger than 18, vacant housing units, renters, restaurants selling all types of alcohol, drug possession arrests, and adjacent area vacant housing.
Conclusions: Violent hot spots were found and adjacent/lagged area characteristics were related to target area violence.

0558

HEAVY DRINKING, ALCOHOL EXPECTANCIES AND BYSTANDER INTERVENTION
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Over the past several decades there has emerged a growing awareness that violence against women is a critical issue facing this country. In understanding cultural norms and sexual violence on college campuses it is imperative to consider the issue of alcohol use. Koss et al.'s (1987) national study found that 73% of all acts identified as rape involved alcohol, and 53% of all acts considered sexually coercive involved alcohol. The bystander approach is a model that has recently been put forth as one innovation that has potential empirical support and programmatic implications for sexual violence prevention (Banyard et al., 2004). This model argues that sexual assault prevention that focuses on engaging the broader context or community in intervening in coercive contexts is more likely to lead to a contextual cultural change. The present study's goal is to gain a greater understanding of the role of alcohol consumption patterns, and the role of alcohol expectancy, and bystander behaviors in coercive contexts. Participants were 637 undergraduate students attending a large mid-western university (M=22.25, SD=2.12). Structural equation modeling utilizing AMOS was used to examine three latent variables: *Alcohol Use, Alcohol Problems,* and *Intervene* (dependent variable). The independent variables were alcohol expectancies and gender. There was an overall good model fit: (X^2 = 710.23 (46) $p < .001$; NNFI = .78; NFI = .86). Alcohol expectancies were negatively and significantly associated with intervening ($\beta = -.28$, $p < .01$), indicating that the more alcohol expectancies students have, the less likely they are to intervene. Alcohol Use ($\beta = -.46$, $p < .001$) and Alcohol Problems ($\beta = -.55$, $p < .001$) were significantly and negatively related to Intervening, indicating that the heavier students are drinking and the more problems they encounter, the less likely they are to intervene in situations that arise with victims of violence. Results indicate that alcohol consumption behaviors and expectations are significantly related to one's willingness to intervene in coercive contexts. Previous research has not examined the role of alcohol in bystander behaviors in contexts of sexual coercion. Given the prevalence of alcohol in college contexts in which interpersonal and peer relationships are unfolding, and in which predatory men are targeting vulnerable women, such findings suggest important empirical, programmatic and safety implications.

0559

PREVENTION TARGETING INDIVIDUALIZED MISPERCEPTIONS OF PEER USE OF ALCOHOL AND MARIJUANA IN A GENERAL MIDDLE SCHOOL POPULATION
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This study with middle school students (N = 1022) 1) examined students' perceptions of peer alcohol and marijuana use, 2) determined the relationship between perceived peer use and students' own alcohol and marijuana use or intended use, and 3) provided individual level feedback on discrepancies between perceptions and actual use reported by students in the survey. Although it is well known that higher perceptions of peer use are related to higher risk for substance use in adolescents and college students, few universal prevention programs have targeted social norm misperceptions in early adolescents. Such programs have used general statistics for feedback, did not assess individual perceptions of use, and have not documented success. By contrast, social norm approaches that have shown great success with college students and at risk populations target misperceptions at the individual level. Individual feedback is most important in early adolescence when individual knowledge about alcohol and marijuana use or intentions are changing rapidly and vary dramatically across students. Our approach provided specific confirmatory or corrective feedback on perceived peer use and peers reported use. Students with accurate perceptions received confirmatory feedback. Students with misperceptions received visual feedback highlighting the discrepancy between their estimate and their peers reported use. They were also asked to explain the discrepancy and were provided information about how the availability heuristic leads to overestimations. We found that many students accurately reported the low levels of use reported by their immediate peers (41.7% for alcohol and 50.3% for marijuana). These students do not need corrections to their normative beliefs. The remaining students, however, reported higher levels of perceived than actual use; some suggesting that 50% or more of their peers had used alcohol (29.4% of respondents) or marijuana (25.1% of respondents) in the past week. Importantly these misperceptions were not only correlated with students' reported use but also their future intentions to use. Quantitative comparisons are in progress, but qualitative results suggest that many students receiving discrepancy feedback were appropriately challenged and reflected on their overestimations. These findings suggest that social norm feedback can be provided and may be useful in an interactive universal prevention program.

0560

BEING ADEPT: A PREVENTION PROGRAM FOR YOUTH SUBSTANCE USE IN MARIN COUNTY
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The middle school years are peak years for alcohol and drug use initiation. Adolescents who initiate substance use at an early age appear to be at greater risk for negative consequences later in life. Being Adept, a multi-component prevention intervention for Middle School students in Marin County, was designed to prevent the onset of substance use through increasing students' knowledge about the effects of these substances and empowering them to resist using alcohol and marijuana through coping skills training. We describe an initial outcomes assessment of adolescents participating in the Being Adept intervention.
In Spring 2011, assessments were administered to 5^{th}–8^{th} graders at one Middle School in Marin County immediately before and 1 day after they received the Being ADEPT intervention. The intervention consisted of one 45-minute session for 5^{th} and 6^{th} grades and two 45-minute sessions for 7^{th} and 8^{th} grades. Measures examined knowledge about alcohol and marijuana, perceived harm caused by moderate and heavy alcohol and marijuana use, and intentions to use alcohol or marijuana within the next year.
There was a significant increase in knowledge about alcohol and marijuana between pre- and post-assessments in all grades (all p<.05). Changes in perceived harms varied by grade: 5^{th} graders reported significant increases in perceived ''great harm'' from occasional alcohol use (13% vs. 22%, p < .0001), binge drinking (52% vs. 64%, p < .01), and occasional marijuana use (29% vs. 39%, p < .01); 6^{th} graders reported significant increases in perceived great harm from binge drinking (51% vs. 36%, p<.01); 7^{th} graders reported significant increases in perceived great harm from occasional alcohol use (26% vs. 55%, p < .0001) and binge drinking (43% vs. 80%, p < .0001); 8^{th} graders reported significant increases in perceived great harm from occasional alcohol use (22% vs. 4%, p<.01). There were no differences in the proportion of students reporting intentions to use alcohol or marijuana in the next year between the two assessments. However, there was a grade effect such that younger students had lower intentions to use alcohol or marijuana than older students.
Being Adept appears to impact some hypothesized mediators of substance use onset. Plans to expand the curriculum will focus on targeting intentions to use and future studies will examine the effects of the expanded curriculum on both hypothesized mediators and substance use outcomes of youth.

0561

DISMANTLING PERSONALIZED FEEDBACK INTERVENTIONS FOR COLLEGE STUDENT DRINKING

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This study examined both variation and commonality in the content of Personalized Feedback Interventions (PFIs) to reduce college alcohol use conducted over the past two decades. A review of the literature on PFIs reveals that although feedback often addresses a few, similar components (e.g., one's drinking patterns, normative beliefs), content is not always the same from one study to the next. Thus, it is difficult to evaluate which components are critical to include when implementing future PFIs. Documenting the consistency with which PFI components are included across studies may help us to better understand the unique role each component plays. In addition, an analysis of PFI materials will highlight trends with respect to both the breadth (total number of components) and depth (extent of feedback specific to each component) of content. Intervention materials analyzed came from Project INTEGRATE, an integrative study of 22 independent, alcohol interventions of which the majority (*n*=15) included personalized feedback. Two expert raters with expertise in the area of PFIs independently reviewed materials to determine whether PFIs included content on 20 different topics. Raters also noted whether content was general in nature, personal to the participant, or both. Results revealed that the number of components ranged from 6 to 15, with PFIs targeting between 10 to 11 topics, on average. Nearly 75% of PFIs included feedback on normative belief discrepancies, dependency factors, family history, and protective behavioral strategies, with all studies covering alcohol use, descriptive drinking norms and use-related consequences. Between one- to two-thirds of PFIs covered expectancies, alcohol-specific sexual behavior, calorie content, financial costs, discussion of change, DWI, and information for special groups. Approximately 25% or less of PFIs covered illicit drug use, biphasic effects, tobacco use, alcohol and mental health, alcohol and drug interactions, and one's decisional balance. Within more commonly included intervention components, the majority of feedback was both personal to the participant, as well as general, or educational, in nature. Although not an exhaustive analysis of all PFI studies, those included in the current analysis are a good representation of the literature, and taken together, indicate that PFIs cover most topics in depth, but there is reasonable variability in what is included, beyond a few components. Funded by: R01 AA 019511

0562

USING ITEM RESPONSE THEORY ANALYSIS TO CREATE LATENT ALCOHOL PROBLEM SCORES FOR COLLEGE STUDENTS FROM MULTIPLE SCALES

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Project INTEGRATE was launched to examine mechanisms of change for the efficacy of brief alcohol interventions for college students. It has been difficult for any study to address this issue because single studies typically examine efficacy in a narrow sample, assess limited measures, and have small sample sizes. To overcome these shortcomings, we initiated an integrative data analysis (IDA) study combining raw data from 22 independent, alcohol intervention studies (N = 24,387). Given that it was not a planned, multi-site study, a critical challenge stemmed from the fact that the existing measures were not comparable across studies. The purpose of this analysis was to develop item response theory (IRT) models to compute latent scores for alcohol problems across the 22 independent studies and time, which could be used in subsequent analyses to examine mediators and moderators of intervention efficacy. Although five major alcohol problem scales were used across the studies (15 included the Rutgers Alcohol Problem Index [RAPI], 6 the Young Adult Alcohol Problems Screening Test [YAAPST], 1 the Brief Young Adult Alcohol Consequences Questionnaire [BYAACQ], 6 the Alcohol Use Disorders Identification Test [AUDIT], and 4 the Alcohol Dependence Scale [ADS]), there was good overlap of scales within studies and of items across scales. The scales were different in terms of the referent time frame and response options used; however, we dichotomized all items, and determined that the different referent time frames would not unduly influence the model. A total of 80 pooled items at baseline were calibrated for item parameters (i.e., severity and discrimination) using a two-parameter logistic (2-PL) IRT model. We created a one-dimension latent alcohol problems score and latent scores for four distinct dimensions of alcohol problems: school/work/responsibility, interpersonal, acute heavy drinking, and dependence-like symptoms. Validation analysis indicated that the latent scores were highly correlated (rs> .79) with the count indices of the RAPI, YAAPST, and BYAACQ, and with the scale scores for the ADS, and AUDIT. Thus, the results demonstrate that it is possible to conduct IDA using data collected independently across studies to examine changes in alcohol problems as the outcome measure and to examine potential mechanisms that account for these changes. Funded by: R01 AA 019511

0563

ADOLESCENT DATING VIOLENCE AND ALCOHOL USE TRAJECTORIES IN THE YEAR FOLLOWING A BRIEF INTERVENTION IN THE EMERGENCY DEPARTMENT

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Dating violence among adolescents is a growing public health concern, with exacerbated rates found among youth in urban emergency departments (ED). A recent study (SafERteens) demonstrated the efficacy of a brief intervention (BI) in reducing peer violence and alcohol-related consequences among adolescents in the ED. This paper presents longitudinal dating violence data from the SafERteens study. Patients (ages 14–18) in an urban ED who screened positive for past year alcohol use and violence were randomized (computer BI, therapist BI, or control) and completed 3, 6 and 12 month follow-ups. First, secondary outcomes of the BIs on dating violence (aggression and victimization) were examined among a subsample of adolescents reporting past year dating violence (n=328; 55%). Compared to controls, participants in the CBI showed significant reductions in moderate dating victimization at 3 and 6 months. Among those reporting more frequent baseline dating violence, the TBI reduced moderate dating victimization at 6 and 12 months and severe dating victimization at 3 months. The BI's did not significantly affect dating aggression. Second, longitudinal trajectories in dating violence, as well as alcohol use and peer violence, were examined among the full sample (n=726). For dating violence, three trajectory groups were identified: Low (43.5%), Moderate (40.4%), and High (16.1%). Baseline risk factors associated with more severe dating violence trajectories included alcohol use, peer violence, other drug use, friends negative influences, parent substance use, and community violence exposure; protective factors included friend positive influences and parental monitoring. Two alcohol trajectory groups were identified: Low (64.1%) and Moderate (35.9%); three peer violence trajectory groups were identified: Low (49.9%), Moderate (33.6%), and High (16.5%). Joint trajectory analysis suggested that dating violence and alcohol use trajectories were moderately associated; dating and peer violence trajectories were strongly associated. An ED-based BI for peer violence and alcohol misuse shows some promise for reducing dating victimization. Given that dating violence trajectories were associated with alcohol use and peer violence trajectories, interventions addressing these concomitant behaviors are warranted. Future studies are needed to refine ED-based intervention approaches to have more robust effects on dating violence. (Supported by NIAAA 014889).

0564

CORRELATION BETWEEN ASSIST SCORE AND 30 MONTH MORTALITY: RESULTS FROM A SAMPLE OF ALCOHOL USERS PRESENTING TO THE EMERGENCY DEPARTMENT

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Excessive alcohol use is the third leading cause of preventable death in the U.S. leading to an estimated 79,000 deaths each year. The signs and symptoms of alcohol-related mortality are often evident long before an individual's death and many deaths could be prevented if programs implemented in health care facilities were able to reliably identify patients at risk for alcohol-related mortality. There is some evidence that SBIRT programs (screening, brief intervention, and referral to treatment) reduce alcohol related mortality by reducing participant's risk for experiencing acute and chronic health consequences related to their alcohol use. This project examines the relationship between ''level of risk'' and other patient characteristics and death within 30 months of presenting to the emergency department (ED). Data are from a sample of 756 alcohol users presenting to the ED between February and May 2009 and enrolled as part of an ongoing SBIRT program in Georgia. Participants were given a health survey which included the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST); a screening tool designed to quantify individual risk (health and social) for various substances including alcohol. Deceased participants were identified through speaking with the participants' friends and family while attempting to reach the participant for follow up and verified through newspaper obituaries or health department death records. Fifty of the 756 patients were identified as deceased within 30 months after intake. Results show an average alcohol ASSIST score at the time of the ED visit of 14.1 for deceased group compared to 13.3 for patients still living after 30 months. This difference was not statistically significant ($p = 0.587$). Deceased participants were significantly older than living participants (51.7 yrs to 40.9 yrs, $p<0.001$), reported significantly worse physical health as measured by the SF-12 (37.6 to 42.1, $p=0.001$) and had significantly more days in the hospital in the six months prior to the ED visit (7.0 days to 2.0 days, $p=0.014$). Results do not support the hypothesis that higher alcohol risk levels, based on ASSIST scores, can be used to identify patients with greater risk of alcohol-related mortality. The current project used only intake data collected during the ED visit. All analyses were bivariate. Future studies will utilize survival analysis techniques to examine potential effects of SBIRT services on alcohol-related mortality.

0565

KIOSK-BASED PRENATAL SCREENING AND INTERVENTION FOR ALCOHOL AND SWEETENED BEVERAGES

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Purpose: Federal guidelines recommend screening for alcohol use among pregnant women. Resource limitations and high patient loads, especially in publicly funded health centers, result in limited time and capacity for alcohol screening and brief interventions. Innovative methods that can be conducted without a health care provider are needed. We describe the development and pilot-testing of a self-administered, computer-based screening and intervention program for beverage consumption during pregnancy for use in public health clinics.
Methods: A self-administered, computerized program focused on beverage drink size was developed and pilot tested at a local Women, Infants and Children (WIC) clinic. Because a majority of women abstain from alcohol during pregnancy but there is an increased risk for gestational diabetes and related pregnancy complications from excessive consumption of sugar added drinks, we added a screening and intervention component for sweetened beverages to our program. The alcohol portion of the computerized program builds on the Early Start Plus intervention evaluated in the Northern California Kaiser programs in 2000. The sweetened beverage portion builds on materials used in Northern California WIC programs. Unique elements of the intervention include personalized feedback based on women's drink size assessment. Materials were reviewed by public health experts and in focus groups of pregnant women attending the clinic.
Results: The computerized program was developed, pre-tested and integrated into a portable touch-screen kiosk. The screening and intervention program software includes computer screens and information brochures (available for print out) for women reporting alcohol use in the past month, alcohol use prior to their pregnancy but not in the past month, and no alcohol use but consumption of sweetened beverages in the past month. The screening assesses beverage-specific drink sizes using actual drinking vessels and additional pictures of drink containers. The intervention provides individualized feedback on drink size, such as discrepancies between the women's drinks and beverage specific standard drinks, and guides women through a plan to reduce consumption if they are unable to commit to not drinking.
Conclusions: Methods to screen and provide brief interventions for alcohol and sweetened beverage consumption among pregnant women in a public health setting without increasing staff work load are feasible.

0566

EFFECTS OF A MULTI-COMPONENT RESPONSIBLE BEVERAGE SERVICE PROGRAM ON VIOLENT ASSAULTS IN SWEDEN

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A multi-component Responsible Beverage Service (RBS) program has been disseminated in Swedish municipalities. The aim of the program is primarily to reduce violence associated with consumption of alcohol at on-licensed premises. The purpose of this study is to analyse the effect of the program on police-recorded assaults after the dissemination during the period 1996–2009.
This study is a natural experiment that uses variation in the level of implementation of the RBS program to predict change in the rate of police-recorded assaults in the municipalities. The municipalities included in the study were those who started to work according to the RBS program no later than 2008. On-licensed premises, which are open during evenings and where violence can occur, must exist in the municipality. Out of 290 municipalities, 240 fulfilled these requirements.
Program fidelity each year in the municipalities during the study period was studied by means of several surveys (response rates: 94–98%). Yearly data on police-recorded assaults, committed during weekend nights, was used as dependent variable. A random-coefficient multilevel linear regression model was used to examine the effect of the RBS program on assaults, where the coefficient of time varied randomly across municipalities.
The results show that the RBS program had a significant effect on police-recorded assaults. However, the effect was mainly seen in smaller municipalities. Of the different components of the RBS program, it was primarily RBS-training and the presence of a community coalition steering group, which contributed to the effect. No significant effect was found regarding supervision of on-license premises.
This study was one of the first studies to estimate the effects of a multi-component RBS program on police-recorded assaults in a large number of municipalities. Our findings suggest that the RBS program can have a significant impact on violent assaults primarily in smaller municipalities.

10. TREATMENT / RECOVERY

0567

THE UTILITY OF CARBOHYDRATE-DEFICIENT TRANSFERRIN, MEASURED USING THE N-LATEX ASSAY, IN A SAMPLE OF SOCIAL DRINKERS AND ALCOHOL DEPENDENT INDIVIDUALS

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Background: Carbohydrate-deficient transferrin (CDT) has been shown to be a sensitive and specific biomarker of alcohol consumption and has been employed to monitor alcohol abstinence during alcohol detoxification treatment and rehabilitation. The utility of CDT has yet to be determined in a sample of heavy drinking social drinkers, e.g. sessional drinkers.
Method: Serum samples from abstainers (consuming no alcohol) (N=2), sessional drinkers (consume >48g (female) and >64 g (male) daily) (N=10) and alcohol dependent individuals (N=14) were analysed for CDT using the N-Latex immunoassay at the Northern General Hospital in Sheffield. Alcohol consumption, expressed as grams, was recorded in self-reported diaries over a 7 day period.
Results: Abstainers exhibited negative %CDT results, compared with the median results in sessional drinker and alcohol dependent individuals, which were above the cut-off value of 2.6%, which is indicative of a positive CDT result with the N-Latex assay. There was a significant linear relationship (p=0.01) between number of drinking days and a positive %CDT within the sample of sessional drinkers. Alcohol dependent individuals CDT% levels significantly reduced (p=0.017) in line with alcohol withdrawal treatment progression.
Discussion: The N-Latex %CDT immunoassay indicated heavy drinking in both a sessional drinking sample and an alcohol dependent sample. This supports the utility of this assay to detect sessional drinking and not solely alcohol dependence. However as this work was a pilot study, it is important that the study be repeated within a larger appropriately powered sample.

0568

ETHYLGLUCURONIDE EXCRETION, FACTS AND MYTHS: RESULTS OF A DOSE RANGING ALCOHOL CHALLENGE STUDY

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Purpose: Ethylglucuronide (EtG), a minor metabolite of ethanol, is a specific marker for alcohol exposure, with a window for detection in body fluids that greatly exceeds that of the parent compound. Most of the focus has been on its forensic use with more limited attention to its possible value as a clinical tool. The considerable excitement about EtG has inflated expectations regarding duration of positivity following alcohol consumption (e.g. ''80 hour test''), and conversely elicited skepticism consequent to evidence regarding risks of false positives following extraneous (non beverage) alcohol exposure.
Method: To better characterize aspects of urinary EtG elimination that might be especially relevant to clinical trials and treatment programs, we carried out a multiple dose alcohol challenge study. Each of ten non-smoking subjects received, on separate days, low, medium and high doses of ethanol calculated to achieve plasma concentrations of 20, 80 and 120 mg/dL respectively. Intensive inpatient sampling for assay of urinary EtG was performed for 24 hours followed by twice daily outpatient collections.
Results: At 12 hours, all doses resulted in urinary EtG concentrations well above 100 ng/mL (averages of 858, 9,607 and 18,219 ng/mL for the low, medium and high doses). At 24 hours following completion of drinking, the percentages exceeding this cut-off were 40, 80, and 100% for the low, medium and high doses. Using 200 and 500 ng/mL cut-offs, these values were 30, 80 and 89%, and 0, 70 and 78%. Peak concentrations averaged 12,002, 63,427, and 192,944 ng/mL following the low, medium and high doses. The mean half-life of EtG was 145 min, which is consistent with published data. The fraction of the alcohol dose eliminated as EtG increased with increasing doses. Concurrent assay for ethyl sulfate yielded comparable results.
Conclusion: Contrary to claims for EtG as an 80 hour test, EtG was infrequently detected beyond 48 hours even with high dosing. Even with the low dose, EtG concentrations exceeded those reported in controlled studies of extraneous exposure. The elimination half-life of EtG is short. Thus, increasing the cut-off value from 100 to 200 or even 500ng/mL is likely to have a modest impact on the duration of positivity, but may significantly decrease the small risk of ''false'' positives from extraneous exposure. Counseling clients to avoid sources of extraneous alcohol exposure is another option.
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0569

DETECTION OF ALCOHOL USE BY A TRANSDERMAL ALCOHOL MONITOR DIFFERS ACCORDING TO GENDER AND NUMBER OF DRINKS

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Alcohol biosensors provide a continuous estimate of blood alcohol concentration based on the concentration of alcohol in perspiration on the skin. The validity of transdermal alcohol biosensors relative to laboratory and field breath alcohol concentration has been established, but more information is needed about how volume of alcohol consumed influences detection rates. In addition, gender differences in detection have not been thoroughly investigated. The objective of this investigation was to establish the ability of the SCRAM alcohol sensor to detect alcohol use at different levels of self-reported consumption, and to determine whether gender influenced detection of alcohol use. Method: Heavy drinking adults (N = 70) were enrolled in one of two investigations of Contingency Management that utilized the SCRAM ankle bracelet to verify reduction in alcohol use. Participants wore the SCRAM bracelet for 1–28 days and reported their alcohol use, including times of drinking, on daily web-based surveys. Participant reports of alcohol use were matched with drinking episodes identified from bracelet readings using day and time of day. Results: The sample was 46% female and 73% non-Hispanic white, with an average age of 30 years. Some bracelet malfunctions were noted and resulted in loss of TAC data on 5.2% of days. On days when bracelets were functional, 690 drinking episodes were reported. Using data from the bracelet, we detected 502 of those episodes (72.8%). Using an episode-level dataset and Generalized Estimating Equations analyses with body mass index controlled, there were no overall gender differences in detection of reported drinking episodes (77% for women and 69% for men). However, at the level of four or fewer self-reported drinks, women's episodes were more likely to be detected, $b = 1.06$, (OR = .35; CI: .18–.68), $p < .01$, and women reached higher transdermal alcohol concentration (TAC) levels ($M = .038$ g/dL) than men ($M = .023$ g/dL). At the level of more than four drinks, there was no gender difference in detection (92.6% of women's episodes vs. 93.4% of men's), $b = .40$, but men showed significantly higher number of drinks per episode ($M = 9.78$ vs. $M = 7.88$), $b = .26$ (OR = .77; CI: .62–.97), $p < .05$. Conclusion: The transdermal alcohol monitor that we tested is very good at detecting heavy drinking levels of more than four drinks; performance of the monitor below this level was better among women due to their higher TAC levels.

0570

CHANGES IN AUDIT-C SCORES REFLECT CHANGES IN DRINKING - RESULTS OF A BIOMARKER STUDY

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Purpose: Alcohol screening questionnaires, such as the AUDIT-C, are increasingly integrated into routine care, and repeat screening is often used to monitor drinking among patients who screen positive. However, it is unknown whether changes in alcohol screening scores reflect changes in alcohol misuse. This study used an alcohol biomarker with a linear dose-response association with alcohol consumption—HDL cholesterol (HDL)—as a proxy measure of alcohol consumption, and evaluated whether changes in AUDIT-C scores were associated with changes in HDL levels.

Methods. This cohort study used secondary clinical data from the Veterans Health Administration (VA Region 1). Eligible outpatients included patients who were screened with the AUDIT-C (0–12 pts) on 2 occasions ≥12 months apart from 2004 to 2007, and had HDLs measured in the year after each AUDIT-C as part of routine care. Changes in AUDIT-C scores and HDL were calculated for each patient. Main analyses were conducted in patients who screened positive on the first AUDIT-C (≥ 5 pts), and used unadjusted linear regression to evaluate changes in mean HDL across varying changes in AUDIT-C scores, compared to patients with AUDIT-C scores that did not change. Secondary analyses adjusted for 3 blocks of covariates. Explanatory post hoc analyses repeated analyses in the entire sample and subgroups based on screening status at baseline and follow-up.

Results. For patients who initially screened positive (n=27,858) and had ≥5 point decreases in AUDIT-C scores at follow-up, the magnitude of decreases in HDL reflected the magnitude of decreases in AUDIT-C scores: HDL dropped 1.4 mg/dl (0.7–2.1) for a 5 pt. decrease in AUDIT-C score, and 3.8 mg/dl (2.5–5.1) for a 12 pt decrease in AUDIT-C score. However, HDL did not increase among patients who increased their AUDIT-C scores. Multivariate adjustment did not meaningfully alter findings. Explanatory analyses among all patients (n=320,944) revealed a dose-response association between increases or decreases in AUDIT-C scores and changes in HDL among patients who screened negative on both AUDIT-Cs, or who screened positive on only one AUDIT-C, but not for patients who screened positive on both AUDIT-Cs.

Conclusion. These findings suggest that AUDIT-C scores reflect changes in alcohol consumption, with the exception of patients who screen positive on two occasions. Repeat AUDIT-C screening may be a useful clinical measure of changes in alcohol consumption.

0571

DIRECT ALCOHOL BIOMARKERS AS TOOLS TO GUIDE MEANINGFUL INTERVENTIONS WHILE MONITORING REPEAT INTOXICATED DRIVERS IN KENOSHA COUNTY

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The goal of this study was to evaluate the performance of two direct alcohol biomarkers as tools to monitor drinking behavior in repeat intoxicated drivers during the 12-month period of their required driver's safety plans. When relapses were detected, the biomarker information was used to conduct a brief intervention to motivate a change in drinking behavior. The study analyzed 32 drivers who came to the Hope Council on Alcohol and Other Drug Abuse for a court-mandated assessment after having been arrested for driving under the influence (DUI). All drivers had at least 3 DUI offenses in their lifetimes, and 50% had a BAC above 0.2% at the time of the arrest. The biomarkers used were ethyl glucuronide (EtG) in fingernails and phosphatidylethanol (PEth) in dried blood spots. Sample collection was done on site by collecting fingernail clippings and blood spots. Samples were sent to USDTL to determine EtG and PEth levels using liquid chromatography and tandem mass spectrometry. Each driver was tested at the assessment interview (baseline) and at 3 and 8 months follow-up. The analysis consisted of classifying drivers into four main groups: 1) Abstainers were drivers who tested biomarker negative at baseline and follow-up; 2) Reducers were drivers who tested biomarker positive at baseline followed by a continuous decline in biomarker values at the follow-up periods; 3) Relapsers were drivers who showed an increase in biomarker levels at any of the monitoring periods; and 4) Non-compliant were drivers who did not comply with biomarker testing at follow-up. The results showed that 19% (6/32) of drivers classified as abstainers; 59% (19/32) of drivers reduced their drinking from baseline to follow-up; 6% (2/32) suffered a relapse; and, 16% (5/32) became non-complaint. Since the reducers represent the largest group in this ongoing analysis, this study supports the value of brief interventions in changing the drinking behavior of repeat intoxicated drivers during follow-up. After drivers discussed the biomarker data with their assessors, most of them experienced a decrease in drinking behavior at follow-up. By using direct biomarkers, Kenosha officials can now more accurately flag the ''extreme high risk'' drivers, conduct more meaningful interventions, and refer them to more frequent monitoring. Developing evidence-based practices is helping Kenosha County allocate resources more effectively and thus increasing public safety by attempting to decrease drunk driving.

0572

ESTABLISHING EVIDENCE-BASED PRACTICES USING TWO DIRECT ALCOHOL BIOMARKERS IN REPEAT INTOXICATED DRIVERS IN KENOSHA COUNTY

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The goal of this study was to evaluate the performance of two direct alcohol biomarkers - ethyl glucuronide (EtG) in fingernails and phosphatidylethanol (PEth) in dried blood spots – when used as tools in the assessment of repeat intoxicated drivers in Kenosha County, Wisconsin. This study was conducted by enrolling 50 repeat-intoxicated drivers undergoing a court mandated assessment after their arrest. Sample collection was done at the assessment center by collecting fingernail clippings and blood spots from each driver. Samples were sent to USDTL to determine EtG and PEth levels using liquid chromatography and tandem mass spectrometry. Reports of alcohol use were obtained using a modified Khavari alcohol test. Demographic of the drivers enrolled showed: 84% males, mean age 41 years, 80% Caucasians and 20% others. Most drivers (64%) were single, 56% had some college education and 62% were full or part-time employed. Their drinking profiles showed 78% with at least three DUI offenses in their lifetime and 92% with prior histories of alcohol treatment. The biomarkers' results showed that 72% (36/47) of drivers tested positive for EtG and 58% (29/45) tested positive for PEth at the time of their assessment interview (baseline); 83% (40/48) tested positive for either EtG or PEth and 59% tested positive for both. Compared to self-reports, 86% (31/36) of drivers reporting some drinking 90 days before baseline tested EtG+ and 55% (6/11) of drivers reporting full abstinence 90 days prior to baseline tested EtG negative. The results for PEth showed that 94% (16/17) of drivers reporting some drinking for 30 days before the assessment tested PEth+ and 54% (15/28) of drivers reporting full abstinence for 30 days prior to baseline tested PEth negative. Repeat testing in the 'presumed' false positive group (5 EtG and 13 PEth) showed that 85% of them had a reduced biomarker value at re-test supporting suspicions of under-reporting at baseline and confirming reduced drinking at follow-up. These findings demonstrate that direct alcohol biomarkers can help the assessor establish evidence based practices to: 1) flag those drivers who are still drinking after their arrest, 2) confirm findings of diagnosis (use/abuse/dependence), 3) identify drivers in denial; and 4) develop a more appropriate treatment plan. Drivers who test biomarker positive despite reporting full abstinence are now tested more frequently and assessors interact more closely with their treatment providers.

0573

PHOSPHATIDYLETHANOL (PETH) IS AN ALCOHOL BIOMARKER AND ANTIGENIC METABOLITE

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Alcohol abuse and related disorders is a major global health problem, and accurate biomarkers are needed to indicate cumulative intake over a given time period, drinking patterns, and alcohol-induced organ damage. Phosphatidylethanol (PEth) is an ethanol-specific, long lived biomarker for alcohol ingestion which can be detected in blood up to two weeks after heavy drinking. However, research into this ethanol metabolite is limited due to lack of regents and accessible methods. We synthesized acyl-modified PEth analogs for efficient coupling to biotin and other biomolecules. These tools were employed to produce antibody clones and to develop an immunoassay for PEth detection in blood. Three high-binding clones produced signals between 15 and 30 times stronger for biotin-PEth compared to other biotin-lipids. Binding of these clones was also selectively competed using PEth with less than 10% cross-reactivity to other abundant phospholipids found in erythrocyte membranes including phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, sphingomyelin, and cholesterol. Standard curve analysis indicates the assay is useful for measuring several PEth species over physiological ranges and as low as 0.5 micromole per liter. We also explored PEth incorporation into washed erythrocytes and PEth generated in vivo; along with the presence of anti-PEth antibodies (See Nissinen, et al. ''Low plasma antibodies specific for phosphatidylethanol in alcohol abusers and patients with alcoholic pancreatitis.'' *Addict Biol* 2011.) We found that treatment of isolated erythrocytes for 4 hours with 0.5 mg/mL PEth resulted in a competitive PEth signal; and determined that human sera from non, moderate, and heavy drinkers contain detectable anti-PEth antibodies. These results demonstrate the feasibility of using high-affinity recombinant monoclonal $F(ab)_2$ antibodies to measure the long-lived ethanol metabolite, PEth, both *in vitro* and from erythrocytes. Further, the identification of anti-PEth antibodies in the circulation is intriguing and indicates we are just beginning to understand the value of PEth as a biomarker for ethanol ingestion and its role as a potential mediator of ethanol induced organ damage.

0574

DETECTION OF SELF-REPORTED SUBSTANCE USE: A COMPARISON OF ALCOHOL AND COCAINE BIOMARKERS

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Low-cost biomarkers of drug use (urine tests) with a detection period of two or more days are increasingly being used clinically as objective measures of drug use and the basis for evidence-based interventions (e.g., contingency management). However, low-cost alcohol biomarkers (breath tests) are less useful clinically due to their brief detection period (0–12 hours).

This study compared the detection of self-reported alcohol and cocaine use using alcohol breath tests and cocaine urine tests in 176 adults with co-occurring severe mental illness who received 3 months of regular alcohol and drug monitoring (urine and breath samples were collected every Monday, Wednesday, and Friday). All participants were cocaine dependent and 80 (45%) also met criteria for an alcohol use disorder. Self-reported days of alcohol and cocaine use were assessed monthly using the Addiction Severity Index -Lite. Descriptive statistics, as well as dependent sample t-tests, were utilized to compare the detection of self-reported use by alcohol and cocaine biomarkers.

Mean days of alcohol and cocaine use were 3.0 (SD=7.2) and 2.5 (SD=5.8), respectfully (not a statistically significant difference). Out of the 6120 days assessed, the total days of self-reported alcohol use was 623 (10.2%) and self-reported cocaine use was 500 days (8.2%). Participants submitted significantly more cocaine-positive urine tests (Mean=1.8, SD=2.7) than alcohol-positive breath tests (Mean=0.2, SD=0.6), $t(359)=11.7$, $p<0.0001$. Out of the 4680 urine and breath samples obtained throughout the study, 689 (14.7%) were positive for cocaine, while 72 (1.5%) were positive for alcohol use. Self-reported cocaine use was detected by cocaine urine tests 92% of the time (82/89 months in which use was reported). In contrast, self-reported alcohol use was detected 29% of the time (23/78 months in which use was reported) across the entire sample and 37% of the time in subjects with alcohol use disorders (13/35 months in which use was reported).

Results provide further evidence that alcohol breath tests are unlikely to detect self-reported use, even when monitoring occurs as often as three times a week. Aside from assessing current intoxication, this biomarker is of little clinical use. The strengths and weaknesses of other biomarkers, such as ethyl glucuronide (capable of detecting alcohol for two or more days after use), will be discussed.

0575

THE ABILITY OF SINGLE SCREENING QUESTIONS FOR UNHEALTHY ALCOHOL AND OTHER DRUG USE TO IDENTIFY SUBSTANCE DEPENDENCE IN PRIMARY CARE

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Background: Single Screening Questions (SSQs) are recommended to identify unhealthy alcohol and other drug (AOD) use. But SSQs may provide information on severity needed to inform brief intervention, thought to be obtainable only from longer questionnaires. We assessed SSQ accuracy for identifying patients with dependence.

Methods: In a cross sectional study in an urban primary care practice, subjects were administered the SSQs asking about AOD use [''How many times in the past year have you had 5 (4 for women) or more drinks in a day?'' & ''How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?''], the Alcohol Use Disorders Identification Test-Consumption items (AUDIT-C), the Drug Abuse Screening Test (DAST), & the Composite International Diagnostic Interview reference standard for current dependence. All possible cutoffs were evaluated by receiver operating characteristic (ROC) curve. Sensitivity (Ss), specificity (Sp), positive predictive value (PPV) and likelihood ratios positive and negative (LR+, LR- & 95% confidence intervals [CIs]) were assessed at cutpoints maximizing the sum of Ss and Sp (alcohol tests for alcohol dependence (AD), drug tests for drug dependence (DD)).

Results: Of 286 patients, 9% had AD and 12% DD. The areas under the ROC curves (AUCs), the probability of distinguishing those with and without dependence, were high: SSQs (alcohol 88%, drug 93%), AUDIT-C (87%), DAST (96%). At optimal cutpoints (OCs) characteristics for the alcohol SSQ for AD (OC ≥8 times) were Ss 88%, Sp 84%, PPV 35%, LR+ 5.6 (CI 4.1, 7.7), LR- 0.1 (CI 0.05, 0.4); for the 3-item AUDIT-C for AD (OC score≥3) Ss 92%, Sp 71%, PPV 23%, LR+ 3.2 (CI 2.5, 3.9), LR- 0.1 (CI 0.02–0.4); for the drug SSQ for DD (OC ≥3 times) Ss 97%, Sp 79%, PPV 38%, LR+ 4.6 (CI 3.6, 5.9), LR- 0.04 (CI 0.01, 0.2); for the 10-item DAST for DD (OC score ≥4) Ss 100%, Sp 84%, PPV 46%, LR+ 6.3 (CI 4.7, 8.3), LR- 0.

Conclusions: Single screening question (SSQ) results are associated with likelihood ratios that can lead to important changes from pre- to post-test probability of dependence. SSQs can be used as brief assessments to identify dependence and may be as or even more accurate than longer tools. SSQs can provide information needed and may overcome a barrier (lengthy questionnaires) to dissemination of screening and brief intervention in primary care settings.

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0576

VALIDATION OF THE ASSIST FOR DETECTING AT-RISK ALCOHOL USE IN URGENT CARE CLINICS

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Substantial evidence has shown that Screening, Brief Intervention, and Referral to Treatment (SBIRT) is effective in reducing alcohol use. While the SBIRT model will identify patients suffering from alcohol use disorders requiring treatment, its major emphasis is on detecting and intervening with patients reporting at-risk alcohol use (patients exceeding the NIAAA recommended daily or weekly limits). In response to the need for an inexpensive international screening test, the World Health Organization developed the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) in 1997 and this instrument is being used by many of the SBIRT projects funded by the Substance Abuse and Mental Health Services Administration (SAMHSA). Much of the research surrounding the development of the ASSIST was focused on the detection of alcohol abuse and dependence rather than at-risk drinking. This study uses a sample of 443 patients visiting three medical center-affiliated urgent care clinics to identify ASSIST scores with the best specificity and sensitivity for detecting at-risk alcohol use. Patients were identified as current drinkers by completing a brief screen in the waiting room. Current drinkers were consented and administered the ASSIST, the Single Alcohol Screening Question (SASQ), a 90 day timeline follow-back (TLFB), and the Diagnostic Interview Survey (DIS). Results reported here show specificity and sensitivity analyses comparing ASSIST scores to the 90 day TLFB, the ''gold standard'' for identifying at-risk alcohol use. While none of the ASSIST scores offer strong sensitivity and specificity, a cutoff score of 4+ has strong sensitivity (Se 83.5) and modest specificity (Sp 42.4) while an ASSIST cut-off score of 6+ has the best combination of sensitivity and specificity when compared to the TLFB (Se 64.2, Sp 63.6). Many of the current SAMHSA funded SBIRT projects are using an ASSIST score of 11+ as the cutoff score indicating the need for a brief intervention. While offering a high specificity (Sp 90.3) these analyses indicate that a cutoff score of 11+ will not detect 60 percent (Se 39.6) of at-risk alcohol users who might benefit from a brief intervention. While more research in varied healthcare settings would help to clarify the results of this study, the use of a lower ASSIST cutoff score is recommended to provide services to the largest possible percentage of at-risk drinkers.

0577

FACTORS ASSOCIATED WITH REPEATED NEGATIVE ALCOHOL SCREENS: IS ANNUAL ALCOHOL SCREENING UNNECESSARY FOR SOME VA PATIENTS?

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Objectives: Alcohol screening and brief interventions are the 3rd highest prevention priority for US adults. The VA requires annual alcohol screening with the AUDIT-C, and >95% of patients are screened annually. However, many patients who screen negative for alcohol misuse may be at low-risk for later screening positive. Identifying low-risk patients who might not need annual screening after an initial negative screen could decrease the burden of unnecessary screening. The purpose of this study was to identify demographic and clinical factors associated with <5% probability of converting to a positive alcohol screen on subsequent routine screening among VA patients who initially screened negative.
Methods: This observational study used data from VA's Corporate Data Warehouse (CDW) Region 1. The study sample included 298,064 male and 19,395 female VA patients who had at least 2 AUDIT-C screens 9–15 months apart (1/04–12/08), screened negative on an initial AUDIT-C (≤3 men; ≤2 women), and had no alcohol or other substance use diagnoses or treatment in the prior year. The main outcome was screening positive on subsequent AUDIT-C screen. Adjusted logistic regression analyses, stratified by gender, evaluated the predicted probability of a positive subsequent screen associated with patient characteristics: age; race/ethnicity; or marital, smoking, co-pay, or mental health status; and tested for interactions with baseline drinking status, nondrinkers (AUDIT-C=0) and drinkers (AUDIT-C>0).
Results: Among 317,459 patients with an initial negative screen, 61% of both men and women were nondrinkers and 39% were low-risk drinkers. Baseline drinking status modified the association between all patient characteristics and the outcome so analyses were stratified by drinking status. In analyses of patients who were nondrinkers on initial screen, only men (6.83%; 95% CI 5.55–8.10%) and women (5.41%; 95% CI 4.14–6.68%) <30 years old had >5% predicted probability of screening positive on subsequent screen. In analyses of patients who reported drinking on initial screen, the predicted probability of a subsequent positive screen was ≥ 5% (11.3–19.1% for men; 5.7–14.4% for women) in all subgroups evaluated.
Conclusions: Nondrinkers ≥30 years old were at relatively low risk of screening positive at their next routine alcohol screening. Health care systems such as VA might choose to selectively screen these low risk patients less often than annually.

0578

SCREENING PATIENTS WITH SOCIAL ANXIETY DISORDER USING THE DRINKING MOTIVES QUESTIONNAIRE

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Introduction: Social anxiety (SA) is a significant risk factor for hazardous drinking, alcohol-related problems, and the subsequent development of alcohol use disorders. Drinking motives, especially those that are negative reinforcers, such as Coping and Conformity, have been thought to be important mediators of the relationship between social anxiety and alcohol use, with Coping motives having the most evidence in the literature. The Drinking Motives Questionnaire (DMQ-R-5) is a validated self-rated instrument that measures drinking motives, and further separates Coping motives into Coping Depression and Coping Anxiety. This separation has relevance in that drinking to cope (DTC) for depression has been associated with alcohol related problems as compared to DTC for anxiety, which has been associated with alcohol consumption. This project evaluates whether specific drinking motives, or a specific question or subset of questions, accurately indicate severity of alcohol use behaviors. If so, it could be a valuable screening tool.
Method: This is a post hoc analysis of an existing data set of 83 subjects with social anxiety disorder and hazardous alcohol use who participated in a randomized clinical trial evaluating the efficacy of an alcohol intervention vs no intervention. Everyone was seeking SA treatment and received the SSRI paroxetine for the treatment of SA. All subjects completed the DMQ-R-5 and were also evaluated for the presence of alcohol dependence (AD). For the purposes of this project, the presence or absence of AD was used as a proxy for severity of alcohol use behaviors as a dichotomous measure. Multiple logistic regression was used to evaluate the contribution of each DMQ-R-5 subscale as well as each individual question to the presence of a diagnosis of AD.
Results: Coping Depression was the only subscale that contributed to the unique prediction of AD. Additionally, question 14 (''to cheer up when you're in a bad mood'') and question 16 (''to numb your pain'') predicted a diagnosis of AD above and beyond their association with each other.
Conclusion: Among patients with SA, questions 14 and 16 on the DMQ-R-5 may be a useful screen for health professionals to predict severity of alcohol related problems. It may also be fruitful to specifically target the motives of ''to cheer up when you're in a bad mood'' and ''to numb your pain'' when providing advice during brief interventions.

0579

ASSESSING YOUTH PARTICIPATION IN AA-RELATED HELPING: VALIDITY OF THE SERVICE TO OTHERS IN SOBRIETY (SOS) QUESTIONNAIRE IN AN ADOLESCENT SAMPLE

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Positive adult outcomes associated with Alcoholics Anonymous related-helping (AAH) has spurred study of the benefits of AAH among recovering adolescents. However, adolescent addiction research is hampered by few validated child assessments of AA activities including AAH. This study provides psychometric findings of a brief AAH assessment ''Service to Others in Sobriety (SOS)'' administered to a large sample of adolescents court-referred to residential treatment (93 boys, 102 girls).
Multi-informant data was prospectively collected from youth self-reports, clinician-rated assessments, biomarkers, and medical chart records after 2-months of residential treatment. Examination of SOS items revealed that very few (7%) juvenile offenders did not participate in any AAH during treatment. Instrument validity analyses supported the SOS as a unidimensional scale, and indicated adequate psychometric properties of the brief tool, including inter-informant reliability (r=0.5), internal consistency (alpha=0.90), and convergent validity (rs=−0.3–0.3). Programmatic forms of AAH discriminated youths who tested negative versus positive on urine toxicology screens during treatment. The cut-point of 40 on the SOS was supported empirically by definite case-ness on the Children's Global Assessment Scale and indicated high AAH participation in approximately one out of four youths.
Most youth engaged in some AAH during treatment at higher levels than other programmatic activities. The SOS appears to be a valid measure of AAH suggesting clinical utility in gauging levels of AAH among adolescents. Given prior positive associations between AAH and treatment outcomes, the SOS might be employed to enhance adolescent treatment, identify accessible service opportunities salient to sobriety, and facilitate juvenile offenders' successful re-entry into the community following treatment.

0580

GENDER DIFFERENCES IN DSM-IV ALCOHOL USE DISORDER CRITERIA IN A REPRESENTATIVE SAMPLE OF NON-COLLEGE AGED YOUNG ADULTS: IMPLICATIONS FOR DSM-V

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Prior research in college student samples has indicated that men and women vary substantially in rates of DSM-IV Alcohol Use Disorders (AUDs). While a substantial body of research exists on the unique developmental trajectories of AUDs in college students, there has been little research that has examined AUD criteria functioning in individuals who never attended college, an understudied group of drinkers. Recently, the DSM-V Substance Use Task Force has provided recommendations for modifying our current AUD diagnostic system. To date, no studies have documented gender differences in DSM-V rates of AUDs or examined differential AUD criteria functioning between males and females in non-college aged young adults. Given this background, the present study examined gender-related differential AUD criteria functioning and documented the prevalence of rates of DSM-V AUDs across gender in a national representative sample of non-college aged young adults. Participants (N = 3805; 58.5% male; between ages 18 to 22) were part of the 2009 National Survey of Drug Use and Health (NSDUH), who reported consuming alcohol in the prior year. As part of this study, participants were asked to report on their alcohol use and endorsement of 11 DSM-IV AUD criteria during the prior year. The percent endorsement for each AUD criterion ranged from 2.6% (unsuccessful efforts) to 22.6% (tolerance) for females and from 5% (larger amounts than intended) to 28.1% (tolerance) for males. Item Response Theory differential criterion functioning (DCF) analyses revealed significant differences in the severity parameters between males and females. The severity parameters indicated that ''tolerance (dependence)'', [$\chi^2(1) = 6.695$, $p < .01$]; and ''legal problems (abuse)'', [$\chi^2(1) = 5.412$, $p < .05$] criteria were more likely to be endorsed (i.e., less severe parameters) among males than females. In contrast, women were more likely to endorse (i.e., less severe parameter) the social/interpersonal problems (abuse) [$\chi^2(1) = 4.783$, $p < .05$] criterion in comparison to males. With respect to rates of the proposed DSM-V diagnostic cut-off (endorsement of ≥ 2 or more criteria), men (28.6%) had a higher prevalence of AUDs than women (20.4%). Collectively, our findings highlight that men and women who never enroll in college have different trajectories in the development of AUDs in young adulthood. The present findings have implications for developing gender appropriate interventions in this understudied group.

0581

VALIDITY OF PROPOSED CRITERIA FOR DSM-5 NICOTINE USE DISORDER AND RELATIONSHIP TO ALCOHOL TRAITS IN 734 ISRAELI LIFETIME SMOKERS

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Background: Extensive evidence supports the DSM-5 proposal to combine substance abuse and dependence criteria into one disorder, remove legal problems and add craving, for a Substance Use Disorder defined by 11 criteria. Applied to Nicotine Use Disorder (NUD), these criteria indicate a single latent trait, but validity evidence is needed. Furthermore, whether the proposed DSM-5 NUD criteria remain related to alcohol variables is unknown.
Methods: The relationship of each NUD criterion to nine external validators was examined in 734 lifetime smokers in an Israeli household sample evaluated with a structured interview. The validators included smoking soon after awakening, number of cigarettes/day, and withdrawal severity; regression analysis was used. Receiver operating characteristic (ROC) curve analysis was used to assess the association of the validators with the set of NUD criteria (number endorsed) and to identify whether DSM-5 NUD or DSM-IV nicotine dependence (ND) provided the most discriminating criterion set. Regression analysis assessed the association of DSM-5 NUD criteria and alcohol dependence, any alcohol use disorder, and weekly at-risk drinking.
Results: All proposed DSM-5 NUD criteria were significantly associated with the validating variables; adjusted odds ratios for validators ranged from 1.26–10.93. Nicotine dependence, abuse and craving criteria showed similar magnitude of associations with the validators. Taken as a set, the proposed DSM-5 NUD criteria were also significantly associated with the validators, with significant ability to discriminate between the presence or absence of the validators (discrimination range, 63.9%–86.9%). ROC curve analysis indicated that the proposed DSM-5 set was significantly more discriminating than DSM-IV ND criterion set (p-value range, .036–<.0001). Finally, the proposed DSM-5 NUD criteria and criterion set were strongly and significantly associated with alcohol variables, consistent with previous studies of smoking and drinking.
Conclusions: Validation of each proposed DSM-5 NUD criterion, validity of the criterion set, increased discrimination compared to the DSM-IV ND set, and the expected relationship with alcohol variables all support the inclusion of nicotine abuse and craving criteria, allowing alignment of the nicotine criteria with those for alcohol and drug use disorders in DSM-5. The proposed changes should overcome some of the concerns expressed about nicotine disorders as defined in DSM-IV.

0582

MEASURING AVERAGE ALCOHOL CONSUMPTION: COMPARISON OF A BRIEF DRINKING QUESTIONNAIRE TO AN ABBREVIATED VERSION OF FORM 90

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Background: Assessing daily drinking using the timeline follow-back procedure is considered the gold standard for obtaining quantity/frequency of drinking for a given time period . However, administration is time consuming and requires training. In response, a 2003 NIAAA Council Task Force developed and released minimal set of core alcohol consumption questions intended for less resource-intensive assessment of alcohol consumption. The current study used data from a large alcohol clinical trial to validate the drinking outcome measures derived from this Brief Drinking Questionnaire (BDQ) against the timeline followback-based measure, the Abbreviated Form 90 (AF 90).
Methods: The BDQ was administered to 130 participants of the NCIG 002 trial, assessing alcohol consumption for the 90 days prior to screening. Immediately following, daily drinking was obtained and recorded using the AF 90; retrospective drinking data collected using a pattern chart, calendar prompt and drinking props. Six drinking outcomes obtained from the two measures were correlated and compared using intraclass correlations (ICC) and sample paired t-tests. An adjustment was made to the BDQ drinks per day outcome by inserting a maximum drinking day value for each maximum drinking day reported.
Results: Compared to the AF 90, the BDQ significantly underestimated the drinks per day, drinks per drinking day, heavy drinking days, maximum drinks in a day (all p<.0001); and overestimated the number of days consuming the maximal drinks (p=.015). The AF 90 and BDQ produced similar estimates of drinking days (p=.746). Intraclass Correlations (ICCs) for all outcomes ranged between 0.25 and 0.65, with the exception heavy drinking days (ICC = −0.01). For the drinks per day outcome, the use of indexing increased the ICC from 0.52 to 0.60.
Conclusion: With the exception of heavy drinking days, outcomes derived from the BDQ are modestly to moderately correlated with those from a daily drinking reconstruction assessment. The use of indexing increased the sensitivity of sporadic drinking events for the number of drinks per day when assessing drinking using the BDQ. The BDQ will be best utilized in clinical trials where drinking is a secondary outcome measure or as a primary measure in studies where a daily reconstruction of drinking is not feasible.

0583

HOW EFFECTIVE IS CONTINUING CARE FOR SUBSTANCE USE DISORDERS? A META-ANALYTIC REVIEW

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Over half the individuals beginning treatment for a substance use disorder relapse within one year. Participating in treatment for more than 6 months is associated with improved outcomes, but most intensive treatment programs last for 3 months or less. Continuing care treatments aim to support clients during the period of high risk following initial, intensive treatment. Several different types of continuing care have been evaluated in randomized trials, but the overall efficacy of these treatments is still unknown. This meta-analysis examined the overall effect of continuing care on substance use outcomes at the end of treatment, as well as the influence of specific ingredients of continuing care, such as whether it is delivered in a clinic or over the telephone, the number of planned sessions, and the modality or treatment approach. A systematic literature search expanded on the sample of continuing care studies reviewed by McKay (2009) and identified 34 randomized trials published since the late 1980's. The length of the tested treatments varied, with some being offered for less than 3 months (n=5), most for 3–6 months (n=19), and the rest for more than 6 months (n=9), up to a maximum of 4 years. Half of the studies (n = 17) tested different types of therapy against each other, such as cognitive behavioral therapy versus 12-step facilitation. The remaining 17 studies tested a psychotherapy against a no treatment control and are the focus here. In the studies with outcome information at the end of treatment (n=16), we found a small (Cohen's *d* approx. = 0.19), but significant (p<0.001) overall effect favoring continuing care over no treatment. Eight of the studies tested CBT-based treatments, whereas the other studies tested general counseling (n=6) or Motivational Interviewing (n=2). However, the modality of treatment was not a significant moderator – i.e., it was not related to effect size. Although the effect is small, with a number needed to treat of about 8 individuals, this analysis provides evidence that continuing care interventions are useful in sustaining initial treatment gains. Further research is needed to identify the specific techniques that best support individuals following intensive treatment.

0584

DO SPOUSES UNDERSTAND HOW THEIR PARTNERS WANT THEM TO CHANGE? PERCEPTUAL ACCURACY OF ALCOHOLIC FEMALE AND ALCOHOLIC MALE COUPLES IN THERAPY

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Perceptual accuracy (PA) is the extent to which a marital partner understands what types of behavior changes his/her partner desires of him/her. This study examined differences in PA between spouses in male or female alcoholic couples seeking alcohol behavioral couple therapy (ABCT). Understanding patterns and content of miscommunication among alcohol dependent men and women and their partners may enhance the efficacy of ABCT for each type of couple. Three research questions were examined: (1) Overall, how accurately do spouses perceive each other's areas of desired change in alcoholic female couples and in alcoholic male couples? (2) What is the PA of alcohol dependent women relative to PA of their male partners? (3) What is the PA of alcohol dependent men relative to PA of their female partners?
Method: Two samples were examined: 92 heterosexual alcoholic male couples in a randomized trial of 3 types of ABCT, and 105 heterosexual alcoholic female couples in a randomized trial of ABCT and individual cognitive behavior therapy. The Areas of Change Questionnaire (ACQ) was used to assess PA in various domains of the relationship. Each partner's PA was determined by comparing his/her response to Part 1 (''I want my partner to…'') with his/her partner's response to Part 2 (''It would please my partner if I…'') of the ACQ. A novel scoring method, counting only direct hits, rather than responses within 1 point on the Likert scale, resulted in a normal distribution of PA for both alcoholic female couples and alcoholic male couples. Number of possible ''hits'' ranges from 0 to 34, and percentages of mean number of hits (out of 34) are reported with means below. Two-tailed, paired t-tests were used to compare partners' PA in each sample.
Results: Among alcoholic female couples, mean number of hits scored by the women (19.23 (sd=5.4), 57%) was not significantly different from the male partner (19.27 (sd=6.1), 57%). Among alcoholic male couples, mean number of hits scored by the men (16.59 (sd=4.9), 49%) was significantly lower (p=.015) than the female partners scored (17.85 (sd=5.9), 51%).
Conclusions: Male alcoholics were less in tune with what their spouses wanted than their wives were. In female alcoholic couples, partners were similar in PA. PA will be examined in 9 specific marital domains (communication, sex, financial, lifestyle, attention, social, domestic, arguing, and alcohol use) for the alcohol dependent participants and their partners.

0585

WITHIN-TREATMENT DRINKING URGES: THE IMPORTANCE OF DRINKING QUANTITY AND TIME SINCE ATTENDING TREATMENT SESSIONS

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Introduction: Many cognitive-behavioral interventions for alcohol use disorders (AUDs) work with clients to understand, predict, and cope with urges to drink. Success in these treatments is indicated in part by how well clients predict and cope with these urges and how much urges decrease over time. The present examines drinking urge trajectories during the course of a behavioral AUD treatment and tests (1) whether daily urges would increase when drinking decreases and (2) whether drinking urges would increase as more time elapses since attending treatment sessions.
Method: The present study is a secondary analysis of data from a randomized trial of individual cognitive-behavioral therapy (CBT) and behavioral couples therapy (BCT) for AUDs (McCrady et al., 2009). Women with AUDs (N = 97) received up to 20 sessions of either BCT or CBT and recorded their daily number of drinks and urges to drink during the treatment period (n = 7326 daily recordings). Longitudinal multilevel modeling was used to examine trajectories of daily drinking urges. Predictors of daily urges included the number of days elapsed since attending a treatment session, dummy variables representing weekend days, the number of sessions attended by that particular day, and changes in mean weekly drinking.
Results: Daily drinking urges were higher on weekends (β = 0.195, p < .001) and urges decreased as participants attended more treatment sessions (β = −.064, p < .001). Urges increased as more time elapsed since attending the previous treatment session (β = 0.061, p = .02), and this effect was not moderated by number of sessions attended. Reductions in weekly mean drinking from the week before predicted fewer daily urges (β = 0.058, p< .001).
Discussion: Daily drinking urges are likely to be higher on weekends, earlier in treatment, and when more time has elapsed since attending a treatment session. We did not find evidence that urges increased when drinking decreased; instead our results suggested that urges and drinking tended to decrease together. There may be a recency effect where having recently attended treatment reduces drinking urges, which suggests that there may be some aspect of treatment attendance that may cause both short- and long-lasting reductions in daily drinking urges. Clinicians should be aware that urges are more likely to occur after more time has elapsed since attending a treatment session, and that urges do not increase substantially when weekly drinking is reduced.

0586

ONE-YEAR OUTCOMES OF GROUP COGNITIVE BEHAVIORAL THERAPY FOR DEPRESSION IN RESIDENTIAL ALCOHOL AND OTHER DRUG TREATMENT CLIENTS

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National data suggest that only 11% of people with co-occurring mental illness and alcohol and other drug (AOD) problems receive treatment for both conditions; therefore, innovative dissemination approaches are needed to provide empirically supported treatments for these clients. This study evaluated the one-year effectiveness of group cognitive behavioral therapy for depression (GCBT-D) delivered by trained AOD counselors to clients receiving residential AOD treatment. We adapted an existing GCBT-D to create a new intervention that increased the likelihood that AOD counselors could implement the intervention with fidelity and that was acceptable and engaging to clients in AOD treatment. We used a quasi-experimental design in which clients at four residential AOD treatment programs received either AOD treatment as usual (n = 88) or treatment enhanced with GCBT-D (n = 96). At baseline, depression symptoms were in the severe range (Mean (SD) = 32.1 (9.0) on BDI-II), 66% had a probable alcohol use disorder, and 65% reported polysubstance use. Clients assigned to the GCBT-D condition attended a mean of 10.1 of 16 sessions, and 65% completed at least half of the sessions. Fidelity data indicated that the average rate of counselor adherence to the manual was 95%, while the average competence score indicated that counselors were delivering competent GCBT. At the 3-month follow-up, GCBT-D clients reported significantly fewer depressive symptoms than the control condition (p<.01), with average BDI-II scores of 5.6 points lower than the control condition. Differences between conditions were not sustained at the 12-month follow-up. Fewer intervention clients met criteria for a current depressive disorder at the 12-month follow-up, but the difference was not statistically significant (12% vs. 19%, *ns*). At 12-months, GCBT-D and control clients did not differ on percent of days using alcohol (14.8% vs. 14.1%; *ns*) or problem substance in past 30 days (10.3% vs. 11.6%; *ns*). Secondary outcomes were not significantly different at the 12-month follow-up (e.g., mental health functioning, anxiety, negative consequences, arrests, employment). Data suggest that GCBT-D delivered by addiction counselors improves depression symptoms faster than residential AOD treatment as usual, but both groups achieve similar symptom reductions by 12 months. Implications for improving long term effectiveness of GCBT-D in clients with co-occurring AOD problems will be highlighted.

0587

A PILOT STUDY OF INTERPERSONAL PSYCHOTHERAPY (IPT) FOR ALCOHOL DEPENDENT WOMEN WITH CO-OCCURRING MAJOR DEPRESSION

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Co-occurring major depression (MD) is prevalent among alcohol dependent (AD) women and is a risk factor for poor treatment outcomes. No study to date has tested a behavioral intervention designed specifically to treat alcohol dependent women with major depression (AD-MD). This pilot study tested the feasibility, acceptability, and initial effects of Interpersonal Psychotherapy (IPT) for AD-MD women in a community addiction treatment program. Participants received 8 individual sessions of IPT in addition to their routine addiction care. Feasibility was determined by the modal and mean number of IPT sessions attended. Acceptability was assessed by participants' reports on the Client Satisfaction Questionnaire (CSQ). Treatment effects were calculated using indices of drinking frequency (percent days abstinent), drinking intensity (drinks per drinking day), and depression symptom severity (measured by the Hamilton Rating Scale for Depression and Beck Depression Inventory-II). Fourteen female patients with current diagnoses of alcohol dependence and major depression participated. Assessments were conducted at baseline, 8-, 16-, 24-, and 32-weeks. Participants attended a mode of 8 individual IPT sessions (mean = 4.79 ± 3.6, range = 0–8) and reported high satisfaction with IPT treatment on the CSQ (M=55.6; SD=11.7). Women's drinking behavior and depressive symptoms improved significantly with treatment. These preliminary findings suggest that IPT is a feasible, highly acceptable behavioral intervention for AD-MD women.

0588

THERAPIST COMPETENCE AS A PREDICTOR OF BEHAVIOR CHANGE FOR PATIENTS IN BEHAVIORAL TREATMENT FOR ALCOHOLISM

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Objective: Pro-recovery behaviors by patients in behavioral treatment for alcoholism have been shown to predict decreased alcohol use after treatment. The current study examined therapist competence as a predictor of pro-recovery behaviors by patients during treatment. Potential mediators of this relationship were examined.
Method: Observer-based ratings of treatment sessions for 192 aftercare patients from Project MATCH were used to assess therapist competence, patient-reported pro-recovery behaviors and mediator variables that measured changes in beliefs about alcohol use. A multiple mediator model was used to examine (1) the relationship between therapist competence and pro-recovery behaviors (i.e., 'Taking Steps') and (2) the extent to which changes in beliefs about alcohol mediated the relationship between therapist competence and pro-recovery behaviors.
Results: Among patients in an aftercare phase of treatment, more highly rated therapist competence in the first treatment session was predictive of increases in pro-recovery behaviors during treatment. The relationship between therapist competence and pro-recovery behaviors was partially mediated by an increase in patients' intention to abstain from drinking alcohol. Changes in other beliefs related to alcohol (e.g., severity of the problem, ability to abstain) did not receive support as mediators.
Conclusions: Among aftercare patients therapist competence plays a role in facilitating pro-recovery behaviors. This effect is substantially accounted for by the effect of therapist competence on increasing patients' intention to abstain from drinking. The specific ingredients of competence in the present study include professionalism, timing, smoothness of interventions, attuning to feelings and focusing on consequences and payoffs for problematic behaviors. Emphasizing these therapist qualities in therapist training and treatment delivery will likely promote positive behavior change among patients.

0589

IDENTIFYING MULTIPLE MECHANISMS OF CHANGE IN ALCOHOLISM TREATMENT
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Cognitive-behavioral therapy (CBT) is an effective treatment for alcohol dependence, but little is known about how CBT works to achieve these effects. Although several possible mechanisms have been proposed to explain the effects of CBT, it is rare that more than one mechanism is studied. However, it may be the case that similar outcomes (e.g., abstinence) may be reached through multiple paths. Therefore, essential to conducting work on behavioral change mechanisms is distinguishing different courses or paths and moderating influences (Kazdin, 2007). In this study, we focused on 2 key mechanisms posited to underlie the effectiveness of CBT specifically, increasing abstinence self-efficacy and reducing positive outcome expectancies for alcohol use, and 2 key mechanisms posited to underlie the effectiveness of a wide range of therapeutic interventions, increasing the therapeutic alliance and reducing/regulating negative emotional states. Participants were 45 alcohol dependent men and women who agreed to participate in a 12-week trial of CBT for alcohol dependence. Comprehensive research assessments were conducted with patients at baseline, end of treatment, and 3-months posttreatment. Results examine the within-treatment week-to-week relationship between ratings of 4 key therapeutic mechanisms and alcohol involvement (operationalized as percent days abstinent {PDA} and drinks per drinking day {DDD}) during treatment. Profiles of the four key mechanisms over the course of treatment in relation to alcohol involvement during treatment and during the 3-month follow-up period will be illustrated. A dominant profile that has emerged is one of increasing self-efficacy and decreasing alcohol consumption. The overarching goal of this presentation will be to map the process of change in successful CBT. As Hayes et al. (2007) state, such a ''map'' would have several important implications, including, (1) further refinement of existing treatment procedures; (2) a clearer picture of the processes of recovery, treatment dropout, poor response, and relapse; and (3) further development of empirically-supported treatment processes.

0590

THE ROLE OF PHYSICAL HEALTH PROBLEMS ON TREATMENT OUTCOMES FOR VETERANS IN TREATMENT FOR CO-OCCURRING DEPRESSION AND ALCOHOL/SUBSTANCE DEPENDENCE
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Both depression and alcohol and other substance use dependence (ASD) are associated with physical health problems. Research has documented increased depression symptoms in the context of chronic medical conditions. In contrast, some acute health events appear to influence positive improvements in substance use.
We examined the relations of pre-treatment acute physical health events (HE) and chronic physical health difficulties (CHD) to depression and alcohol/drug use during treatment in a sample of 205 predominantly male veterans meeting DSM-IV criteria for alcohol, cannabis, and/or stimulant dependence and major depressive disorder enrolled in a randomized clinical trial comparing two psychotherapy interventions. The interventions (Integrated Cognitive Behavioral Therapy and Twelve Step Facilitation Therapy) were provided in an outpatient group setting, with twice weekly sessions for 12 weeks (Phase I) followed by once weekly sessions for 12 weeks (Phase II). Alcohol/substance use and depression were assessed at baseline, Phase I, and Phase II using the Timeline Follow Back and Hamilton Depression Rating Scale, respectively.
30 participants (15%) reported a HE in the 90 days prior to entering treatment and 144 (70%) had CHD. Type of treatment received was not related to HE or CHD or relations between health and outcomes. Recent HE predicted greater depression symptoms at intake ($p = .03$), but not during treatment, while CHD were predictive of greater depression symptoms at intake ($p = .001$) and Phase II ($p = .04$) with a trend observed at Phase I ($p = .06$). HE predicted abstinence in Phase I ($p = .02$) but was not related to abstinence in Phase II. HE predicted higher percentage of days abstinent in Phase II ($p = .02$) but not Phase I. CHD were not predictive of alcohol/substance use at any time.
In summary, HE and CHD had differing relationships to treatment outcomes for veterans with co-occurring depression and ASD. Findings suggest that addressing HE during addiction treatment may be beneficial, whereas CHD may be a significant barrier to reducing depression in treatment. Future research is needed to explore ways of incorporating a focus on HE to improve addiction outcomes and ways to successfully address depression for those individuals with CHD.

0591

SOCIAL NETWORK CHARACTERISTICS AND MOTIVATION TO ABSTAIN FROM ALCOHOL AND MARIJUANA AMONG ADOLESCENT SUBSTANCE USERS IN TREATMENT
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Peer substance use is a robust predictor of adolescent substance use and is often involved in relapse among treated youth. This cross-sectional study examined associations between peer network characteristics and treated adolescents' readiness to change substance use shortly after the start of treatment. We hypothesized that the proportion of abstinent peers in the network would be positively associated with: motivation to abstain, motivation to reduce contact with substance using peers, and confidence to abstain. To date, data from 90 youth (ages 14–18; mean age=17.1; 77% male; 83% White), recruited from 5 sites of a community-based intensive outpatient addictions treatment program, have been analyzed. Almost all (98%) had a past year marijuana diagnosis, and 31% had an alcohol diagnosis. Shortly after starting treatment, adolescents reported on substance use prior to treatment, motivation to abstain (1=low to 10=high motivation), confidence to abstain (1=low to 10=high), and social network characteristics. Motivation to abstain from marijuana mean=8.6 (SD=2.3), and alcohol motivation mean=7.8 (SD=3.0); Confidence to abstain from marijuana mean=8.4 (SD=2.4), and alcohol mean=8.1 (SD=2.9). Adolescents reported an average of 3 household members and 8 peers (total network members=10.7, SD=2.0). A minority of network peers, on average, abstained from marijuana (39%) and alcohol (38%) in the past month. As predicted, a greater proportion of abstinent network peers was associated with higher motivation to abstain from both alcohol ($r=.45$, $p<.01$) and marijuana ($r=.21$, $p<.05$). Further, a greater proportion of network peers who abstained from marijuana was associated with higher motivation to reduce contact with marijuana using network peers ($r=.40$, $p<.01$). Although proportion of alcohol abstaining peers was positively associated with confidence to abstain ($r=.23$, $p<.05$), proportion of marijuana abstaining peers was not associated with confidence to abstain. Results indicate that a minority of peers in a treated adolescent's social network abstained from substance use, and that a higher proportion of abstinent peers is associated with readiness to change. Interventions that aim to increase the proportion of abstinent peers and to reduce contact with substance using peers in the adolescent's network warrant attention.
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0592

LISTENING TO YOUTH: ADOLESCENTS' SELF-REPORTED REASONS FOR ALCOHOL AND DRUG USE AS A UNIQUE PREDICTOR OF TREATMENT RESPONSE AND OUTCOME
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Background: Clinical efforts have focused on improving the quality of adolescent substance use disorder (SUD) treatment, yet average improvements have been modest. Because adolescents are noteworthy for heterogeneity in their clinical profiles, treatment might be enhanced by the identification of markers identifying clinical subgroups for whom interventions could be more effectively tailored. Some of these, such as abstinence motivation, substance involvement, justice-system involvement, and psychiatric status, are promising candidates. In addition, this study examined the unique predictive utility of adolescents' own self-reported reasons for use.
Methods: Adolescent outpatients (N=127; 24% female, aged 14–19) were assessed at treatment intake on their predominant self-reported reason for alcohol and other drug use as well as a variety of demographic, substance use, and psychological and psychiatric variables, and re-assessed 3, 6, and 12 months later.
Results: Reasons fell into two broad domains: using to enhance a positive state (positive reinforcement [PR]; 47% of youth) and using to cope with a negative state (negative reinforcement [NR] 53% of youth). Compared to PR patients, NR patients were found to be significantly more substance-involved and report more psychological distress and a more extensive treatment history. Additionally, NR patients showed a significant and strong treatment response during outpatient care, whereas PR patients showed no treatment response. Importantly, PR/NR status uniquely predicted treatment response and outcome over and above a variety of other variables including abstinence motivation, self-efficacy, coping, justice-system involvement, and prior treatment.
Conclusion: Adolescents' own reasons for using substances appear consistent with conceptual models of addiction (e.g., Koob, 2004) and appear to provide unique clinical information that may inform treatment planning. PR patients may benefit from a greater focus on problem recognition and risk using motivational enhancement strategies, whereas NR patients may benefit more from coping skills training.

0593

HOW DO JUSTICE-SYSTEM INVOLVED ADOLESCENTS FARE IN OUTPATIENT ALCOHOL AND DRUG TREATMENT?

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Background: Approximately 50% of all adolescents treated for alcohol and other drug use disorders in the United States are referred by the criminal justice system (JS). A substantial number of these JS involved youth are mandated to attend treatment (JSI-M). However, little is known about the characteristics of mandated patients and how they fare during treatment and in the longer-term compared to non-mandated, justice-system-involved (JSI) patients and patients not involved in the justice system (No JSI). Greater knowledge in this arena would inform the utility of youth justice system treatment mandates.
Method: Adolescents (N=127; M age 16.7; 24% female; 87% White) enrolled in a study of outpatient treatment effectiveness were assessed at intake and 3, 6, and 12 months later using validated assessments. Outcomes were modeled using controlled Generalized Estimating Equations (GEE).
Results: Patients fell into three groups: JSI-M (n= 24; 19%), JSI (n=40; 31.5%), and No JSI (n=63; 50%). At intake, compared to JSI-M and No JSI patients, JSI patients were more likely to be expelled, suspended, or to have quit high school (p=.001), but both JS groups reported significantly more motivation to not use drugs (p=.001) and reported greater lifetime 12-step meeting attendance (p=.05) than the No JSI group. There were no differences between groups on during-treatment change on important clinical indices, and all three groups showed similar positive change with regard to increased abstinence. GEE results revealed this treatment benefit disappeared following treatment for the JSI-M group who exhibited a greater decline in abstinent days compared to the No JSI group.
Conclusions: Compared to No JSI patients, JS patients entering outpatient treatment may be more motivated for abstinence and, in keeping with the notion that treatment does not have to be self-initiated to be effective, show a similar magnitude positive treatment response. Despite early treatment gains, however, JSI-M adolescents may deteriorate more quickly following treatment. Consistent with recovery management models of addiction care, longer term monitoring, linkage, and support may be necessary to increase the chances of ongoing recovery in this high risk group.

0594

SELF-EFFICACY AND COPING RESPONSE IN THE TREATMENT OF ADOLESCENT ALCOHOL USE DISORDERS

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Most recent research efforts on psychosocial interventions for youth with alcohol use disorders (AUD) has emphasized the necessity of further studies of predictors of treatment outcomes and on mechanisms of behavioral change. This study assesses the importance of self efficacy as well as coping response in predicting post-treatment alcohol use outcomes for adolescents with AUD. After participating in an 8-session common cognitive-behavioral group therapy, 144 AUD adolescents aged 13 to 18 were randomly assigned to one of three experimental aftercare groups: (1) In-Person, (2) Telephone, or (3) No Active Aftercare, and were assessed at three subsequent time points: End of Aftercare, 3- and 12-months. There was an increase in frequency of alcohol use among youth overall, and this increase was independent of aftercare group (Burleson, Kaminer, & Burke, 2011). Two additional measures were collected at the beginning of aftercare: (1) the 39-item Situational Confidence Questionnaire (SCQ; Annis, 1997) assessed the perceived confidence to resist alcohol use urges, and (2) the 48-item Coping Response Inventory-Youth (CRI-Y; Moos, 1993) measured the perceived frequency of use of coping responses to stressful life circumstances. The overall scale scores of these measures were used due to their high reliability (SCQ standardized a = .95; CRI-Y standardized a = .89), as well as the high intercorrelation among their respective subscales. Among those youth assessed (n = 138) the SCQ and the CRI-Y were completely uncorrelated at the beginning of aftercare ($r = -.002$, $p = .98$), and were subsequently utilized as fixed covariates in the analyses of change in frequency and quantity of alcohol use. Hierarchical linear modeling (HLM) analyses indicated that the more confident the youth to resist urges, the lower the increase in frequency of use across time ($p = .026$); whereas the more frequent the reliance on coping responses, however, the higher this increase ($p = .034$). For quantity of alcohol use, the same results occurred for the SCQ ($p = .020$), but there was no significant predictive effect for the CRI-Y ($p = .53$). All of these effects were independent of experimental treatment group. Self efficacy to resist alcohol use across situations is a promising predictor of positive treatment outcomes among adolescents, while reliance on coping responses to stress showed mixed results. Future efforts will explore the differential predictive ability of the respective SCQ and the CRI-Y subscales (AA-012187).

0595

TRACKING ADOLESCENTS' SESSION-TO-SESSION CHANGE IN MOTIVATION TO ABSTAIN FROM ALCOHOL AND MARIJUANA IN COMMUNITY-BASED TREATMENT

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Research has shown the importance of motivation to change in predicting substance use treatment outcome. The aims of this on-going study were to track changes in adolescents' motivation to abstain from alcohol and marijuana after each outpatient treatment session, and to identify distinct trajectory types and patient characteristics associated with each trajectory type. To date, data from 61 youth (ages 14–18; mean age=17.0±1.0; 77% male; 88% White), recruited from 5 sites of a community-based intensive outpatient (IOP) addictions treatment program, have been analyzed. Adolescent IOP treatment, focusing on relapse prevention and 12-step facilitation, involves attending 3 3-hour sessions per week for a recommended length of 6–8 weeks (~18–24 sessions). Ratings of motivation to abstain (1–10 scale: 1=not motivated to 10=very motivated) from alcohol and marijuana were obtained after each IOP session (mean sessions attended=14.1, SD=6.5). Growth mixture modeling was used to identify distinct alcohol and marijuana motivation trajectory types. Almost all (98%) youth had a lifetime marijuana diagnosis, 33% alcohol diagnosis, 36% conduct disorder (CD), and 15% major depression (MD). For both alcohol and marijuana, 4 trajectories were identified: High Motivation (alcohol: 34%, marijuana: 46%), Increasing (alcohol: 29%, marijuana: 20%), Moderate (alcohol: 18%, marijuana: 23%), and Low Motivation (alcohol: 18%, marijuana: 11%). Across sessions, motivation to abstain from marijuana (mean rating: 8–9) was generally higher than alcohol (mean rating: 7–9). Trajectory groups for alcohol and marijuana did not differ by gender, age, treatment site, CD, or MD. For alcohol, those in Increasing and High groups had, on average, fewer alcohol symptoms compared to the Moderate group ($p<.05$); marijuana trajectories did not differ on marijuana symptom count. For alcohol and marijuana, youth in Low Motivation were referred to IOP either by family or court. For marijuana, those in High Motivation were more likely to complete IOP (68%) compared to those in Low Motivation (14%) ($p<.03$). Emerging data suggest that for some youth, IOP increases and maintains high motivation to abstain from alcohol and marijuana, with increases in motivation tending to occur early (first 1–2 weeks of IOP). However, enhancing motivation and retention in treatment remain key targets for a subset of youth with low motivation, many of whom were referred by family or the courts. (AA014357, AA017128, AA018195)

0596

PRELIMINARY EFFICACY OF A SINGLE GENDER FEMALE-SPECIFIC COGNITIVE-BEHAVIORAL THERAPY (CBT) GROUP THERAPY FOR ALCOHOL DEPENDENT WOMEN

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Accumulating evidence of gender differences in many aspects of alcohol use disorders (AUDs) has resulted in efforts to identify and develop effective treatments for women. Since most therapy for AUDs and other substance use disorders in the U.S. is delivered in groups, the current study reports on the development and initial testing of a modification of individual female-specific cognitive behavioral therapy for women with AUDs (I-FS-CBT) to a group format (G-FS-CBT). Women are randomized to 12 weekly outpatient individual or group therapy sessions. Drinking is assessed at baseline, within treatment, and for a year after using the Timeline Followback Interview and Form-90. Potential mechanisms of change are assessed before and after each session. Cost-effectiveness of the group versus individual treatment is assessed. Two core themes - the woman as an active agent in her own life, and the woman's right to self-care - are integrated into the the manual. Psychoeducation on female alcoholism and core CBT elements are covered. 7 areas of concern are addressed explicitly in the treatment: (a) heavy drinkers in the social network; (b) anxiety, (c) depression; (d) stress and strong emotions; (e) social network support for abstinence; (f) anger management; (g) assertiveness. The G-FS-CBT manual was written and piloted on2 groups. Repeated measures ANOVAs for pilot data showed a significant reduction in drinking frequency ($F=13.37$, $p<.01$)and intensity ($F=6.68$, $p<.05$) over time. Depression decreased significantly from baseline to post-treatment ($t = 3.61$; $p < .01$); there was a trend for anxiety to decrease ($t = 2.17$; $p = .07$) and autonomy to increase ($t = 2.13$; $p = .07$) from baseline to post-treatment. Following the pilot groups, the manual was revised and recruitment for the randomized trial of I-FS-CBT compared to G-FS-CBT is underway. Of 203 telephone screens thus far, 107 clinical intakes have been conducted; 44 women have been randomized to G-FS-CBT and 44 to I-FS-CBT; 7 groups have been run, with a 72% completion rate. Women on average are middle-aged, married, with diverse ethnicity, high rates axis I disorders, and drink daily and heavily. Preliminary data will be provided on drinking outcome, therapy process, and potential mechanisms of change (coping skills, self-efficacy, autonomy, social support for abstinence, emotion regulation, alleviation of negative affect, therapeutic alliance, and group process) for the group therapy treatment condition.

0597

THE WOMEN'S RECOVERY GROUP STUDY: GENDER AND ALCOHOL USE CHARACTERISTICS

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There is a narrowing gender gap in the prevalence of alcohol use disorders. In addition, compared to men, women progress more rapidly from drinking onset to alcohol-related problems (i.e. 'the telescoping effect'). Among those who drink, women have greater vulnerability to a more accelerated course of illness than men accompanied by increased incidence of alcohol-related negative health effects. The Women's Recovery Group Study is a two-site, randomized controlled trial comparing single-gender (WRG; Women's Recovery Group) to mixed-gender group therapy (GDC; Group Drug Counseling). The primary aim of the trial is to examine treatment outcomes in women receiving GDC compared to WRG. Participants 18 years or older were included if they were alcohol or substance dependent and had used alcohol or other drugs at least once within the past 60 days. 158 participants (100 women, 58 men) were enrolled. Women were randomized to WRG (n = 52) or GDC (n = 48), and 58 men participated in GDC. For the current analyses, we examined baseline data to investigate gender differences in alcohol use. Participants were predominately white (94%) with a mean age of 47 years. The majority of participants met criteria for current alcohol dependence (89%) and 74% listed alcohol as their primary substance of abuse. There were no gender differences in rates of alcohol dependence or designation of primary substance. Results showed that compared to men, women had a later age of first alcohol use (16 vs. 14 years; t = 0.24, df = 155, p < .05) and fewer years of lifetime alcohol use (17 vs. 22 years; t = 1.03, df = 155, p < .01). However, women and men did not significantly differ in number of days of alcohol use, number of heavy drinking days, or age of first treatment. Women reported fewer drinks per drinking day (8 vs. 12 drinks; t = −3.56 df = 156, p < .001) than men. These results indicate that although women started drinking later than men, the age of initiation of treatment did not significantly differ for women and men (37 vs. 35 years, respectively), and there were few gender differences in alcohol use at enrollment to treatment. These findings contribute to the evidence that support the telescoping course of alcohol dependence in women compared with men. Intervention early in the course of problematic drinking is important for men and women, but may have additional relevance for women due to the accelerated course of drinking severity. 2R01DA15434 (NIDA), 2K24DA019855 (NIDA)

0598

IMPACT OF A PERFORMANCE MEASURE FOR BRIEF ALCOHOL INTERVENTION ON GENDER DIFFERENCES IN ALCOHOL-RELATED CARE IN THE VETERANS AFFAIRS HEALTHCARE SYSTEM

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Brief alcohol interventions (BI) are recommended for all patients with alcohol misuse but are more commonly offered to men than women. The VA Healthcare System requires annual alcohol screening with the AUDIT-C questionnaire. Although AUDIT-C scores ≥3 for women and ≥4 for men are optimal screening thresholds that maximize sensitivity and specificity, VA implemented a performance measure (PM) requiring BI among all patients with AUDIT-C ≥5 in order to minimize clinical burden of false-positive screens. We used chart review data collected for the VA Office of Quality and Performance (07/06 – 06/10) to evaluate rates of documented BI in men and women and whether PM implementation (10/1/07) modified associations between gender and BI in two samples: 1) patients with AUDIT-C scores ≥3 for women and ≥4 for men (AUDIT-C ≥3/4 sample), and 2) patients with AUDIT-C scores ≥5 (AUDIT-C ≥5 sample). BI was defined as documentation of advice to reduce or abstain from drinking and/or feedback relating alcohol use to health. In each sample, logistic regression models, adjusted for important clinical covariates, tested whether associations between gender and BI varied based on PM implementation and estimated the prevalence of BI for men and women before and after the PM. Among 261,234 (211,742 men and 49,492 women) screened patients, 28,810 (14%) men and 5,460 (11%) women screened positive at AUDIT-C ≥3/4, while 16,176 (8%) men and 1,837 (4%) women screened positive at AUDIT-C ≥5. In the AUDIT-C ≥3/4 sample, BI was more common overall among men than women (p-value <0.01), and associations with gender varied based on PM implementation (p=0.01). Before PM implementation, 26% (95% CI 23%–29%) of men and 23% (20%–26%) of women with AUDIT-C ≥3/4 had documented BI. After PM implementation, 40% (38%–42%) of men and 31% (29%–33%) of women with AUDIT-C ≥3/4 had documented BI. Parallel analyses conducted in the AUDIT-C ≥5 sample identified no gender differences overall (p=0.15) and no variation in the association based on PM implementation (p=0.33). In both samples, rates of BI increased for both genders after implementation of a performance measure for BI. Although care appears to be equitable across genders among patients for whom BI is incentivized in the VA, implementation of the PM for BI was associated with a nearly three-fold increase in the gender disparity in BI among patients who screened positive for alcohol misuse at optimal thresholds.

0599

RATES OF ALCOHOL MISUSE AND FOLLOW-UP CARE AMONG OEF/OIF VETERANS IN VA: ASSOCIATIONS WITH SUBSTANCE USE DISORDERS AND PTSD

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Objectives: VA is seeking to improve access to care for alcohol misuse among Operations Enduring and Iraqi Freedom (OEF/OIF) Veterans, who are at heightened risk for alcohol use disorders (AUD), drug use disorders (DUD), and post traumatic stress disorder (PTSD). However, little is known about the management of alcohol misuse among OEF/OIF Veterans with and without these disorders. This study evaluated the management of alcohol misuse among OEF/OIF VA outpatients with and without documented AUD, DUD, and PTSD diagnoses.
Methods: This study used VA Office of Quality and Performance medical record review data from a national sample of VA outpatients (≤ 55 years old) with documented alcohol screening (AUDIT-C) from 2006–2010. Among OEF/OIF patients with alcohol misuse (AUDIT-C ≥ 5), we used logistic regression to compare the adjusted prevalence of documented brief intervention (BI; advice to abstain or drink within recommended limits and/or feedback linking drinking to health) and/or referral (to alcohol treatment or discussion of referral), for those with and without diagnoses for AUD, DUD, and PTSD. Models were adjusted for gender, age, marital status, alcohol misuse severity, and addictions treatment utilization.
Results: We identified 6,618 OEF/OIF Veterans (n=932 women) with documented AUDIT-C screens. Among 1,243 (18.8%) who screened positive for alcohol misuse, 61.1% (n=759) had BI (n=482) or referral (n=54) only, or both BI and referral (n=223). Unadjusted rates of AUD, DUD, and PTSD were 39.6%, 14.5%, and 61.9%, respectively. The adjusted prevalence of BI or referral was significantly higher for screen positive Veterans with AUD (71.8%, 95% CI: 66.5 – 77.2) compared to those without an AUD diagnosis (52.6%, 48.1 – 57.2), and Veterans with co-occurring AUD/DUD (75.9%: 95% CI: 67.8 – 84.1) compared to those without a substance use disorder (SUD) (51.7%, 46.9 – 56.5). Rates of BI or referral were not significantly different among screen positive Veterans with or without PTSD.
Conclusions: Results indicate AUD, DUD and PTSD are common among OEF/OIF Veterans with alcohol misuse. Rates of BI or referral were higher for Veterans with co-occurring AUD/DUD than for those without, although even in these high risk groups, approximately 25% with alcohol misuse did not receive BI or referral. Results highlight the need for systems to ensure returning Veterans with alcohol misuse and diagnosed SUDs and PTSD receive follow-up care.

0600

FEASIBILITY AND ACCEPTABILITY OF A PROGRAM TO PROMOTE MEDICATION TAKING AND SUBSTANCE USE REDUCTION, STEP-BY-STEP

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Purpose: While the Veterans Administration promotes primary care mental health integration, a continued challenge in primary care is the provision of behavioral interventions to modify health behaviors and improve health outcomes. For example, Veterans taking antidepressants have poor adherence and even more so for those using alcohol and other drugs. The complex and interactive nature of depression, alcohol and drug use, and antidepressant medication taking suggests that a multi-faceted and integrated approach is needed. The purpose of this pilot study was to test the feasibility and acceptability of a 5-week group psychoeducational program (MEASURED Steps) in primary care among Veterans taking antidepressants and drinking alcohol . MEASURED Steps was developed based on the transtheoretical model framework and evidence-base related to the neurobiological bases of depression and substance abuse.
Methods: Veterans with a positive screen for depression (PHQ-2 score > 2), reporting alcohol use (AUDIT>1), and active antidepressant prescription were recruited in cohorts from primary care settings. The length of time to recruit and session attendance were used to assess feasibility. A client satisfaction questionnaire (4-point Likert type scale with higher scores reflecting higher satisfaction) and exit interview were used to assess acceptability. Payment ($5) was provided for each session attended.
Results: Two cohorts were recruited for the study. Cohort 1 (n=13) was recruited within 22 weekdays and Cohort 2 (n=7) within 61 weekdays. Of the n=11 assigned to MEASURED Steps, three individuals never failed to attend a single session, with the remainder, on average, attending 4.62 sessions. Satisfaction scores were high (mean = 3.53). Exit interviews revealed several barriers to attendance, including travel expenses (e.g. private and public transportation costs) and scheduling conflicts. A web-based delivery of the program appealed to several participants, while others valued the interaction with the nurse leader and/or peers in the group.
Conclusions: Increased efforts are needed to recruit for a larger study, such as engaging the primary care teams for support. Translating this intervention for on-line delivery may be a practical approach so more Veterans can access this integrated treatment and enhance the VA's efforts directed toward mental health integration in primary care.

0601

THERAPEUTIC ASSESSMENT OF PERSONALITY FOR VETERANS IN ALCOHOL AND DRUG TREATMENT: A PILOT STUDY OF A BRIEF INTERVENTION

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Objective: The overarching goal of this pilot project (*N*=9) was to prepare for a large-scale study that seeks to develop a personality assessment feedback intervention for veterans entering alcohol and drug treatment. This brief intervention is based on the Collaborative Model of Therapeutic Assessment (Finn & Tonsager, 1997) and is intended to increase veterans' engagement in substance use disorder (SUD) treatment. The specific goal of the pilot project was to obtain quantitative and qualitative data on veterans' acceptability of the brief intervention.
Method: Within the first week of treatment, an omnibus measure of normal personality (Multidimensional Personality Questionnaire; MPQ; Tellegen & Waller, 2008) was administered to participants, all of whom had a diagnosis of alcohol dependence. A feedback session was conducted one week later, and participants' reactions to the session were evaluated with the Assessment Questionnaire-2 (AQ-2; Finn & Tonsager, 1997) and a brief, structured interview.
Results: Mean scores on the MPQ trait scales were similar to other SUD populations – i.e., lower well-being, social closeness, harm avoidance, positive emotionality, and constraint; higher stress reaction, alienation, and negative emotionality. However, for all trait scales the amount of variance was comparable to the MPQ normative sample. Regarding veterans' reactions to the feedback sessions, mean scores on the AQ-2 were similar to norms established by the Center for Therapeutic Assessment in terms of new self-awareness, positive accurate mirroring, positive relationship with the assessor, negative feelings about the assessment, and overall satisfaction. In addition, qualitative results indicated that participants found the feedback sessions to be helpful, positive, and accurate, and all reported that they would take part in the feedback session in the future and would recommend the intervention to other veterans.
Conclusions: Findings provide preliminary support for the acceptability of conducting therapeutic assessments of personality for veterans in alcohol and drug treatment, which may serve as a useful clinical tool for increasing engagement in treatment.

0602

DRINKING REDUCTION IN HIV PRIMARY CARE: A RANDOMIZED TRIAL OF HEALTHCALL, A TECHNOLOGY-BASED ENHANCEMENT TO BRIEF MOTIVATIONAL INTERVIEWING

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Aims: Among patients with HIV, heavy drinking increases mortality and fosters HIV transmission behaviors. A large literature shows the value of brief drinking-reduction motivational interviewing (MI) in general primary care patients without alcohol dependence. However, little information is available on brief MI among primary care patients with more complex problems. In resource-limited HIV primary care clinics, interventions must be effective, yet require little staff time. We tested the efficacy of a technological enhancement, HealthCall, to brief MI to reduce heavy drinking among HIV primary care patients with and without alcohol dependence. HealthCall utilizes automated telephone Interactive Voice Response (IVR) to involve patients in brief (1–3) min daily calls to report alcohol and health behaviors. At 30 and 60 days, call drinking data are presented to patients in graphical form as personalized feedback.
Method: MI+HealthCall, MI-only and advice/education (control) were compared in a 3-arm randomized trial in a large New York City HIV primary care clinic. Participants were English- or Spanish-speaking HIV-infected patients (N=258) who drank ≥4 drinks at least once in the prior 30 days. Brief MI was administered at baseline in the two MI arms. At 30 and 60 days, patients were assessed and briefly discussed drinking behaviors. Pre-designated study outcomes were mean number of drinks per drinking day (NumDD) and percent days abstinent (PDA), measured with the Timeline Followback at baseline, 30 and 60 days.
Results: Of randomized patients, 226 (88.6%) provided post-treatment data. NumDD and PDA decreased in all three treatment groups, which did not differ significantly when patients with and without alcohol dependence were combined. A time x treatment x alcohol dependence interaction (p=.09) suggested that results differed between those with and without alcohol dependence. Among alcohol dependent patients, NumDD was lower at 60 days than in the control (t=3.53, df=93, p=0.0007) or MI-only groups (t=2.17 df=93, p=0.03), representing a large and moderate effect size, respectively.
Conclusions: IVR-based enhancements to brief interventions are feasible in urban HIV primary care, acceptable to staff and patients, and may be effective in reducing drinking among alcohol dependent HIV primary care patients.

0603

BRIEF ALCOHOL INTERVENTION AMONG HAZARDOUS AND HEAVY DRINKING HIV INFECTED WOMEN

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Objective: Hazardous and heavy alcohol use is associated with worse HIV treatment outcomes and increased mortality among women with HIV. We examined the effectiveness of brief alcohol intervention among HIV infected women.
Methods: We performed a randomized trial of hazardous and heavy drinking women receiving care in the Johns Hopkins HIV Clinic. Women were randomized to either a 2-session brief alcohol intervention with 2 booster phone calls or control. Ninety-day alcohol use, measured using the Time Line Follow Back, was measured at baseline and 3, 6, 12 month follow-up visits. Our main outcomes included 90-day frequency of alcohol use (%days alcohol was consumed), number of standard drinks per drinking day, and % binge drinking days, defined as days when >3 standard drinks were consumed. Changes in outcome from baseline for visits 2–4 were analyzed with general linear mixed effects regression models for three factors with interactions. The factors included treatment group, visit (longitudinal), and a high/low alcohol group designation based on the overall median of the baseline outcome across all subjects. Treatment group differences at each visit were calculated from these models.
Results: 153 women were randomized to intervention (n=76) and control (n=77). At baseline, their median age was 46, 86% were African American, 70% used illicit drugs. Overall, the median % drinking days was 24, the median %binge drinking days was 14%, and the median drinks per drinking day was 7.7. The two groups did not differ significantly in their baseline characteristics. The, 90-day frequency of alcohol use decreased significantly at 3 (decreased 13%, p=0.045) and 6 months (decreased 20%, p=0.001) among women in the high frequency group, but was not sustained at 12 months. Drinks per drinking day also decreased significantly among women with higher levels of daily drinking at 3 months (decrease in 5 drinks/occasion, p=0.008), but this effect was not sustained at 6 or 12 months. We found no difference in the %binge drinking days at intervention follow-up in either group.
Conclusions: Brief alcohol intervention resulted in decreased frequency of alcohol use among HIV-infected women at 6 months with higher frequency of use, but not at one year. Additional booster sessions may be necessary for a sustained effect.

0604

CHOOSING A DRINKING GOAL IN MI AMONG HIV PRIMARY CARE PATIENTS: CLINICAL AND DEMOGRAPHIC PREDICTORS

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Aim: Motivational interviewing (MI) to reduce excess drinking permits patients the choice of drinking-reduction goal. Some evidence suggests that a low-reduction drinking goal is associated with worse outcome. Little is known about pre-treatment patient characteristics that predict choice of drinking-reduction goal. Heavy drinking among HIV-infected individuals is associated with increased mortality and disease transmission behaviors. Thus, knowledge of patient characteristics associated with choice of drinking reduction goals could be clinically useful in strengthening the efficacy of a brief MI in resource-limited HIV primary care clinics.
Method: As part of a randomized clinical trial, 152 HIV urban, English- or Spanish-speaking primary care patients who drank ≥4 drinks at least once in the prior 30 days participated in a brief MI session aimed at drinking reduction. We analyzed patients' drinking reduction goals set during the MI session as a binary outcome variable, characterizing a drinking goal representing less than 50% reduction compared to prior drinking (mean drinks/drinking day in the 30 days prior to baseline) as a low-reduction goal, with the rest characterized as having a high-reduction goal. Patient characteristics tested as predictors of a low- or high-reduction drinking goal included age, sex, race, depression (Beck Depression Inventory; BDI), and DSM-IV alcohol dependence. The relationship of these to choice of drinking goal was tested with a logistic regression model.
Results: Overall, 78% of the patients chose a high-reduction goal and 22% chose a low-reduction goal. Age, sex, race and alcohol were unrelated to drinking goal. Depression (BDI >20) was a significant predictor of drinking reduction goal (p=0.003). After controlling for age, sex and race, depressed patients were three times as likely to choose a low-reduction goal than those who were not depressed (Odds ratio 3.13; 95% CI 1.28–7.68). Note that abstinence as a drinking goal did not differentiate patients within the high-reduction group in terms of depression.
Conclusion: Among HIV primary care patients in a brief MI for drinking reduction, depression at a moderate to severe level predicted a choice of drinking goal associated with poor drinking reduction outcomes. Targeting and addressing depression and self-efficacy during MI sessions or other brief interventions may assist these patients to choose drinking reduction goals more likely to result in a positive outcome.

0605

SINGLE SESSION OF MOTIVATIONAL INTERVIEWING FOR NON-TREATMENT SEEKING ALCOHOL DEPENDENT PATIENTS: AN OPEN LABEL TRIAL

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Motivational interviewing (MI) is a non-directive, patient-centered approach shown to reduce heavy drinking and promote behavior change. Although MI is frequently used in treatment studies, findings for non-treatment seeking alcohol dependent samples are limited. The purpose of this pilot study is to examine an open label trial of MI for non-treatment seeking alcohol dependent patients (n = 33, 8 female) enrolled in a research study of alcohol administration. All participants completed a baseline assessment at study entry, which included the Structured Clinical Interview for DSM-IV (SCID) to determine alcohol dependence. Participants received a single session of motivational interviewing upon completion of the alcohol administration portion of the study. The participants who completed the MI session were invited back for a 1-month follow-up. A total of 33 participants from the alcohol administration completed the MI, and 28 returned for the follow-up (an 85% retention rate). At each visit patients completed measures of alcohol use (30-day Timeline Follow Back) and motivation for change (The Stages of Change Readiness and Treatment Eagerness Scale - SOCRATES). A series of multilevel models were used to examine the effects of the motivational interviewing session on alcohol use (i.e., drink days, total number of drinks in past 30 days, and drinks per drinking day) and motivation for change (i.e., ambivalence, recognition of drinking problems, and taking steps to change). Results revealed a significant effect of the intervention (pre-post) on measures of motivation for change, such as increased recognition of problems and reduced ambivalence (*ps* < .05). In addition, there was a significant pre-post intervention effect on drinking outcomes, namely number of drinking days ($p < .01$) and total number of drinks over the past 30 days ($p = .05$). There were no intervention effects on taking steps to change ($p = .32$) or drinks per drinking day ($p = .39$). Together, these results provide initial support for the effectiveness of a single session of motivational interviewing for non-treatment seeking alcohol dependent patients. Further randomized controlled studies are warranted to more fully evaluate this brief intervention.

0606

AUDIT-C AS A SCREENING TOOL FOR BRIEF INTERVENTION WITH TRAUMA PATIENTS: CAVEAT EMPTOR

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The AUDIT-C is a brief alternative to the full AUDIT which is often used to identify patients who are most likely to benefit from brief intervention. In this study, we examine the specificity, sensitivity, positive predictive value and negative predictive value of the AUDIT C to determine its potential impact on the effectiveness of brief intervention. A total of 703 trauma patients were screened using the AUDIT as inclusion criteria for a randomized clinical trial comparing brief advice, brief intervention and brief intervention plus booster. In this study, we compare the total AUDIT score to the first three items of the AUDIT (i.e., AUDIT-C). We considered a score of 8 or more on the AUDIT positive and a score of four or more for women and five or more for men on the AUDIT-C as positive. The sample was predominately male (72%) and 51% (512) White, non-Hispanic, 30% (213) Black, non-Hispanic and 16% (110) Hispanic with an average age of 42. A total of 58% (409) screened negative and 54.5% (383) screened negative on both the AUDIT-C and total AUDIT. Nearly 19% (129) screened positive on the AUDIT C but not the full AUDIT and, thus, would have been eligible for the study based on the AUDIT C but not the AUDIT. Only 3.7% (26) screened negative on the AUDIT C but positive on the full AUDIT. The sensitivity and specificity were adequate at 86% and 75%, respectively. The positive predictive value was 56% and the negative predictive value was 94%. Thus, using the AUDIT-C alone may have led to the enrollment of a significant number of patients who were false positives. Given that brief intervention in the trauma center has been found to work more effectively for those with moderate or severe problems using the AUDIT-C as a screening tool for receiving a brief intervention may negatively impact its effectiveness. Caution should be used when applying the AUDIT-C for screening purposes when identifying patients who are most likely to benefit from brief intervention. Given the brevity of the AUDIT C and the preference for a brief screening tool in the trauma department setting, the AUDIT C may serve as an effective pre-screening tool.

0607

BRIEF SURGICAL ADVICE IS COMPARABLE TO BRIEF INTERVENTION AND SUPERIOR TO STANDARD OF CARE IN REDUCING CONCERNING ALCOHOL USE

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Purpose: Alcohol use disorders are a concerning factor associated with injury. A brief intervention (BI) administered during hospital admission for treatment of injuries at trauma centers has been shown to have a positive effect on reducing subsequent reported alcohol use. This study compares efficacy of BI administered by motivational interviewers (BMI) and brief surgical advice (BSA) offered by specially trained trauma surgeons to standard care (SOC) on subsequent self reported alcohol use.
Methods: Patients admitted to a Level I Trauma Center after injury either positive for Blood Alcohol Content (BAC) over 80 mg/dl and or positive screen on the Alcohol Use Disorder Identification Test (AUDIT) were eligible for inclusion. Those agreeing to participate in the study were randomized to SOC, BMI or BSA. Self-reported alcohol use was monitored at three month intervals after discharge for 12 months.
Results: There were 119 patients randomized: 41 in the BMI group, 40 in the BSA group and 38 into SOC. Baseline characteristics were mean age 31, 83% male, 45% white, 33% African American and 19% Hispanic.Mechanisms of injury included traffic related incidents (31%), gunshot/stabbing (24%), burns (17%), assault (13%), and falls (10%). Severity of baseline alcohol use disorder was the same for all groups (mean AUDIT score = 10). All groups showed an improvement in the number of days on which alcohol was consumed (drinking days) at 3 months, but only SOC and BMI showed decreases in drinks per drinking days and heavy use days at 3 months. The BSA showed decreases on all 3 use parameters by 6 months. After 3 months, the SOC group gradually returned to baseline alcohol consumption whereas both intervention groups remained below baseline although at a level higher than the 3 month point.
Conclusion: Both BSA and BMI are more effective than SOC in reducing degree of subsequent self reported alcohol use. Because hospitalization for injury appears to have a deterrent effect on alcohol use for approximately 3 months, BI outcome studies on alcohol use after hospitalization should be extended beyond this time period. These findings also suggest that ''booster'' encounters may be most beneficial after 3 months to sustain positive effects. Further work should delineate differences between the two types of BI and why they appear to have a differential impact on alcohol consumption.
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0608

INDIVIDUAL AND ORGANIZATIONAL DETERMINANTS OF ALCOHOL SCREENING AND BRIEF INTERVENTION IMPLEMENTATION IN EMERGENCY DEPARTMENTS (SIPS-ED)

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Objectives: This study explored individual and organisational barriers to and facilitators of effective implementation of alcohol screening and brief intervention in 9 Emergency Departments (EDs). This study was part of a large UK research programme on Screening and Intervention Programme for Sensible Drinking (SIPS).
Methods: Nine EDs were recruited in three regions of England and 282 ED staff (mean 31.3 per ED; range 8–82) were trained in the study and intervention procedures. ED staff were required to deliver one of three screening tools and one of three brief interventions. All staff received appropriate training and support. Staff attitudes were measured before (T1) and straight after training (T2) as well as post implementation (T3) using the Short Alcohol and Alcohol Problems Perception Questionnaire (SAAPPQ). Additional questions on organisational factors affecting the implementation of SBI were asked at T2 and T3. Data were also collected to measure the performance of screening and delivery of intervention in each setting.
Results: While staff were keen to be trained and while their attitudes and motivations significantly improved after training (p <.o1), there were several barriers to implementation which limited SBI activity across most settings, including workload pressures, lack of time, perceived lack of importance of alcohol in ED, high staff turnover, other competing priorities and feeling forced to take on extra work.
Only 3 of 9 EDs were able to implement the protocol without additional input from the research team beyond training and regular support. In the remaining EDs it was necessary to deploy researchers and Alcohol Health Workers to complete screening and intervention. Successful sites were noted to have a keen 'clinical champion' who prioritised the screening and brief intervention activity, voluntary participation of ED staff, supportive managers, and a small number of core staff who were keen to participate and able to be engaged by the research team. Training large numbers of staff yielded less screening and intervention activity.
Conclusions: Implementation of SBI in ED will be difficult in clinical practice due to the exigencies of ED care, and is likely in most cases to require delivery by dedicated outside specialist alcohol staff. Successful implementation also depends on local clinical and managerial champions and having a small number of dedicated staff who have responsibility for delivery of SBI.

0609

MEDIATOR AND MODERATOR EFFECTS OF A SIGNIFICANT OTHER INVOLVED BRIEF INTERVENTION DELIVERED IN AN EMERGENCY DEPARTMENT

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Evidence suggests the inclusion of significant others (SO; e.g., romantic partner, family member) improves alcohol treatment outcomes, but comparatively little is known about differential processes in individual compared to SO-involved alcohol interventions. The aim of the current study was to examine whether SO and Patient characteristics influenced mediating processes and outcomes in an individual motivational intervention (IMI) including a SO (SOMI) delivered to patients in an Emergency Department (ED). Data was from a large, randomized controlled trial (N = 406). Patients were adults who met one of 3 criteria: a) scored an 8 or higher on the AUDIT, b) were alcohol positive upon hospital admission or c) had consumed alcohol 6 hours prior to injury resulting in hospital admission. Initial OLS regression analyses examined each lagged a and b path of treatment condition (SOMI vs IMI) to the candidate mediators (SO behavior–support sobriety, support drinking, punish drinking, withdraw from drinker; patient self-efficacy and motivational readiness) and to the outcome variables (number of drinking days [ndd], number of heavy drinking days [nhdd], peak BAL, drinks per drinking day [dkdd]). Based on initial OLS results, we next examined 6-mo SO withdraws from patient and patient self-efficacy as mediators of the effect of the SOMI condition on 12-mo patient drinking frequency (ndd, nhdd). Results showed a portion of the effect of the SOMI condition on reduced drinking frequency at 12-mo was explained by differential increases in patient self-efficacy (ndd, b= −4.62(2.31), 95%CI: −13.86, −0.58; nhdd, b= −4.56(1.99), 95%CI: −13.67, −0.54). For SO withdrawal behavior, mediation effects were conditional upon the SO relationship type. Here, the SOMI condition was associated with reductions in 6-mo SO withdrawal behavior, which in turn was associated with greater drinking frequency at 12-mo. This protective mediation effect was seen only in contrast with IMI performed with non-romantic partner SOs (nhdd, b= −5.34(2.5), 95%CI: −11.71, −1.70; ndd, b= −6.12(2.85), 95%CI: −13.07, −1.8). Results indicate two pathways of SOMI effects: one through increased patient self-efficacy and one through reductions in romantic partner SO withdrawal behavior. Although trial results identified no significant differences between the IMI and SOMI conditions, these analyses suggest involving a SO in brief alcohol interventions may play a valuable role in reducing frequency of drinking.

0610

SUSTAIN TALK PREDICTS WORSE OUTCOMES AMONG MANDATED COLLEGE STUDENT DRINKERS RECEIVING A BRIEF MOTIVATIONAL INTERVENTION

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The construct of change talk (within-session client language conveying intention to change drinking) has become of increased interest in the literature on motivational interviewing (MI). Change talk has been linked to improved treatment outcomes, but many studies have ignored the role of sustain talk, language against change or that favors the status quo of drinking. The aim of this study was to examine the role of both client change talk (CT) and sustain talk (ST) within an MI session in predicting drinking outcomes. Participants were college students who had been mandated to receive a brief motivational intervention following an infraction of college alcohol policy (n = 94). Audiotapes of these sessions were coded using therapy process coding systems. We examined the relationships between client CT and ST, and drinking outcomes. Contrary to prior research, CT was not predictive of outcomes. However, greater ST predicted worse drinking outcomes across a variety of domains at the 3-month follow-up, including number of heavy drinking days ($p < .01$), average drinks per drinking day ($p < .05$), alcohol-related problems ($p < .05$), maximum number of drinks ($p < .01$), and peak blood alcohol level (BAL; $p < .01$). All of these effects persisted through the 12-month follow-up. At both follow-ups, these associations were present even controlling for baseline drinking levels. Gender and event severity (negative consequences experienced as part of the referral incident) emerged as significant moderators of the relationship between ST and 3-month drinking outcomes. Females who exhibited greater levels of ST during the session had higher average drinks per drinking day ($p < .05$), more alcohol problems ($p < .01$), and a higher peak BAL ($p < .05$). Those with a greater event-level severity who exhibited higher levels of within-session ST had more alcohol problems ($p < .001$), a higher level of maximum drinks ($p < .05$), and higher peak BAL ($p < .05$). Results suggest that researchers and clinicians should pay more attention to client sustain talk in addition to focusing on change talk. Students who are mandated to receive a brief motivational intervention following an alcohol-related incident and still seem resistant to changing their drinking (as evidenced through higher levels of ST), are likely to experience worse outcomes up to a year later.

11. EPIDEMIOLOGY

a. Alcohol consumption rates, drinking patterns **289–299/611–621**

0611

ALCOHOL OR CANNABIS FIRST? DIFFERENCES BY ETHNICITY AND RISK FOR RAPID ONSET OF PROBLEM USE IN WOMEN

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The aims of this study are to examine differences by ethnicity in the sequence of initiation of alcohol and cannabis use in women and to test for associations between sequence of initiation and risk for rapid progression to problem use. Data were drawn from a female twin study of alcohol-related psychopathology (n=3,787) and a high-risk alcoholism family study (n=315). Participants were 18 to 32 years of age; 18% African-American (AA), 72% European-American (EA). Data were collected with structured psychiatric telephone interviews. Just under half of AAs (49.7%) and EAs (44.4%) had used cannabis. AAs were equally likely to have initiated cannabis use before (35.0%) as after alcohol (36.3%). EAs were five times more likely to have tried alcohol before cannabis (13.1% vs. 64.8%). Two Cox proportional hazard regression analyses were conducted to predict rate of transition from first use to symptom onset for cannabis and alcohol, using sequence of initiation of substance use. Analyses were adjusted for age at first use, age at time of symptom report, and sample design, as well as significant covariates: ethnicity, childhood sexual and physical abuse, maternal and paternal alcohol problems, major depressive disorder, regular smoking, and conduct disorder. After accounting for the contribution of alcohol use (HR=2.71, CI:1.79–4.09), initiation of cannabis use before (HR=1.58, CI:1.17–2.12) or at the same age as first alcohol use (HR=1.37, CI:1.04–1.80) was associated with elevated rate of transition to cannabis use disorder symptoms. AA ethnicity also independently predicted rapid symptom onset (HR=1.46, CI: 1.11–1.92). After accounting for the contribution of cannabis use (HR=2.54, CI:2.16–2.99), initiation of cannabis before alcohol use was associated with slower transition from first drink to alcohol use disorder symptom onset (HR=0.68, CI:0.56–0.83), whereas never using cannabis was associated with elevated rate of progression (HR=1.33, CI:1.16–1.54). AA ethnicity independently predicted slower transition time (HR=0.55, CI: 0.46–0.66). Results indicate that use of cannabis before alcohol is associated with elevated rate of progression to problem cannabis use but slower transition from first drink to problem drinking. This sequence of initiation is more common in AA than EA women, but differences by ethnicity do not fully account for these associations, nor do differences in sequence of initiation fully account for differential outcomes for AA vs. EA women.

0612

AN EXAMINATION OF AGE AT FIRST DRINK AMONG ASIAN AMERICAN ADULTS IN NATIONAL LATINO AND ASIAN AMERICAN STUDY

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For Asian American (AA) adults, alcohol use has become an increasing concern. Between 1991/1992 and 2001/2002, rates of DSM-IV alcohol abuse increased significantly among Asian females ages 18–29 and rates of alcohol dependence increased significantly among Asian males in this age group (Grant et al., 2004). Age of first drink is an important predictor of alcohol use and related problems. Comparing to later onset drinkers, early onset drinkers were more likely to report heavy drinking (Rothman et al., 2008) and experience alcohol use disorders in adulthood (Dawson et al., 2008). To date, limited research has examined age at first drink in the AA population. Thus, this study will address gaps in the literature by assessing differences of age at first drink by ethnicity, nativity (foreign- vs. U.S.-born) and self-reported language proficiency (Poor/fair vs. good/excellent).

The sample was extracted from the National Latino and Asian American Study (N = 2095). Descriptive statistics indicate that age at first drink in this sample was similar to the general population (Dawson et al., 2008). Specifically, 7.6%, 18.4%, and 74% reported age at first drink being lower than 15, between 15 and 17, and higher than 18 years old resectively. Consistent with the parent study (Takeuchi et al., 2007), subsequent analyses were conducted separately for men and women. Results from a one-way ANOVA suggest that age at first drink differed among men with different ethnic backgrounds, $F_{(3,\ 631)} = 11.368$, $p < .001$. There was no ethnic difference of age at first drink for women. U.S.-born men (M = 18.51) reported significantly lower age at first drink relative to foreign-born men (M = 20.60) ($t_{(632)} = -4.31$, $p < .001$). Women also showed a similar pattern ($t_{(329)} = -4.24$, $p < .001$). Men with lower English proficiency (M = 21.09) reported significantly higher age at first drink relative to those with higher proficiency (M = 19.55) ($t_{(630)} = 3.219$, $p < .001$). This pattern was also exhibited for women ($t_{(329)} = 2.276$, $p < .001$). Men with lower Asian language proficiency (M = 18.92) reported significantly lower age at first drink relative to those with higher proficiency (M = 20.78) ($t_{(519)} = -3.61$, $p < .001$). A trend level significance was exhibited for women ($t_{(257)} = -2.85$, $p = .05$). Additional analyses on language variables (thinking in a language) will also be presented. Results suggest a consistent effect of nativity and language proficiency on age at first drink.

0613

NEIGHBORHOOD PERCEPTIONS AND ALCOHOL CONSUMPTION AMONG MEXICAN AMERICANS RESIDING IN U.S.-MEXICO BORDER AND NON-BORDER AREAS

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Objective: This research examines the association between neighborhood perceptions (informal social control, social cohesion, and perceived neighborhood violence) and alcohol consumption (volume of drinks consumed per week) among Mexican Americans residing in U.S.-Mexico border and non-border areas.
Methods: Respondents are from two surveys, both of which utilized a multistage cluster sample design. Data for the border sample were collected in the U.S.-Mexico border regions of Texas, Arizona, New Mexico and California between 3/09–6/10 (N=1307). The response rate was 67%. The non-border sample is from the 2006 Hispanic Americans Baseline Alcohol Survey (HABLAS) and includes 1288 Mexican Americans from 5 U.S. metropolitan areas: Houston, Miami, Los Angeles, New York and Philadelphia. The response rate for HABLAS was 76%.
Results: The multiple regression analysis for women showed no significant effect of informal social control, social cohesion, or perceived neighborhood violence on the number of drinks consumed per week. Employment status (retired, disabled, not working by choice versus full- or part-time employment) (b = 0.52, P value= < .01) and religious affiliation (Protestant versus Catholic) (b=0.47, P value= < .01) were associated with a lower volume of consumption, while U.S. birthplace (versus foreign birth) was associated with higher consumption (b=1.33, P value=.04). Among men, the only neighborhood variable associated with the volume of consumption was perception of neighborhood violence. A perception of increased neighborhood violence was associated with a higher volume of consumption (b=1.05, P value=.03). Among men, employment status (retired, disabled, not working by choice versus full- or part-time employment) (b=0.52, P value= < .01) and religious affiliation (Protestant versus Catholic) (b=0.47, P value= < .01) were associated with a lower volume of consumption. In addition, there was a statistically significant association between living on the border and a higher volume of alcohol consumption (b=1.33, P value=.03).
Conclusion: Neighborhood perceptions had no effect on the volume of alcohol consumption among women. But among men, increased perceptions of neighborhood violence were associated with increased drinking. The stress associated with perceived lack of safety may contribute to an increase in drinking as a coping mechanism.

0614

CO-OCCURRENCE OF LIFETIME REGULAR ALCOHOL AND CIGARETTE USE AMONG HINDUS, TAMILS, CREOLES, AND MUSLIMS IN MAURITIUS

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The current study examined the co-occurrence of regular alcohol and cigarette use among the four major religioethnic groups in Mauritius, a developing country in the Indian Ocean. Participants were 1,170 (518 women and 652 men) of the original 1,795 participants of the Joint Child Health Project, an ongoing longitudinal study started in 1972 when the cohort was 3 years old. As part of the current data collection phase (mean age 36.9 years), we assessed lifetime regular cigarette use and lifetime regular drinking. Rates of lifetime regular drinking and smoking differed across gender and religioethnic groups. In men, rates of lifetime regular drinking were similar among Hindu, Tamil, and Creole men (85–89%), but lower in Muslim men (19%; $\chi 2 = 246$, 3 df, $p < .01$). Lifetime regular smoking was highest in Creole men (57%), followed by Tamil and Muslim men (49%), and lowest in Hindu men (39%; $\chi 2 = 13.4$, 3 df, $p < .01$). The correlation between cigarette use and drinking was significantly higher among Muslim and Creole men than among Hindu men ($r = .37–.39$ vs. .17; $zs > 2$, $p < .05$); the correlation in Tamil men was similar to that in Hindu men ($r = .17$, $p < .01$). Being a lifetime regular smoker increased the odds of being a lifetime regular drinker by almost 28 times in Creole men, almost 12 times in Muslim men, over 5 times in Tamil men, and over 3 times in Hindu men. In women, about half of Creole women (54%) were lifetime regular drinkers compared with about a third of Tamil and Hindu (30–33%) women; no Muslim women were lifetime regular drinkers or smokers ($\chi 2 = 83$, 3 df, $p < .01$). Creole women had the highest rate of lifetime regular smoking (17%), with significantly lower rates in Tamil and Hindu women (1–3%; $\chi 2 = 54$, 3 df, $p < .01$). Being a lifetime regular smoker increased the odds of being a lifetime regular drinker by over 9 times in Creole women, but was not predictive of lifetime regular drinking in Hindu or Tamil women. These findings suggest discrepant patterns of co-occurrence of drinking and smoking by gender and religioethnic group in Mauritius that may be associated with varying cultural and religious influences. This research was funded by grants from NIH (K08 AA14265, R01 AA18179, and R01 AA10206) and the Mauritian Ministry of Health.

0615

DRINKING, BINGEING, AND MORTALITY: RE-THINKING THE J-SHAPED CURVE

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Background: The dose-response association between alcohol consumption and mortality has been repeatedly demonstrated to be J-shaped, with low to moderate consumption associated with reduced mortality risk, and higher levels of consumption predicting sharply elevated mortality risk, relative to abstention. However, very few studies of mortality have considered drinking patterns in conjunction with, or in lieu of average daily dose measures.
Objectives: (1.) To examine the epidemiology of drinking patterns, operationalized as frequency of heavy *versus* non-heavy drinking, differentiated using the ''5-or-more'' drinks threshold to define heavy drinking or ''binge'' episodes. (2) To determine the association of these frequencies with mortality, assuming additivity of effects of heavy and non-heavy drinking episodes.
Methods: Data from 1997–2001 administrations of the National Health Interview Survey (NHIS) were aggregated to yield data on 128,203 subjects between the ages of 18 through 64 at time of interview. Mortality data through 2006 was obtained from NHIS-linked mortality files, maintained by the Centers for Disease Control. RESULTS: Regarding the joint distribution between heavy drinking frequency and non-heavy drinking frequency, 48.6% of past-year drinkers reported mostly non-heavy drinking days, 9.1% reported mostly heavy drinking days and 37.5% reported drinking infrequently (less than twice a month, any amount). Only 4.7% of drinkers reported a mixed pattern of heavy and non-heavy drinking. When considered as separable behaviors, heavy-drinking frequency bore a linear relationship to mortality risk (HR=1.08 / day-per-week; p<.0001). Non-heavy drinking frequency was associated with a J-shaped mortality curve, albeit with a shallow ascending slope; e.g., daily non-heavy drinking did not predict elevated mortality risk relative to abstention.
Conclusions: Heavy drinking and non-heavy drinking are distinct behaviors, and only a limited number of people engage in both. The ascending arm of the conventional J-shaped curve is likely driven by individuals who engage primarily in heavy-drinking episodes. Operationalizing total population alcohol consumption as a combination of heavy and non-heavy drinking episodes, rather than an average daily dose, could add substantial value to prevention-oriented research.

0616

PROSPECTIVE ASSOCIATIONS OF PSYCHIATRIC DISORDERS WITH HEAVY DRINKING: A THREE-YEAR FOLLOW UP STUDY

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Our goal was to examine the prospective associations of psychiatric disorders with risky drinking behaviors. Psychiatric disorders have been documented to increase risky drinking behaviors in numerous cross-sectional studies, but nationwide longitudinal data of the prospective associations are still scarce. Using data on the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) the incidence of heavy drinking during a three-year follow up was examined among 13,029 drinkers aged 18 and older who were free from heavy drinking at baseline examination (2001–2002). The outcome, heavy drinking was defined as two or more drinks of all types of alcohol a day, and one or more drinks a day for men and women respectively. The DSM-IV past year diagnoses of specific mood, anxiety, any drug abuse, dependence, and tobacco dependence, as well as personality disorders were used to predict the incidence of heavy drinking. Multivariate logistic analyses were conducted to estimate the associations of psychiatric disorders with heavy drinking while controlling for sociodemographic characteristics and psychiatric comorbidity. Antisocial personality disorder, any drug abuse and dependence were positively associated with heavy drinking during the three-year follow up (Odds Ratios=1.54, 3.17 and 3.45, respectively, all p Values < 0.05). Psychiatrists should be vigilant and recognize the heavy drinking implications of psychiatric morbidity when care to patients is provided.

0617

PROSPECTIVE DEVELOPMENTAL SUBTYPES OF ALCOHOL DEPENDENCE FROM AGE 18 TO 32 YEARS: IMPLICATIONS FOR NOSOLOGY, ETIOLOGY, AND INTERVENTION

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The purpose of the present study was to identify child and adult correlates that differentiate (a) individuals with persistent alcohol dependence from individuals with developmentally-limited alcohol dependence and (b) individuals with adult-onset alcohol dependence from individuals who never diagnose. Participants are 1,037 members of the Dunedin longitudinal study, a birth cohort followed prospectively from birth until age 32. Past-year DSM-IV alcohol dependence diagnoses were ascertained with structured diagnostic interviews at ages 18, 21, 26, and 32. Individuals were classified as developmentally-limited, persistent, or adult-onset subtypes based on their time-ordered pattern of diagnoses. The persistent subtype generally exhibited the worst scores on all correlates, including family psychiatric history, adolescent and adult externalizing and internalizing problems, adolescent and adult substance use, adult quality of life, and coping strategies. The prospective predictors that distinguished them from the developmentally-limited subtype involved family liability, adolescent negative affectivity, daily alcohol use, and frequent marijuana use. Furthermore, young people who developed the persistent subtype of alcohol dependence were distinguished from the developmentally-limited subtype by an inability to reduce drinking and by continued use despite problems, already by age 18. The adult-onset group members were virtually indistinguishable from ordinary cohort members as children or adolescents, but, in adulthood, adult-onset cases were distinguished by problems with depression, substance use, stress, and strategies for coping with stress. Information about age-of-onset and developmental course is fundamental for identifying subtypes of alcohol dependence. Subtype-specific etiologies point to targeted prevention and intervention efforts based on characteristics of each subtype.

0618

CHANGES IN DRINKING BEHAVIOR DURING PREGNANCY IN KOREAN WOMEN BETWEEN 1997 AND 2008

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Objective: Drinking alcohol during pregnancy can result in various negative consequences. A few studies have been conducted in Korea to investigate alcohol consumption in pregnant women, but no study has investigated whether alcohol drinking habits of Korean pregnant women have changed over time. Therefore, we compared the results of two surveys conducted in 1997 and 2008 that investigated whether pregnant women drank alcohol before and during pregnancy.
Method: Pregnant women who were <30 days before their expected delivery date and who visited a specialized hospital for obstetrics in 1997 and 2008, respectively, were asked to complete a self-report questionnaire. Demographic and obstetric characteristics as well as alcohol history were investigated.
Results: 1) Comparing the 2008 survey (n = 476: group B) with the 1997 survey (n = 731; group A), the average age and education level of group B were significantly older and higher than those in group A (30.6 ± 3.7 vs. 28.0 ± 3.4, $p < 0.001$; 14.9 ± 1.7 vs. 13.6 ± 2.3, $p < 0.001$). Moreover, the proportion who were positive on the CAGE test or who had a blackout history was significantly greater in group B than that in group A (18.7% vs. 11.9%, $p = 0.001$; 28.1% vs. 8.9%; $p < 0.001$). 2) The rate of subjects who consumed alcohol before their last menstrual period (LMP) in group B was significantly higher than that in group A (83.3% vs. 78.5%, $p = 0.045$). In contrast, the rate of subjects who consumed alcohol after LMP was significantly lower in group B than that that in A (40.0% vs. 57.6%, $p<0.001$).
Conclusion: During the 11 years between 1997 and 2008, the pregnant women were older and had more alcohol-related problems but more pregnant women intended not to drink alcohol during their pregnancy. These results suggest that an appropriate anti-drinking educational strategy for pregnant women to effect these changes might be needed.

0619

EARLY LIFE EXPOSURE TO VIOLENCE AND SUBSTANCE MISUSE IN ADULTHOOD—THE FIRST BRAZILIAN NATIONAL SURVEY

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Background: Substance misuse has been a major source of health and social problems in developing societies as it has been elsewhere. There is a growing body of evidence from developed nations linking early exposure to violence in childhood with substance misuse in adulthood. The role of depression on this association is not clear. This study estimates the association between early life exposure to violence, alcohol disorders and illegal substance use in adulthood and the role of depression on these associations using a national Brazilian sample.
Methods: The first Brazilian National Alcohol Survey gathered information on early exposure to violence and use of psychoactive substances in 1880 participants aged 20 to 60 years old selected at random from the Brazilian household population. The survey response rate was 66.4%. We used weighted logistic regression to calculate adjusted odds ratios for the associations between early exposure to violence and substance misuse. To assess the mediating effect of current depression on these associations we used the Sobel-Goodman Mediation Test.
Results: Witnessing violence during childhood or adolescence was reported by nearly 20% of the participants whilst over 8% reported having been victims of at least one form of violence and 2.6% were victims of two or more different forms of violence during their childhood. There was a statistically significant association between early exposure to violence and alcohol abuse and/or dependence and use of illegal substances in adulthood. There was a dose-response relationship between severity of exposure to violence and substance misuse (OR: 3.56, CI95%: 1.72–7.36). Depression partially explained the association between early exposure to violence with alcohol dependence (18.77% $p<0.001$) and had no mediating effect on the association with illegal substance use (5.83% $p=0.220$).
Conclusions: Adverse early life events may affect individual's susceptibility to substance misuse which can be partially mediated by depression. Prevalence of substance misuse in adulthood may be in part attributed to prevalence adverse childhood experience. While prevention is the ideal goal detection and intervention with children exposed to violence must be prioritized.

0620

ALCOHOL CONSUMPTION ACROSS THE LIFESPAN: THE FIRST BRAZILIAN NATIONAL SURVEY

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Brazil is amongst the developing nations with the highest estimated alcohol consumption levels. Only recently Brazil has started to develop comprehensive population studies on the pattern of alcohol consumption.
We estimate the prevalence of alcohol in a national representative sample and analyzed how socio demographics characteristics and mental health are associated with the use.
This is a cross-sectional study using data from the first Brazilian National Alcohol Survey, which gathered information on alcohol use and comorbidities in 3007 participants. Data was analyzed in three age groups separately (Adolescents (14 to 19 years old) N=761; Adults (20 to 60) N=1880 and Elder (61 and over) N=366). Weighted logistic regression was used to calculate adjusted odds ratios.
More than half of the adolescents were regular alcohol users and one out of ten were abusers and/or dependents. Older male adolescents living in urban areas were more likely to present alcohol related disorders. Adolescents with alcohol abuse/dependence were more likely to have depression.
In the adult group 28% reported binge drinking and 11% presented alcohol abuse and/or dependence. Gender and depression were associated with alcohol abuse/dependence whilst education, marital status and income were not.
Among the elderly participants 10.4% were binge drinkers and the prevalence of alcohol abuse/dependence was 3.2%. Heavy drinking was more common among those who were single. Income and depression were associated with alcohol dependence.
Abstinence is high in the Brazilian population, however, elevated proportions of those who drink consume alcohol in a high risk pattern leading to increased levels of alcohol related problems. The high prevalence of alcohol use and related disorders among the young population must lead to the intensification of law enforcement strategies to prevent availability. There is a rapid increase of the elderly population in Brazil, even though rates of alcohol problems are much lower in this age group, prevalence of heavy drinking among the elderly is higher than in most developing countries in the world. There is a need to develop more focused interventions targeted to each age group separately. Prevention and treatment strategies should aim to tackle mood disorders as much as addiction. The overall high prevalence of alcohol related problems in the Brazilian population should instigate changes in health and enforcement sectors urgently.

0621

ALCOHOL USE AMONG WOMEN OF CHILDBEARING AGE – UNITED STATES, 2006–2010

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Purpose: Alcohol consumption during pregnancy is a risk factor for fetal alcohol spectrum disorders (FASD) and other adverse reproductive health outcomes. The purpose of this study is to examine annual trends in the prevalence of any alcohol use and binge drinking among pregnant and non-pregnant women aged 18–44 between 2006 and 2010. Additionally, patterns of binge episodes and maximum alcoholic beverages consumed on a single occasion were explored.
Methods: Five years of data, collected from 2006 through 2010, from the Behavioral Risk Factor Surveillance System (BRFSS) were combined and analyzed. The study population included 13,880 pregnant and 331,196 non-pregnant women aged 18–44. Annual and five-year prevalence estimates of any alcohol use and binge drinking (defined as four or more drinks on one occasion) in the past 30 days were calculated for pregnant and non-pregnant women. The average number of binge drinking episodes and the average maximum number of drinks consumed on one occasion in the past 30 days among binge drinkers were also estimated.
Results: The estimated prevalence of any alcohol use from 2006–2010 among pregnant women and non-pregnant women was 7.6% (95% Confidence Interval (CI) = 6.9–8.4) and 51.5% (95% CI = 51.2–51.8), respectively. The estimated prevalence of binge drinking from 2006–2010 among pregnant women and non-pregnant women was 1.1% (95% CI = 0.8–1.4) and 13.5% (95% CI = 13.2–13.7), respectively. There was little annual change in either set of prevalence estimates over the five years of data collection. The reported average number of binge drinking episodes was only slightly lower among pregnant women compared to non-pregnant women (2.5 vs. 3.0, respectively). The average maximum number of alcoholic beverages consumed on one occasion was found to be 6.2 drinks among both pregnant and non-pregnant women who binge.
Conclusion: The relatively stable prevalence estimates of any alcohol use and binge drinking from 2006 to 2010 among women of childbearing age indicate that continued efforts are necessary to address this public health concern and further reduce FASD risk. Women who binge drink appear to binge with similar frequency and intensity, regardless of pregnancy status. Women who binge drink are an important population for targeted interventions. Increasing screening and brief intervention may help to address this issue.

0622

OUTPATIENT TREATMENT ENGAGEMENT AND POST-TREATMEN T DETOXIFICATION ADMISSIONS: AN EXPLORATION OF RACIAL/ETHNIC DIFFERENCES

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Although treatment for alcohol and other drug (AOD) disorders has been shown to be effective, a limited research literature on racial/ethnic disparities in AOD treatment suggests that the quality of treatment may differ based on client's race/ethnicity. Treatment engagement is a process-based performance measure which has been adopted by the National Committee for Quality Assurance (NCQA) and endorsed by the National Quality Forum. This study is focused on two questions: 1) Is engagement in outpatient treatment associated with a detoxification admission, a negative outcome? and 2) Is any association of treatment engagement and detoxification admission moderated by clients' race/ethnicity? This study used administrative data of client treatment services received in specialty treatment facilities licensed in Massachusetts linked with data from the National Survey on Substance Abuse Treatment Services on facility-level attributes and Census data on neighborhood attributes. The sample consisted of 12,146 adult clients (77% White, 12% Latino, 11% Black) who began an outpatient treatment episode in 2006. Treatment engagement was defined using the NCQA/Washington Circle specifications: receipt of at least one treatment service within 14 days of beginning a new outpatient treatment episode and receipt of at least two additional treatment services in the next 30 days. Survival models were used to answer the research questions, with time to detoxification admission as the dependent variable. For the first question, engagement was the main independent variable. For the second question, interactions between race/ethnicity and engagement were added to the model. Overall, 40% of clients met the engagement criteria, although Latinos had significantly lower engagement rates than the other two racial/ethnic groups. Clients who met the engagement criteria had a lower hazard of having a detoxification admission during the year following the index outpatient visit than those who did not engage (Hazard Ratio = 0.84, $p < .01$). Interactions between race/ethnicity and engagement were not significant. Treatment engagement is a useful measure for monitoring AOD quality of care, and works equally in predicting detoxification admission as a treatment outcome for clients from diverse racial/ethnic backgrounds. Treatment programs should aim to improve treatment engagement among their clients, with increased attention to engage Latino clients, as they have lower engagement rates.

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THE ASSOCIATION OF ALCOHOL AND OTHER DRUG TREATMENT ENGAGEMENT WITH EMPLOYMENT OUTCOMES

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Employment is a key outcome for individuals treated for alcohol and drug disorders (AOD) which has been shown to improve their stability, health and social wellbeing. This study explores the association between meeting a process-based performance measure for outpatient treatment engagement and employment in the formal sector. Treatment engagement was defined using the NCQA/Washington Circle specifications: receipt of another treatment service within 14 days of beginning a new outpatient treatment episode and at least two additional treatment sessions within the next 30 days. We linked secondary data from two Washington State sources on adult clients receiving outpatient treatment in 2008: treatment admission and encounter data for 2007–2009 from the Division of Behavioral Health and Recovery and quarterly data on wages and hours worked from the Employment Security Department. Our analyses (N=8,185) were based on Full-Information Maximum Likelihood sample selection models accounting for clustering within sites, to investigate the association between engagement and any employment, number of quarters worked, amount earned, and hours worked. Each model consisted of two jointly estimated equations: (1) a probit equation predicting employment in any quarter in the year after a new episode of treatment, and (2) a linear regression equation predicting number of quarters employed, number of hours worked, or total wages earned in the same time period. Engagement was marginally associated with any employment in the year following the beginning of a treatment episode ($p < .10$). When the second equation outcome was number of quarters worked, neither the facility's engagement rate nor the client's own engagement demonstrate a significant impact on employment. When the second equation outcome was number of hours worked or total wages, the facility's engagement rate had a positive significant effect on employment in any quarter (Coeff: 0.30, 95% CI: 0.06, 0.54). Engagement by the client had a significant positive effect at the second equation for number of hours worked (Coeff: 69, 95% CI: 5, 134) and wages (Coeff: 1,202, 95% CI: 25, 2380). Although employment in the formal sector may under-estimate total employment, these results suggest that engagement in outpatient treatment can be a useful performance measure for publicly-funded specialty treatment settings.

0624

THE ASSOCIATION OF ALCOHOL AND OTHER DRUG TREATMENT ENGAGEMENT WITH SUBSEQUENT CRIMINAL JUSTICE OUTCOMES

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This study examines the relationship between client-level engagement in outpatient treatment and facility engagement rates with a treatment outcome for subsequent criminal justice involvement. Adult clients who began an outpatient AOD treatment episode in 2008 in publicly-funded, specialty treatment facilities in New York, Oklahoma, and Washington made up the sample (N = 105,449). Administrative treatment data were linked to criminal justice data. Engagement was defined using the NCQA/Washington Circle specifications: receipt of another treatment service within 14 days of beginning a new outpatient treatment episode and at least two additional treatment sessions within the next 30 days. Shared frailty survival (time-to-event) models were used to examine the relationship between outpatient engagement and three dependent variables: time (in days) to any arrest, a drug arrest, or a violent arrest. Survival analyses model hazard rates (HR), which then allow comparison across groups of their relative probabilities of arrest at any particular time during the follow-up time period. All models controlled for client characteristics and facility characteristics (percent of clients in the treatment facility that had prior criminal justice involvement, and percent who used hard drugs). Across states, overall outpatient engagement rates ranged from 50% to 77%. In all states, clients who engaged had a lower hazard of arrest during the year following the index outpatient visit than those who did not engage (New York HR: 0.76, 95% CI: 0.70, 0.83; Oklahoma HR: 0.74, 95% CI: 0.66, 0.83; Washington HR: 0.83, 95% CI: 0.75, 0.92). Also, in New York and Oklahoma but not Washington, clients who engaged had a lower hazard of arrest for a drug-related crime and for a violent crime. In addition, in New York and Oklahoma but not Washington, clients treated in outpatient facilities with higher engagement rates had a lower hazard of arrest. We conclude that outpatient treatment engagement is a useful process measure for monitoring quality of care in publicly-funded specialty treatment settings as it associates with criminal justice outcomes. Providers may be able to improve criminal justice outcomes by focusing efforts on having more clients return for timely treatment services.

0625

IMPACT OF A SYSTEMS INTERVENTION ON ENGAGEMENT IN ADDICTION TREATMENT

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Patients seeking treatment in Emergency Departments (ED) often suffer from underlying but undetected health problems including addiction. Clinicians in busy EDs face many barriers to detecting substance abuse or dependence and making successful treatment referrals. Specialists trained to conduct screening, brief intervention and referral to treatment (SBIRT) can improve detection of alcohol problems including alcohol dependence, but getting patients needed services is challenging. Accessing the treatment system can be difficult, as needed services are often unavailable. Patient-level barriers also exist including transportation problems and patient denial. As a result, only a small percentage of ED patients needing treatment ever successfully engage in treatment. The purpose of this study was to test the impact of systems interventions designed to increase ED patients' engagement in addiction treatment.

Health education specialists (HES) in the ED conducted assessments using the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) to identify patients with alcohol and other drug disorders. Based on ASSIST scores, patients received a brief intervention (BI), BI plus referral to brief treatment (BT), or BI plus referral to addiction treatment (RT). Patients with ASSIST scores >26 were referred to the local state-funded treatment provider. To monitor treatment engagement, quarterly reports were generated by working with the local treatment provider to identify RT patients receiving treatment within one week of their ED visit.

Beginning in July 2010, systems changes were made to improve treatment engagement including regular meetings between SBIRT and treatment provider administrators, signing release forms to permit sharing of patient information between HES and treatment provider, and implementing a weekly meeting in the ED between HES and a treatment representative to collect information on referred patients.

The number of referrals per quarter ranged from 51 to 99. Results from quarterly reports show an increase in treatment engagement from 19.3% in the 3rd quarter of 2010 to 32.8% in the 3rd quarter of 2011 with a high of 34.4% in the first quarter of 2011. Bus passes purchased in September 2011 for RT patients reporting problems accessing transportation may show further improvements in treatment engagement in future reports. This study demonstrates that ongoing efforts to increase treatment engagement can be successful.

0626

CRIMINAL JUSTICE INVOLVEMENT AND ALCOHOL TREATMENT AND TREATMENT NEED: RESULTS FROM A NATIONAL SAMPLE

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The purpose of this study was to investigate the associations of recent criminal justice involvement with perceived need for alcohol treatment and alcohol treatment utilization in a large national sample (N=4545) of individuals with alcohol use disorders. We analyzed data from the 2006 National Survey on Drug Use and Health (NSDUH). 310 (6.6%) reported past year alcohol treatment and 104 (2.6%) reported no treatment but felt need for treatment in the past year. Almost 20% reported criminal justice involvement in the past year, including being arrested and booked (one time, 8.8%, two or more times, 4.4%), being on probation (7.8%), on parole or supervised release (2.6%), arrested and booked for drunkenness (3.9%), possession/sale of drugs (2.7%), and DUI (4.5%) (not mutually exclusive, other types of arrest were < 1%). Bivariate analysis found significant associations between all criminal justice measures and received/needed treatment. Multinomial logistic models regressed perceived need for alcohol treatment and past year treatment utilization (versus neither) on past year legal involvement, adjusting for demographic (gender, age, race/ethnicity, marital status, education, income) and clinical characteristics (alcohol dependence vs. abuse, serious psychological distress, major depression, overall health). Strong associations between frequency of criminal justice involvement were found for treatment utilization compared to perceived need for treatment alone. The odds of treatment utilization and needing treatment were significantly greater for being booked/arrested one time (perceived need OR=3.4, treatment utilization OR=3.3) and 2+ times (perceived need OR=5.8, treatment utilization OR=5.9). Treatment utilization was also associated with being on probation (OR=5.0), but perceived need was not. Individual types of arrests were not significantly associated with utilization/need when adjusting for clinical and demographic characteristics. Significant clinical variables were alcohol dependence (vs. abuse) for both utilization and need, major depression (utilization only), and excellent/good health (inversely for utilization). Study results suggest opportunities for active interventions in criminal justice locations to increase treatment rates or treatment need, a major correlate of treatment utilization.

0627

BARRIERS TO HELP-SEEKING FOR PROBLEM DRINKING/DRUG USE AMONG THE NATIONAL GUARD

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Problem alcohol/drug use is highly prevalent among military personnel, but help-seeking is low. This newly funded VA study is an in-depth ethnographic investigation of the complex interactions between alcohol/drug use, perceptions of benefit and harm of substance use, and attitudes and intentions to seek treatment among a sample of current and former National Guard (NG) soldiers. A total of 90 current/past NG personnel with past year alcohol/drug disorders who have deployed overseas will be interviewed. Participants are being recruited via respondent-driven sampling. With the help of numerous key informants in the NG, ongoing ethnographic mapping techniques are being used to identify participants. Ongoing participant observation is being used to gather background information on military culture and the context of alcohol/drug use and help-seeking. Participants complete structured diagnostic instruments and a semi-structured in-depth interview. The in-depth interviews explore substance use histories, barriers to help-seeking, and soldiers' perspectives on already-emerging and new treatment ideas. A sub-sample is participating longitudinally via in-depth follow-up interviews. Focus groups will be conducted later in the study to brainstorm new intervention approaches. Preliminary data from the ethnographic research indicate that the problems associated with treatment-seeking do not appear to be linked to availability of treatment. Rather, the problems appear linked to a relative lack of perceived need/desire for treatment, and numerous privacy and stigma concerns which make anonymous and consequence-free treatment attendance difficult. Some NG soldiers attend mandated treatment as a result of failing a random drug test. Others choose to leave the NG or are discharged after failing a drug test. Many do not seek help for treatment until ''a crisis'' of some kind occurs. Drinking alcohol is normative and consequences of drinking are often under-emphasized. Younger service members express interest in online resources for help-seeking.

0628

EXAMINING PATTERNS OF SPECIALTY CARE UTILIZATION BY VETERANS WITH SUBSTANCE USE DISORDERS AND PTSD

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Previous research among returning soldiers serving in Afghanistan and Iraq (OEF/OIF) has documented concerning rates of both substance use disorders (SUDs) and Posttraumatic Stress Disorder (PTSD). This study examined if comorbid SUD and PTSD diagnoses present a barrier to patient utilization of specialty SUD and/or PTSD treatment services among returning OEF/OIF Veterans in the VA healthcare system. Historically, SUD treatment providers have been concerned that trauma-focused therapies may trigger a relapse while PTSD treatment providers have felt that individuals actively misusing substances are not appropriate for trauma-focused therapies. Given the fact that rates of SUD and PTSD treatment utilization varies by gender, there is also a need to examine male and female Veterans separately. This was a cross-sectional study that used national VA administrative data from Fiscal Years 2008 and 2009. The sample is composed of OEF/OIF Veterans who had at least one face-to-face outpatient mental health or primary care clinic encounter at a VHA facility and had a SUD and/or PTSD diagnosis (N=80,228 patients) with 25.7% (n=2,0651) with alcohol-related disorders. Logistic regression was used to compare three groups (SUD only, PTSD only, comorbid) on SUD and PTSD treatment utilization adjusting for demographic and military service characteristics. Findings were that male comorbid patients were slightly but significantly more likely to utilize outpatient and inpatient SUD treatment than those with SUD alone, and female comorbid patients were more likely to utilize inpatient SUD treatment than those with SUD alone. Male and female comorbid patients were more likely to utilize outpatient and inpatient PTSD treatment than patients with PTSD alone. We also found that only 9% of female and 14% of male comorbid patients utilized concurrent SUD-PTSD treatment. Comorbid patients appear to utilize and engage in equal or more specialty SUD and PTSD treatment relative to those with a single condition contrary our hypothesis. However, relatively few comorbid patients receive both SUD and PTSD care. Thus, among patients with comorbid SUD and PTSD, a comorbid diagnosis of PTSD does not appear to present a barrier to treatment of SUD, nor does a comorbid diagnosis of SUD present a barrier to PTSD treatment. However, our findings highlight the need for continued focus on increasing opportunity and access to receiving care for both PTSD and SUD among returning OEF/OIF veterans.

0629

THE EFFECT OF ALCOHOL USE ON UTILIZATION OF MENTAL AND PHYSICAL HEALTH SERVICES

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The goal of this study is to examine the utilization of mental and physical health services among alcohol users. The purpose of this is to understand if alcohol use affects an individual's desire to seek help from available services for concerns which may or may not be related to alcohol use. Data were collected from an anonymous online health survey which collects information on demographic depression, smoking, alcohol, and service utilization. There were 599 participants, 81.6% English speaking and 2.7% Spanish speaking, 5.5% Latino and 57.8% non-Latino individuals from 55 countries. Of these participants 68.6% are female, and 31.4% are male, 29.7% are single, 40.1% is married, with a mean age of 40, SD 16.5. Within this survey is a screening tool which measures for possible problems with alcohol called the CAGE questionnaire. Participants score on the CAGE ranged from 0 – 4 points; 52.3% of participants had a score of 0, 18% had a score of 1, 14.5% had a score of 2, 10% had a score of 3 and 4.2% had a score of 4. In the study a high score on the CAGE was a score of 2 and above, which was 28.7% of participants. In regards to finances the participants reported spending on average $21.12, SD 62 per week, and $1098.31 SD 3224.027 per year. In regards to web use related to alcohol. 92.5% of participants reported that they did not use the internet to search for information on alcohol use. 27.2% of participants said they would use online interventions if they had the information on these, 71.1% said they would not,. The data was analyzed using a Pearson correlation, there was no correlation found between a high score on the CAGE and utilization of health services r .044, p .305, and participant's health insurance r –.026, p .558 A correlation was found between a high score on the CAGE and a higher amount of visits to mental health providers .107,p .013, and a higher amount of visits to the participant's doctor or primary care in which participants discussed personal or emotional problems, including substance abuse r .169, p .002. In conclusion, this study shows that the web can be a useful way to gather data for future research. The data collected suggests that more information needs to be gathered on how alcohol affects use of mental health services.

0630

PEDIATRICIAN SCREENING FOR ADOLESCENT SUBSTANCE USE DISORDER RISKS

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The American Academy of Pediatrics (AAP) recommends that pediatric primary care providers (PPCPs) assess family and individual risk factors to engage in adolescent substance use disorder (SUD) prevention. AAP advises PPCPs to assess adolescent mental disorders [i.e., attention deficit hyperactivity disorder (ADHD), conduct disorder (CD) and major depressive disorder (MDD)], adolescent substance use, and parental substance use. We conducted a survey of PPCPs to determine attitudes and self-described practices regarding these risk factors. In this study, 35 PPCPs (69% MD pediatricians, 23% pediatric nurse practitioners, 8% others) were recruited through an established urban practice-based research network. Most PPCPs indicated they screened the majority of patients for ADHD (74% of PCPs), CD (60%) and MDD (57%) by age 12, and for cigarette (100%), alcohol (97%) and marijuana use (100%) by age 14. On the other hand, a substantial proportion viewed assessment of parental marijuana use as ''inappropriate'' (49%) and most (62%) ''never'' screened for parental marijuana use. Most PPCPs (63%) were interested or enthusiastic about substance screening and intervention with computer assisted tools. These results suggest that most PPCPs attitudes and practices are consonant with AAP recommendations for adolescent risks but not for parental risk factors. Programs to engage PPCPs in SUD prevention will need to address this obstacle. Computer administered assessment and intervention may provide a viable option for assisting PPCPs provide screening and preventive services. Supported by PA-HEAL SPH00010, R01AA016482 and P50DA05605.

0631

INCREASED UTILIZATION OF COMPUTED TOMOGRAPHY IS ASSOCIATED WITH ALCOHOL INTOXICATION IN PATIENTS ADMITTED TO A LEVEL I TRAUMA CENTER FOR ASSAULT

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Increased utilization of radiologic resources has been demonstrated in adult trauma patients presenting with alcohol-related injuries; however, few studies have evaluated this utilization for specific injury mechanisms. The purpose of this study was to evaluate the association between alcohol intoxication and the use of computed tomography (CT) for trauma patients admitted for assault-related injuries. We conducted a retrospective cohort study linking the trauma registry (2005–2009) of Harborview Medical Center (HMC),the only level I trauma center in northwest of the US, to HMC billing data which contained detailed information on all radiologic procedures performed for each patient. The primary exposure of interest was whether the patient was intoxicated, which was defined as a blood alcohol content (BAC) >80mg/dl. The main outcome of interest was the number of CTs per body region (head, pelvis, abdomen, thorax, lower and upper extremity, cervical spine, and maxillofacial). Negative binomial regression was used to evaluate whether the utilization rate of body region specific CT procedures was associated with intoxication status after adjusting for potential patient and injury related characteristics that could affect utilization rates. A total of 799 patients were admitted to HMC for assault related injuries from 2005–2009. Over 40% of assault-related injuries were in individuals who were intoxicated. In general alcohol intoxication was associated with increased utilization of CT (incidence rate ratio [IRR]: 1.24; 95% CI: 1.11–1.39) even after adjustment for the potential confounders of gender, mechanism of injury, injury severity score, ICU admission, length of hospitalization, final disposition, and year of admission. Pelvis (IRR: 1.42; 95% CI: 1.05–1.92), abdomen (IRR: 1.58; 95% CI: 1.16–2.15) and cervical spine (IRR: 1.40; 95% CI: 1.09–1.79) demonstrated increased utilization rates for intoxicated patients compared to non-intoxicated patients with assault-related injuries. Alcohol related assault injuries were found to be associated with increased utilization of radiologic procedures in a level I trauma center. These data suggest that alcohol related trauma injuries have a major impact on radiology departments and investigations to investigate there appropriateness are required.

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THE ALCOHOL AND OTHER DRUG TREATMENT WORKFORCE IN MASSACHUSETTS: PERSPECTIVE OF PROGRAM DIRECTORS AND CLINICAL STAFF ON WORK ENVIRONMENT

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Difficulties in recruiting and retaining counseling staff impact the quality of care that a treatment facility is able to deliver. Using data collected from 48 outpatient substance abuse treatment facilities in Massachusetts in 2011 this study provides an in-depth insight into the alcohol and other drug treatment workforce. The specific goal of this study is to determine the individual and facility factors that impact addiction treatment counselors' perceptions of their work environment. The research questions are: (1) How does perception of work environment vary at the individual counselor level, controlling for counselors nested within facilities? (2) How does perception of work environment vary across facilities, taking into consideration within-facility variation? Two survey instruments were developed for this study: a counselor-level work environment survey (CS) completed by the counseling staff (n=293) working within participating facilities and a facility-level workforce survey (FWS) completed by the Program Director at each facility (n=48). The CS instrument provides counselor demographics, education, employment history and current employment, workload, perception of work environment, feelings towards work, income, and overall impressions. The FWS provides facility/agency characteristics, range of services and service delivery information, staffing, and wage and benefits information. Facilities varied by type of ownership, services provided, and staffing. 54% of facilities offered regular or intensive outpatient services, 15% provided opioid treatment only, and 31% offered both. Among counselors, 74% are female, 80% have a master's degree, and 19% reported feeling burned out at least once a week. Hierarchical linear models were used to analyze within- and between-facility variation in counselor's attitudes and perceptions of their work environment. Preliminary findings indicate that counselor burnout is significantly related to counselor perception of work environment regardless of facility level differences. By focusing on counselors and their workplace, this research creates an opportunity to gain knowledge and insights about the counselors and the challenges they face as they seek to deliver quality care. Findings from this study can inform future workforce development policy in Massachusetts with implications for other states.

0633

EFFECTIVENESS OF INTEGRATED CHRONIC DISEASE MANAGEMENT FOR CO-OCCURRING SUBSTANCE DEPENDENCE AND MENTAL HEALTH DISORDERS IN A PRIMARY CARE SETTING

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Purpose: People with co-occurring addiction and mental disorders typically have worse outcomes than those with a single disorder alone. Given the majority of those with mental disorders are seen exclusively in primary care, an intervention that integrates addiction and mental health care in a primary care setting may be more effective and reach more patients. We performed secondary subgroup analyses of a randomized clinical trial to study the effect of integrated chronic disease management (CDM) on substance use and mental health outcomes among people with substance dependence (SD) and 1) major depressive disorder (MDD) and 2) post-traumatic stress disorder (PTSD).
Methods: Subjects were adults with alcohol and/or drug dependence recruited from a detoxification unit, a medical center or from advertisements. CDM was provided by a nurse care manager, social worker, internist and psychiatrist. The control group was given a primary care appointment but no access to CDM. Outcomes (past 3 months assessed at 3, 6, and 12 months) were 1) abstinence from opioids, stimulants or heavy drinking; 2) depressive symptoms (Patient Health Questionnaire [PHQ-9]); and 3) anxiety symptoms (Beck Anxiety Inventory [BAI]). Randomized groups were compared using longitudinal regression models adjusted for the following baseline characteristics: race, gender, baseline dependence, outpatient addiction treatment, depression, anxiety, and lifetime injection drug use.
Results: Of 553 subjects with SD, 435 (79%) met diagnostic criteria for MDD and 204 subjects (37%) for PTSD at baseline. No significant effect of CDM was observed for any outcome: 1) abstinence from opioids, stimulants or heavy drinking in those with MDD (adjusted odds ratio [AOR]=0.88; 95%CI 0.65–1.19; p=0.40) or PTSD (AOR=1.17; 95%CI 0.71–1.92; p=0.55); 2) fewer depressive symptoms in those with MDD (AOR=1.00; 95%CI 0.75–1.33; p=0.99) or PTSD (AOR=0.99; 95%CI 0.64–1.51; p=0.94); or fewer anxiety symptoms in those with MDD (AOR=1.01; 95%CI 0.76–1.36; p=0.92) or PTSD (AOR=1.13; 95%CI 0.73–1.77; p=0.58).
Conclusions: Although an integrated approach to care for people with co-occurring disorders may hold promise, it was not more effective for improving substance use, depression or anxiety than usual separate care in this study. A larger study exploring different sub-populations may be needed in order to determine whether and what kind of integrated care is an effective approach for people with co-occurring disorders.

0634

IN AN AGE OF PARITY AND HEALTH REFORM: ORGANIZATION AND BENEFITS FOR ALCOHOL AND OTHER DRUG SERVICES IN PRIVATE HEALTH PLANS

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Health plan decisions can directly influence patients' access to care and cost and quality of care. Rapid changes in the healthcare system, most recently the federal parity law and national healthcare reform legislation, require significant changes to health insurance for alcohol and other drug (AOD) services. Health plans face many decisions regarding their services and organization in responding to this changed environment. We present findings from the third round of a nationally representative, in-depth survey of health plan executives, previously conducted in 1999 and 2003. The 2010 telephone survey (n = 389 health plans, 939 products, 89% response rate) included an administrative module addressing plan characteristics, contracting arrangements, AOD benefit design, cost-sharing, network management and provider payment and a clinical module addressing wellness programs, treatment of AOD conditions in primary care, entry into specialty AOD care, disease and care management, delivery of specialty AOD care, and quality measurement to provide a current picture of the delivery and management of AOD services. Each plan was asked about its top three commercial products. The 2010 survey captures pre-parity (2009) and post-parity (2010) benefit years. Coverage of AOD services was generally very high and showed little change between 2003 and 2010. However, residential treatment services remain less likely to be covered. Additionally, disease management programs for alcohol problems are less likely to be offered than disease management programs for depression and chronic medical conditions. In 2003, prior authorization was required by the vast majority of products to access most AOD services, except by only 58% for outpatient AOD treatment. In 2010, many plans no longer require prior authorization for AOD services and may use other approaches to manage services. The use of technology in AOD treatment services has increased. In 2010, online counseling was offered to 60% of health plan enrollees while more than 70% of products offered online personalized response to questions or problems. Important changes occurred in the organization and delivery of AOD services since 2003. Findings indicate products cover the majority of AOD treatment services and no longer require prior authorization.

0635

ORGANIZATIONAL COMMITMENT TO THE USE OF MEDICATIONS FOR THE TREATMENT OF AUDS: UPDATED DATA FROM THE US SPECIALTY TREATMENT SYSTEM (2009–2011)

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Despite the priority place on improving the quality of substance use disorder (SUD) treatment by federal agencies, a research-to-practice gap persists with limited use of medications for the treatment of alcohol use disorders (AUDs). This study provides updated data on the availability of AUD medications from an ongoing national study of privately funded treatment programs. Data were collected via face-to-face interviews with administrators of 292 SUD treatment programs from 2009–2011. Organizational commitment to the use of AUD medications was measured by a count variable that summed the number of AUD medications prescribed by treatment programs. Results showed that a majority of programs (56%) did not prescribe any AUD medications, 13% prescribed a single AUD medication, 16% prescribed two medications, 9% prescribed three AUD medications and 6% of programs prescribed all four medications. The most commonly prescribed AUD medication was acamprosate (34%), followed by tablet naltrexone (28%), disulfiram (22%), and injectable naltrexone (14%). Compared to data from 2007–2008, there was a small decrease in the availability of disulfiram, tablet naltrexone, and injectable naltrexone and a small increase in the use of acamprosate. Consistent with prior research, several organizational characteristics were associated with organizational commitment to the use of AUD medications. Results of negative binomial regression showed that location in a hospital setting, program size, access to a staff physician, and percentage of patients covered by private insurance were positively associated with the expected number of AUD medications prescribed, while for-profit status and percentage of referrals from the criminal justice system were negatively associated with the expected number of AUD medications prescribed. Our findings revealed a relatively flat rate of AUD medication adoption in privately funded SUD treatment programs, indicating that the research-to-practice gap remains significant. Results also suggest that program funding and access to medical resources including staff physicians continue to play a key role in organizational commitment to implementation of AUD medications and lack of coverage of AUD medications in criminal justice contracts remains a key barrier to wider implementation of AUD medications.

0636

ACCESS TO ADDICTION PHARMACOTHERAPY IN PRIVATE HEALTH PLANS

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Advances in pharmacotherapy for addiction continue; an increasing number of medications now are available to treat alcohol and opiate addictions. To understand access to addiction medications, it is essential to consider the role private health plans and pharmacy benefit managers may exert through benefit design. To contain escalating prescription expenditures, health plans often use cost-sharing and administrative controls, which may impact physicians' prescribing and patients' use of addiction medications. In 2003, coverage exclusions and assignment to the highest cost-sharing tier were common for buprenorphine, the newest addiction medication at the time. The purpose of this study was to explore health plans' current approaches to benefit design with a focus on the most recently available addiction medications. Understanding the facilitators or barriers to addiction medications is essential because medication-based approaches to addiction are a widely endorsed evidence-based practice. We used 2010 data from a nationally representative survey of private health plans (n = 385 health plans, 925 products; Response rate: 89%) to examine plans' management of naltrexone, extended-release naltrexone, acamprosate, and suboxone. We further considered how health plans encourage use of pharmacotherapy for alcohol and opiate dependence. 96% of products covered extended-release naltrexone, and of those, 50% considered it part of the medical benefit rather than the pharmacy benefit. Other addiction medications were commonly covered (acamprosate 91%, naltrexone 99% and suboxone 100%). Prior authorization was common for only for extended-release naltrexone and rare for other medications. Extended-release naltrexone and acamprosate were usually on the most expensive payment tier in terms of patient cost sharing. Health plans used a variety of ways to encourage addiction pharmacotherapy including providing feedback to providers and offering financial incentives. In addition plans used coverage and cost-sharing mechanisms that may affect access to addiction medications. Exclusions and placement on higher cost-sharing tiers were common and may lead to restricted access to effective treatment options for addiction.

0637

COST OF CO-MORBID MAJOR DEPRESSIVE DISORDER AND ALCOHOL DEPENDENCE AMONG PATIENTS COVERED BY PRIVATE INSURANCE OR MEDICAID

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It is estimated that approximately 11% of patients with major depressive disorder (MDD) in the US that are over age 18 also have co-morbid alcohol dependence. The literature characterizing this patient population is limited. The objective of this study is to describe healthcare costs among MDD/alcohol dependence co-morbid patients in US population covered by private insurance or Medicaid as compared to a general MDD population and alcohol dependence population.
Cases for this retrospective study were drawn from a managed care administrative claims databases (Thomson MarketScan®). Three patient diagnostic groups were compared: patients with at least one coded diagnosis of 1) MDD *and* alcohol dependence, 2) MDD alone, and 3) alcohol dependence alone. From the privately insured Commercial and Encounter databases, sample sizes drawn between August 1, 2009 to September 30, 2010 were as follows: n=4,443 for MDD/alcohol dependence co-morbid, n= 225,918 for MDD only, and n=17,201 for alcohol dependence only. Patients were required to have at least 1 year of continuous pharmaceutical and medical benefit enrollment during the study period. From the Medicaid database in 2009 sample sizes were as follows: n=1,022 for MDD/alcohol dependence co-morbid, n= 27,917 for MDD alone, and n=3,496 for alcohol dependence alone. Annualized healthcare costs were calculated as reimbursements to providers for medical services and prescription drugs.
In this retrospective analysis, the MDD/alcohol dependence co-morbid patients had higher healthcare costs than patients diagnosed with MDD alone or alcohol dependence alone. Among the privately insured patients, the mean annual total direct healthcare cost were $34,405 for MDD/alcohol dependence co-morbid patients, $18,464 for MDD only patients, and $19,613 for alcohol dependence only patients. The same trend is observed among Medicaid patients (mean annual total direct healthcare cost: $37,288 for MDD/alcohol dependence co-morbid, $21,116 for MDD alone, and $23,133 for alcohol dependence alone).
Mean annual per-patient healthcare costs for MDD/alcohol dependence co-morbid patients were nearly 2-fold higher than among patients with MDD alone or alcohol dependence alone. This pattern of higher economic burden in the MDD/alcohol dependence co-morbid condition suggests that targeted interventions for this specific co-morbid population may be warranted.

13. QUANTITATIVE / COMPUTER METHODS 316–321 / 638–643

0638

A COMPARISON OF SEVEN BRAC ESTIMATION METHODS UTILIZING TRANSDERMAL ALCOHOL SENSOR, BREATH ANALYZER, AND DRINKING DIARY DATA FROM REAL-TIME DRINKING EPISODES

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We evaluated the performance of BrAC estimation methods that utilized various combinations of three types of real-time data collection methods: 1) transdermal alcohol sensor (TAS) data, 2) breath analyzer data, and 3) detailed drinking diary. Seven estimation methods were used: 1) breath analyzer data (“Raw BrAC”); 2) breath analyzer data fit to a spline-based curve (“Spline BrAC”); 3) raw TAC data produced by the WrisTAS™ 7 device (TAC BrAC); 4) BrAC Estimator software, a first principles mathematical model MATLAB code that creates individualized models of TAC data from a calibration session (“Est BrAC”); 5) BrAC Estimator software further tuned with breath analyzer data (“Cal BrAC”); 6) drinking diary model by Matthews and Miller (1979; “DD BAC”); and 7) drinking diary model adjusted to include percent alcohol in the drinks (“DD-PA BAC”). The fits of three BrAC-curve-based statistics: 1) peak BrAC, 2) time of peak BrAC, and 3) area under the BrAC curve, were compared using absolute and relative differences to assess relative performances of these BrAC estimation methods. We analyzed data from 11 drinking episodes collected by a single subject. For all three BrAC measures, the Cal BrAC estimation method did the best; this is not surprising since this approach uses the most available data. Among the other methods, the TAC BrAC method provided the next best estimate of peak BrAC, but a less accurate estimate of the area under the BrAC curve; it yielded a poor estimate of the time of peak BrAC. The two drinking diary methods were good at capturing the time of peak BrAC, but they were poorest at estimating the area under the BrAC curves. The Est BrAC software method did almost as well as the Cal BrAC method at estimating the time of peak BrAC and although it was not as accurate as Cal BrAC at estimating the area underneath the BrAC curves, it was considerably better than the other methods in this regard. Across drinking episodes, the fit of the Est BrAC models was affected more by the shape of the drinking curve than by the level of peak BrAC or stomach content. Given the increased accuracy in BrAC estimates from the BrAC Estimator software program and the low real-time subject burden, this software program appears to be an effective way to improve real-time BrAC estimates compared with other BrAC estimation methods. This research was funded by grants from the Alcoholic Beverage Medical Research Foundation and NIH (K08 AA14265, R01 AA11257, R21 AA17711).

0639

TIMELINE FOLLOW “BACK TO THE FUTURE:” THE USE OF WEB-BASED TECHNOLOGY IN THE ASSESSMENT OF ALCOHOL DRINKING AND CIGARETTE SMOKING BEHAVIORS

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The Timeline Followback (TLFB) is the gold standard in the retrospective assessment of daily drinking or smoking patterns. However, its administration by in-person or telephone interview is both time intensive and resource consuming. While the use of internet technology in research is growing, it is unknown whether the TLFB could be reliable in a web-based self-administered format. Thus, the goal of the current investigation was to test the psychometric properties of a self-administered web-based version of the TLFB against a previously validated telephone interview version of the TLFB.
The study used a within-subjects design to compare estimates of daily drinking and smoking behaviors obtained by a self-administered web-based version of the TLFB for the previous 4 weeks. The sample consisted of 120 nonalcoholic young adults (65 men) who were regular consumers of alcohol and cigarettes. Participants completed both the validated telephone version as well as the newly developed web-based version of the TLFB, and did so with 3 to 7 days time between the two surveys to minimize any practice effects. They also completed the Alcohol Use Disorder Identification Test (AUDIT) and Fagerström Test of Nicotine Dependence (FTND), which were used as secondary validation measures.
Results indicated that the correlations between the telephone and web-based TLFB were high for total drinking days, binge episodes and total number of drinks consumed in a 4-week period (aggregate estimates of *r*s ranged from .83 to .93). Similarly, correlations for aggregate estimates were also high for smoking days, heavy smoking days (10+ cigarettes/day), total cigarettes smoked over the 4 weeks as well as co-use (alcohol drinking and cigarette smoking) days, ranging from .90 to .95. Estimates from the online TLFB also correlated significantly with scores from the AUDIT and FTND (r=.32 and r=.69 respectively).
Overall, the current study shows that the future has arrived for the web-based TLFB. The results demonstrate strong support is use to capture concurrent reports of drinking and smoking behaviors in research designs such as longitudinal studies with multiple follow-up assessments or large-scale epidemiological studies.

0640

QUADRATIC GROWTH MIXTURE MODELING: IMPACT OF MODEL MISSPECIFICATION

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Studies of alcohol outcomes from intervention programs often collect data at several time points. Growth mixture modeling (GMM; Muthén, 2001a, 2001b) is a useful longitudinal data analytic technique for alcohol and drug intervention research due to its ability to examine heterogeneity in change. The present study examined the impact of model misspecification, especially involving a quadratic slope term, in GMM through a Monte Carlo (MC) simulation study. Many extant GMM studies assume linear growth trajectories even when nonlinear growth trajectories are suspected, and the present study examined this misspecification. One common approach to modeling nonlinearity is to add polynomial terms of a time variable. Specifically, if we add the squared term of the time variable, quadratic growth trajectories are tested. When a quadratic slope indeed exists (i.e., when it is statistically significant), model misspecification (i.e., omitting the quadratic slope) may result in misclassification and consequently misinterpretation of data. For this MC study, data sets were generated using quadratic GMM with various model settings, and those simulated data sets were estimated using both linear and quadratic GMMs. Class enumeration (counting the correctly specified models) was then performed with respect to two perspectives: (1) general performance of information criteria, such as BIC, across estimation difference (correct specification vs. misspecification) under crossed conditions of factors (e.g., missingness, class separation, number of indicators, and sample size), and (2) impact of each individual factor while holding the other factors constant. The results showed that linear GMM underestimated the true number of latent classes when BIC, the most recommended IC in mixture models was used. However, when the sample size adjusted BIC (Sclove, 1987) was used, that underestimation problem was quite mitigated. The present study further examined sample size requirements for the accurate estimation of quadratic as well as linear GMMs. The required sample sizes were quite comparable for linear and quadratic GMMs, even though quadratic GMM has been thought to be more complex than linear GMM. In sum, specifying a quadratic growth term in mixture models does not cost much in terms of sample size while it results in more correct classification. Therefore, the inclusion of a quadratic term should be considered, whenever feasible, with the use of GMM.
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0641

A NONLINEAR STATISTICAL MODEL FOR MEDICATION AND PLACEBO EFFECTS
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Background: It can be difficult to detect the usually modest effects of psychotropic medications against the background of placebo, motivational, and other effects on outcome. Current statistical methods for medication outcome data, however, are badly mis-specified and frequently yield inconsistent results. Creating a better-specified model involves representing mathematically the key processes that affect outcome.
Methods: A novel nonlinear statistical model was developed using a one-parameter moving average sub-model to represent the underlying time course of key model components, including medication effects, placebo effects, and behavioral treatment effects. The model takes medication compliance into account. The model was tested on a random half-sample of Project COMBINE data (N=524), and replicated on the other half-sample, using number of drinks per week as the dependent variable.
Results: The nonlinear model explains 93% of the variation in alcohol consumption in the developmental sample, and 48% of the variance in the replication sample, using fewer parameters than the linear model. In contrast, a classical linear model applied to the same data accounts for only 6% of the variance. Significant naltrexone (p<.0001), acamprosate (p<.0001), and placebo (p=.0164) effects were detected, though effect sizes were modest. The model allows the calculation of an analog of the half-life of intervention effects, which is useful in understanding the dynamics underlying treatment outcome over time.
Conclusions: The nonlinear model accounts for a high proportion of variance, and replicates well. It offers more power than linear models for detecting intervention effects, though because it uses post-randomization information it would not be used as an intent-to-treat analysis. While the initial model development was done using an alcohol treatment study, the model could be applied to many psychotropic medications. Much work remains to be done to improve the model, and to explore the multiple possible pathways by which interventions affect long-term treatment outcome.

0642

MODELING LONGITUDINAL POST-TREATMENT CLIENT OUTCOMES FROM OPEN-ENROLLMENT THERAPY GROUPS
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In studies of group therapy interventions delivered in alcohol and other drug (AOD) treatment settings, primary client-level outcomes such as AOD use are frequently measured following group therapy. We present an analytic approach that accounts for the complex correlation structure of client post-treatment outcomes induced by open enrollment. We employ multiple membership (MM) modeling to link the effect of each session attended by a client to his/her outcomes. Under standard MM, post-treatment outcomes are modeled using conditionally independent random session effects. We combine MM with conditional autoregression (CAR) to relax this assumption, allowing the analytic model to better reflect the overlap in client attendance session-to-session. We also employ longitudinal growth modeling, under which the posterior distribution of growth parameters is estimated using a non-parametric approach that overcomes parameter identification limitations of standard parametric growth models. We demonstrate these methods in the context of an intervention to deliver group cognitive behavioral therapy to clients with depressive symptoms who are enrolled in residential alcohol and other drug treatment. We find that MM modeling, with or without correlated session effects, improves upon models that ignore client session attendance with respect to model fit statistics. MM-CAR produces a modest improvement in model fit but provides sharper visualization of session effects. Nonparametric modeling of growth parameters results in improved model fit and greater flexibility to capture the scope of change over time in client outcomes. Our approach provides a way to account for correlation of client post-treatment outcomes due to open-enrollment into group therapy and to address researchers' concerns about the robustness of the statistical significance of treatment effect estimates given the correlation of outcomes among clients attending open-enrollment therapy groups.

0643

SCORING OF COLLEGE STUDENTS' ALCOHOL EXPECTANCIES USING ITEM RESPONSE THEORY ANALYSIS ACROSS STUDIES AND TIME
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The present study was aimed at developing latent alcohol expectancy scores across multiple studies and time as part of Project INTEGRATE. The development of latent trait scores that are based on a common, standard metric across multiple studies is one of the more critical challenges of integrative data analysis (IDA). IDA utilizes recent advances in research methodology and computing technology and benefits from data sharing to overcome limitations of single studies and generate new knowledge. Project INTEGRATE utilizes this IDA approach to examine mechanisms of change for the efficacy of brief alcohol interventions for college students (22 studies, $N = 24{,}387$). In the original studies, alcohol expectancies and drinking motives were assessed using the Alcohol Expectancies Questionnaire (AEQ), the Comprehensive Effect of Alcohol (CEOA), Expectancy/Context Questionnaire (ECQ), Drinking Motives Questionnaire (DMQ), Athlete Drinking Scale (ADS), and other items. We matched items that were similarly or identically worded, dichotomized item responses, and conceptually derived four distinct dimensions: Social enhancement, tension reduction, negative alcohol expectancies, and drinking motives. Although 17 out of the 22 studies assessed alcohol expectancies or drinking motives, the item overlap across studies was rather minimal. Thus, we combined a few items to provide a link across studies. A total of 122 items at baseline were calibrated separately for each dimension using a two-parameter logistic item response theory analysis (2-PL IRT). We developed a Markov chain Monte Carlo algorithm to efficiently calibrate a large number of item, as well as model, parameters for the four dimensions simultaneously for this large data set. Different latent mean values across the studies were estimated but the correlational structure of the four dimensions was assumed to be the same across the studies. We correlated these new latent trait scores with original alcohol expectancies/drinking motives scale scores and typical weekly drinking in the past month. The new scores were highly correlated with original scale scores (.6–.8), and moderately correlated with drinking (.2–.4). Using the calibrated item parameters at baseline, we then computed latent trait scores for longitudinal data. The results demonstrate that even for a highly sparse, large data set, IRT can provide reasonable estimates, which is encouraging for an IDA approach to existing data. Funded by R01 AA 019511.

TUESDAY – Posters 1–321 / Abstracts 644–964
1. GENETICS
a. Human **1–18/644–661**
b. Lab animal – transgenics/knock-outs/inc **19–32/662–675**

0644

CHRM2 AND GABRA2 GENOTYPES INFLUENCE ACTIVATION DURING A RESPONSE INHIBITION FMRI TASK IN HIGH-RISK ADOLESCENTS
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The GABRA2 SNP rs279871 has been associated with fMRI response to alcohol cues in areas thought to code reward value (Kareken et al. 2010) and higher the risk of substance use and conduct disorders across the lifespan (Dick et al. 2006). Additionally, the CHRM2 SNP rs1455858 has been associated with alcohol, drug, and affective disorders (Luo et al. 2005) greater disinhibition and substance use in adolescents (Hendershot et al. 2011). To further assess the association between these genotypes, risk behavior, and brain-based intermediate phenotypes, 175 participants were recruited from a juvenile justice diversion program. Participants completed the Rutgers Alcohol Problem Index (RAPI), DNA collection, and an fMRI assessment. During the fMRI, participants took part in a Go/No-Go Task in which they were instructed to respond to the target stimulus 'X' (.80 probability) appeared and not to respond to the 'K' (.20 probability). A correct response to a Go event is a Hit and a correct inhibition of response to a No-Go event is a Correct Reject. To evaluate response inhibition, we examined Correct Rejects vs. Hits. The GABRA2 SNP rs279871 was not significantly correlated with RAPI scores in this sample of high-risk adolescents. However, the fMRI analyses revealed that GABRA2 rs279871 is significantly correlated with activation during response inhibition. Those with more genetic risk (more A alleles) show less activation during the task than those with less genetic risk. The significant activation difference ($p < .001$, FDR corrected) was located in the right parahippocampal gyrus and right precuneus, regions associated with self monitoring and attention. Furthermore, the risk allele of the CHRM2 SNP rs1455858 was significantly positively correlated with RAPI scores ($r = .222$, $p = .003$) in our sample. The fMRI analyses also revealed that CHRM2 rs1455858 was positively correlated with activation during response inhibition. Those with higher genetic risk (more A alleles) show less activation than those with less genetic risk. The significant activation difference ($p < .001$, FDR corrected) was located in the left and right superior frontal gyrus, regions associated with cognitive control. These findings suggest that risk alleles in the GABRA2 and CHRM2 genes are associated with lower ability to inhibit prepotent responses and therefore might contribute to increased risk taking and alcohol consumption in adolescents.

0645

INFLUENCE OF *GABRA2* ON TRAJECTORIES OF ALCOHOL USE FROM ADOLESCENCE TO EARLY ADULTHOOD

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The goal of this study was to identify the effect of the gamma-aminobutyric acid receptor subunit alpha-2 gene (*GABRA2*) on trajectories of alcohol use from adolescence to early adulthood. Previous studies on the effect of *GABRA2* have mostly employed cross-sectional designs using adult samples. Given evidence that the effect of *GABRA2* varies over time, cross-sectional designs are limited in their ability to examine the dynamic nature *GABRA2* genetic effects. In this study, the effect of *GABRA2* on trajectories of alcohol use behaviors was examined using longitudinal data from the Collaborative Study on the Genetics of Alcoholism (COGA) on individuals assessed at multiple time points between 12 and 25 years. Specifically, the focus was on the differential effect of *GABRA2* on trajectories of alcohol use in adolescence (younger than 19 years) and in early adulthood (equal or older than age 19), as well as genotypic effects on the change of alcohol use between adolescence and adulthood. Piecewise linear growth curve models, which can incorporate different growth trajectories across different periods of time, were fit to the data. After adjusting for multiple testing, the most consistent finding was a significant difference by *GABRA2* genotype on the change in alcohol use between age 18 and 19. Individuals who carried the genotype previously associated with adult alcohol dependence in COGA showed a greater increase in alcohol use and drunkenness in the transition from adolescence to young adulthood. The effect of *GABRA2* on the change in alcohol use between age 18 and 19 may reflect an interaction between *GABRA2* and the many environmental changes that accompany the increasing independence associated with the transition from adolescence to adulthood. This study also illustrates the importance of using a longitudinal perspective to better understand genotype effects on the etiology of alcohol problems.

0646

SUBJECTIVE RESPONSES TO CLAMPED ALCOHOL INTOXICATION AS A FUNCTION OF FAMILY HISTORY AND GABA-RELATED GENOTYPES

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Background: Subjective responses to alcohol intoxication have long been believed to influence whether, how much, and how often a person chooses to drink, and thus play a role in the development of problem drinking. In the present study, intravenous (IV) administration of ethanol (EtOH) was used to maintain blood alcohol concentration at 60 mg%, eliminating the substantial variability in blood alcohol concentration that follows oral alcohol administration. Subjective responses to alcohol intoxication were then examined as a function of a family history of alcoholism (FHA), and of genes encoding GABA receptor subunit expression (*GABRA2*, *GABRG1*).
Methods: One hundred and fourteen heavier drinking male and female non-dependent drinkers (4.71 drinks/drinking day, ages 21–27) rated their perception of alcohol intoxication on a continuous scale assessing 9 dimensions (anxiety; desire for more or less alcohol; intensity of that desire; perceived number of drinks, enjoyment, intoxication; relaxation; stimulation; and tiredness). Ratings were obtained twice at each of 3 time periods: at baseline; during the initial block of the alcohol clamp (at approximately 5 and 30 minutes after a stable clamp was achieved); and during the terminal block of the clamp (at approximately 2.5 and 3 hours after a stable clamp was achieved). Subjective perceptions were assessed as a function of gender, FHA, recent drinking history, and *GABRG1* (rs2350439) and *GABRA2* (rs279871) genotypes. Effects were quantified as both initial responses (departure from baseline perceptions) and adaptive responses (change from initial response after 3 hours at the clamped target concentration).
Results: Initial responses to alcohol were unrelated to either FHA or GABA genotypes. Adaptive responses to alcohol displayed a trend toward influence by *GABRG1* genotype, with AA genotypes (n=21) showing a consistent pattern of greater tolerance on almost all measures as compared to AG (n=55) or GG (n=28) genotypes. This trend reached significance only for stimulation (p<.03).
Conclusions: *GABRG1* genotype appears to affect tolerance (adaptive responses) to alcohol intoxication, highlighting the importance of this gene as a potential factor in alcoholism risk.
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0647

GABRG1 MARKERS MODERATE AMPHETAMINE-INDUCED STRIATAL DOPAMINE RELEASE

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Risk of alcohol dependence (AD) has a substantial genetic component. Alcohol exerts many of its effects via interactions with gamma-aminobutyric acid (GABA) receptors, which populate limbic and reward-related areas and help regulate mesolimbic dopamine (DA) neurotransmission. AD is associated with markers in the $GABA_A$ γ-1 receptor subunit gene (GABRG1) and the intergenic region 5'GABRG1-3'GABRA2. However, research has yet to show an association between these polymorphisms and human brain's reward system function. The rewarding effects of most drugs of abuse are via enhancement of mesocorticolimbic DA neurotransmission. PET imaging has demonstrated that amphetamine (AMPH) increases mesolimbic DA concentrations. Given that the mesolimbic system is a mediator of drug reward, it is important to understand the genetic factors that modulate its function. Therefore, we determined if DA responses to AMPH is related to variation in $GABA_A$-receptor subunit genes.
Methods: 86 healthy social drinkers [57% males, 70% Caucasian, 22.9 yrs (SD=3.2)] completed two positron emission tomography (PET) scans with high-specific activity [^{11}C] raclopride. The first scan was preceded by intravenous (i.v.) saline and the second by AMPH. The major outcomes were: Baseline global striatal DA binding potential (BP) following i.v. saline and AMPH-induced striatal DA release. Genotype effects were analyzed using linear regression analysis model, controlling for gender. Ancestry was estimated by the Structure software and was adjusted for in the association analyses. We applied a Bonferroni correction for Type I error.
Results: Baseline global striatal DA BP: carriers of the minor allele for a single nucleotide polymorphisms (SNP) in the GABRG1 region demonstrated on average significantly higher baseline BP (rs993677 p=0.010) compared to those homozygous for the common allele. AMPH-induced striatal DA release: carriers of the minor allele for SNPs in the GABRG1 gene and intergenic region 5'GABRG1-3'GABRA2 showed on average lower DA release compared to those homozygous for the common allele (rs1497577 p=0.002; rs488447 p=0.010; rs479277 p=0.007).
Conclusion: Our results suggest that the proposed variations modulate AMPH induced striatal DA release and thus may affect the rewarding effects of drugs of abuse, including alcohol. Consistently, carriers of the minor allele for SNP rs1497577 (GABRG1) have been associated with AD. [Supported by NIH grants AA017466 (M Uhart), AA10158 (GS Wand)]

0648

ACUTE SENSITIVITY AND ADAPTATION TO ALCHOL ASSOCIATED WITH FAMILY HISTORY OF ALCOHOLISM AND *GABRG1* GENETIC STATUS USING THE STOP SIGNAL TASK

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Introduction: Genetic polymorphisms associated with GABA receptor subunits are associated with increased risk for alcohol abuse and dependence; however, there lacks a clear understanding of the underlying mechanisms. While an effect on fast EEG has been associated with *GABRA2*, generally little electrophysiological data has been reported in relation to either *GABRA2* or *GABRG1*. More specifically, how such polymorphisms are related to brain activity during behavioral inhibition—a construct also related to alcoholism risk—has yet to be examined.
Methods: For this study, 119 young non-dependent drinkers, aged 21–27 participated; 59 with positive and 60 with negative biological family history of alcoholism (FHA). Subjects were genotyped for a single nucleotide polymorphism rs2350439 in *GABRG1*. Of the participants genotyped, 28 were GG, 20 were AA, and 52 were heterozygous. Subjects participated in a placebo controlled 60mg% intravenous alcohol clamp. Two 4.5 minute blocks of a stop signal task (SST) were conducted at 3 times during each session; at baseline prior to the infusion, after initial exposure 15 minutes following establishment of the clamp, and after maintenance of the clamp for 3 hours. Data was collected for 64 monopolar scalp leads, with preliminary analyses limited to lead CPZ. Data was concatenated for each block, filtered, and epoched with a window of −200 ms to 800 ms. ERPs were generated for all 'Go' trials and all 'Stop' trials (trials requiring subjects to withdraw their prepotent 'Go' response). Peak amplitude differences were derived by subtracting the P300 amplitude of all 'Stop' trials from that of all 'Go' trials and tested for differences between FHA and *GABRG1*.
Results: Family history positive (FHP) subjects had lower peak amplitude differences than family history negative (FHN) subjects across all time points. Peak amplitude in FHN, but not FHP subjects, exhibited a return to baseline during the final block, demonstrating tolerance to the effects of ethanol. The electrophysiological response in *GABRG1* GG homozygotes was acutely sensitive to the effects of EtOH— a response not observed in individuals with other genotypes.
Conclusions: FHA and *GABRG1* alter ERPs generated by behavioral inhibition both during baseline, as well as a function of alcohol intoxication. This suggests that a genetic proclivity for alcoholism alters brain mechanisms involved in inhibiting behavior. Supported by P60 AA007611 and UL1RR025761.

0649

GABRA2 AND THE EXTERNALIZING SPECTRUM IN ADOLESCENCE

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Externalizing disorders (e.g. attention-deficit hyperactivity disorder (ADHD), conduct disorder (CD), and substance use disorders (SUD)) are highly comorbid. Although some studies have found evidence for a one-factor model of these disorders (e.g. Krueger, 1999), others have found a two-factor model (Farmer et al., 2009) in which SUD and CD share a common liability that is unique from that of ADHD. The current study tested this two-factor model in adolescence against one- and three-factor models. Moreover, evidence suggests that a single latent factor including SUD and CD is heritable and that the GABRA2 gene confers risk for both (Hicks et al., 2004; Kendler et al., 2003; Dick et al., 2006) whereas no studies have shown a relation between GABRA2 and ADHD. The current study tested whether a SNP in the GABRA2 gene (rs279858) significantly predicted substance experimentation (SE) and CD but not ADHD.

Participants were from a larger longitudinal study of parent alcoholism risk (N=302, ages 12–18 years) and were either non-Hispanic Caucasian or Hispanic. ADHD and CD symptoms were measured with the CBCL. Substance experimentation (SE) assessed whether the adolescent got drunk and used 8 other drugs in the past year. Measures at each of 3 annual assessments were used as indicators of ADHD, CD, and SE. Ethnicity was not correlated with genotype. Confirmatory factor analyses showed that the three-factor model, with SE, CD, and ADHD on separate factors, was the best fit (χ^2=29.694, df=21, p=0.098; RMSEA=0.037; CFI=0.989; WRMR=0.684). Structural equation models controlling for age, gender, and parent alcoholism showed that those with the AA genotype reported more SE compared to those with the AG (*B*=–0.431, *p*=.047) and GG (*B*=–0.774, *p*=.028) genotypes but the AG and GG groups did not differ in SE. Findings were similar for alcohol and illegal drugs tested separately (marginally significant for alcohol and significant for illegal drugs). Genotype did not significantly predict the ADHD or CD factors. These findings suggest that, in adolescence, ADHD, SE, and CD are correlated but have some distinct underlying vulnerabilities, including those associated with the rs279858 SNP of GABRA2. These findings highlight the etiological differences among externalizing disorders in adolescence and suggest that biological mechanisms may contribute to these differences.

0650

GENETIC VARIATION IN HTR2A AND PTPRB ARE ASSOCIATED WITH ALCOHOL DEPENDENCE AND WHITE MATTER INTEGRITY IN THE POSTERIOR THALAMIC RADIATA

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The etiology of alcohol use disorders is known to involve both neurobiological and genetic factors. Compromised integrity of white matter connectivity represents one neurobiological risk factor that has been linked to alcoholism. We undertook a preliminary genomewide association study (GWAS) of genetic variants associated with compromised white matter integrity in a sample of heavy drinkers (n = 249). Integrity of white matter was assessed using fractional anisotropy (FA). DNA was obtained from saliva samples and analyzed using the Illumina Human 1M Duo DNA Analysis BeadChip. The most significant associations with white matter integrity in the posterior thalamic radiata (PTR) came from 2 genes, *HTR2A* and *PTPRB*. In *HTR2A*, 3 single nucleotide polymorphisms (SNPs), rs1745837, rs622337 and rs655854, were significant at p<.0001. In *PTPRB* the top significant SNPs (p<.0001) were rs17814313, rs3752702, and rs919594. We attempted to replicate our top findings for *HTR2A* and *PTPRB* in the Study of Addiction: Genetics and Environment (SAGE) sample of individuals with substance dependence (n = 3,838). In the SAGE sample, we examined four *HTR2A* SNPs falling within 2,000 bases of the strongest *HTR2A* signal from our initial analysis, for an association with alcohol dependence symptom count. Correcting for multiple tests, one SNP in this range demonstrated a significant association with alcohol dependence (rs1923886, p=.012). In the SAGE sample, two PTPRB SNPs which were found to be significant in our initial analysis also demonstrated a significant association with alcohol dependence (rs3752702, p=.031; rs919594, p=.023). These findings suggest that both *HTR2A* and *PTPRB* are related to alcohol dependence and are associated with compromised white matter integrity in the posterior thalamic radiata.

0651

WHOLE GENOME SCREEN OF COPY NUMBER VARIATION: AN INVESTIGATION OF GENE DOSAGE AFFECTS ASSOCIATED WITH ALCOHOLISM

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To determine if copy number variation in the genome may be associated with alcoholism risk a pilot arrayCGH study was conducted on 54 males comprised of alcoholics and controls provided by the Collaborative Studies of Genetics of Alcoholism (COGA). DNA samples from individuals were run on custom whole genome Agilent 2x400k arrays. While several candidate genes were identified, the gene dosage finding most strongly associated with alcoholic individuals was the loss of copy number in PDE4DIP. This gene interacts with PDE4D, a regulator of cAMP and PKA, indicating it may play an important role in the regulation of CREB and NMDA receptors. For these reasons it was chosen for follow up analyses to determine if these trends would hold up in a larger, more diverse cohort of individuals. An additional 100 samples made up of an additional 50 COGA alcoholics and controls and 50 caucasian controls were investigated for PDE4DIP copy number. It was found that alcoholics continue to trend towards a lower copy number of PDE4DIP than controls. The analysis of a larger sample size should help clarify these initial suggestive associations. The copies of PDE4DIP fall on chromosome 1q21.1 a highly dynamic region of the genome that is copy number variable across individuals. Given that PDE4DIP is part of an important brain-related pathway, change in gene dosage provides a compelling potential mechanism for influencing individual susceptibility to alcoholism and other forms of drug abuse.

0652

THE MTHFR$_{(C677T)}$ POLYMORPHISM: IT'S PREVALENCE AND LINK TO ALCOHOL CONSUMPTION

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Introduction: The enzyme 5,10-methylenetetrahydrofolate reductase (MTHFR) has a key function in the folate cycle and contributes to homocysteine metabolism. The mutant enzyme variant, known as MTHFR$_{(C677T)}$ causes reduced activity, resulting in high circulating plasma homocysteine level and risk of cardiovascular disease. Studies with alcoholic dependent patients have shown a higher prevalence of the MTHFR$_{(C677T)}$ polymorphism. However this has not been investigated in healthy individuals who consume alcohol in a range of non-dependent patterns. The aim of this work was to investigate the prevalence of the MTHFR$_{(C677T)}$ polymorphism in a sample of individuals with a range of alcohol consumption patterns, from abstaining through to dependency.

Methods: DNA was extracted from healthy individuals (N=35) and clinically diagnosed alcohol dependent patients (N=17), who were undergoing treatment for dependency within a detoxification clinic. DNA was extracted using published methodology and the presence of the MTHFR$_{(C677T)}$ polymorphism determined using Real-Time PCR. Alcohol consumption was recorded in 7 day self-report diaries and expressed in grams. Plasma homocysteine was analysed using HPLC-ED.

Results: No alcohol dependent individuals, within the sample, were shown to carry the MTHFR$_{(C677T)}$ polymorphism. Of the healthy individuals, 17.1% (N=6) tested positive for the MTHFR$_{(C677T)}$ polymorphism. Within this small group a significant linear relationship was identified (p<0.05, R=0.975) whereby increasing alcohol consumption was associated with increasing plasma homocysteine levels. Furthermore the MTHFR$_{(C677T)}$ polymorphism carriers were shown to have statistically significantly (p=<0.05) higher ratio's of plasma homocysteine (μmol/l) levels to amount of alcohol consumed per drinking day (grams) in comparison to those individuals who did not carry the polymorphism.

Discussion: This pilot study has shown there is an association between the presence of the MTHFR$_{(C677T)}$ polymorphism, plasma homocysteine and alcohol consumption in healthy individuals who consume alcohol. Further work is required, within a statistically powered sample, to investigate the prevalence of the MTHFR$_{(C677T)}$ polymorphism and its effect on elevated plasma homocsyteine and resulting cardiovascular disease risk. This further work must also take into consideration different alcohol consumption patterns, including dependency.

0653

ASSOCIATION OF GENETIC VARIATIONS IN MIR-9 GENES WITH ALCOHOLISM

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Alcoholism has a strong genetic component, however the exact genetic/molecular underpinnings of this debilitating disease are yet to be determined. Others and us have recently indicated that one of microRNA species, miR-9, is regulated by alcohol. We discovered in an animal model that the development of molecular tolerance to alcohol in neurons depends on miR-9. microRNAs belong to a family of short, non-coding RNAs. They don't encode proteins but regulate stability of various mRNA transcripts encoding proteins. microRNAs are very important master regulators of gene expression, with one microRNA regulating simultaneously expression of hundreds of transcripts. Since alcoholism is a multigenic disease, microRNAs' control of expression of many genes makes them a very attractive model of the development of alcoholism. miR-9 is encoded by three different genes located on separate chromosomes: miR-9-1 on chromosome #1, miR-9-2 on #5, and miR-9-3 on #15. Remarkably, two out of three miR-9 genes are located in the susceptibility loci for alcohol dependence. Interestingly, each miR-9 gene is a mirtron, a microRNA gene situated within a different, longer gene (a host). Thus, expression of each miR-9 gene is controlled by its own, proximal promoter and by the distal, host gene promoter. Here, we describe genetic variations in proximal promoters of miR-9 genes in alcoholics. We scanned 3–5 kb of each miR-9 region in 282 COGA samples (239 families) using qRT-PCR, nested PCR and direct sequencing. PCR products were purified using Qiagen PCR kits. Restriction digestion was used to ensure specificity of the PCR products. Sequencing was performed in both directions to ensure high accuracy. SNPs were identified using the Geneious Pro. We detected SNPs in all proximal promoters. Some of the SNPs have been previously detected in the general population. However, some of the SNPs were not observed previously. We observed around ten new SNPs per region. We detected also around the same number of known SNPs per region. Interestingly, all the SNPs were located in the promoters, before or after each gene, but not within miR-9 gene per se. In summary, our results show that a specific set of SNPs located within miR-9 proximal promoters is associated with alcoholism. These miR-9 SNPs could contribute to the mechanism of the development of alcohol tolerance, as well as serve as an important biomarker of an individual susceptibility to alcohol dependence.

0654

ASSOCIATION OF SNPS IN PROMOTERS OF MIR-9 HOST GENES WITH ALCOHOLISM

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Alcoholism has strong genetic component but the exact genetic underpinnings of alcoholism are unclear. It is proposed that multiple genes contribute to susceptibility to alcoholism. microRNAs are recently discovered, powerful master regulators of gene expression with each microRNA regulating expression of hundreds of genes. We hypothesize that genetic variations in genomic regions controlling expression of microRNA can explain, at least partially, multigenic nature of alcoholism. Alcohol affects expression of several microRNAs. One of the best examples is microRNA called miR-9. We showed previously importance of miR-9 in the development of tolerance to alcohol, one of the first steps toward addiction. Here we used 282 COGA (the Collaborative Studies on Genetics of Alcoholism) samples of alcoholics (239 families) to determine SNPs in genomic regions controlling miR-9 expression. 3 miR-9 genes (miR-9-1, –2 and –3) are located on chromosome #1, #5 and #15, respectively. Interestingly, each miR-9 gene is a mirtron, a microRNA gene situated within a different, longer gene (a host). miR-9-1 is located within the C1orf61gene encoding CROC4 protein, miR-9-2 is positioned within non-coding CR599257 gene, while miR-9-3 is embedded within the non-coding CR612213 gene. The host gene promoter although located several thousands nucleotides away from a particular miR-9 gene, can still control expression of this miR-9 gene. Changes caused by mutations in the host genes promoters could have a significant effect on the production of their respective miR-9 genes. We scanned around 2-6 kb of each host promoter region using qRT-PCR, nested PCR and direct sequencing. PCR reactions were optimized to obtain a single product (determined on Bioanalyzer). Products were purified and specificity ensured by restriction digestion. Sequencing was performed in both directions for high accuracy. SNPs were identified using the Geneious Pro. We found several SNPs located in the promoters of miR-9 genes hosts. Some SNPs were described previously in general population as described in dbSNP database, however some were newly found. In general we detected more new SNPs then the known ones. In some families SNPs were present in multiple generations suggesting their hereditability. In summary, SNPs in miR-9 host promoter regions could serve as valuable biomarkers of susceptibility to alcoholism, helping to determine predisposition of an individual to the development of alcoholism.

0655

SNPS IN PROMOTERS OF MIR-9 GENES IN ALCOHOLICS CAN ALTER BINDING OF TRANSCRIPTION FACTORS

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microRNAs are small, non-coding, RNA molecules of tremendous biological importance. They are very powerful regulators of mRNA levels and protein expression.Each microRNA cancontrol cellular fate or activity by simultaneous regulation of multiple genes. Alcoholism is a multigenic disorderof unclear molecular underpinnings. Using animal models, others and us indicated that a particular microRNA, miR-9, is regulated by alcohol. Particularly, we showed the essential role of miR-9 in the development of molecular tolerance to alcohol. Here, we wanted to establishinvolvement of miR-9 in the development of alcoholism in humans.We used 282 DNA samples from the COGA(the Collaborative Studies on Genetics of Alcoholism) collection to search for COGA-specific SNPs in genomic regions related to miR-9.In humans, there are three miR-9 genes located on distinct chromosomes and embedded within host genes. We sequenced on averagetwo 3,000 nucleotide regions per miR-9: one surrounding each miR-9 gene and including its promoter, and the other being the respective host gene promoter of each miR-9. We observed the presence of several SNPs, particularly in the promoter regions.Promoters serve as recruitment areas for transcription factors and initiation of transcription.SNPs that occur within a promoter can change binding oftranscription factorsand subsequent gene expression. Weanalyzed the effects of SNPs in miR-9promoterson binding of transcription factorsusingMAPPER2, a reliableonline software suite, whichusesthe TRANSFAC and JASPAR databases as a source of transcription factor binding site information. We tested around twenty SNPs per promoter. We determinedthat some SNPs were located outside thebinding sites of any transcription factor and thus would have no effect on association of transcription factors with the promoters. However, some of theseSNPs were located within the binding sites. Importantly,theycould change the binding affinity of these factors. Some SNPs coulddecrease the affinity several fold, while others create new binding sites of high affinity.Together, described changes in binding of transcription factorstomiR-9 promotersmay alterbasal or stimulated expression levels of miR-9, leading to faster development of drug tolerance in alcoholics.

0656

A POLYMORPHISM OF THE FERROCHELATASE GENE IS RELATED TO NEUROBIOLOGICAL RESPONSE TO ALCOHOL CUES, SUBJECTIVE RESPONSE TO ALCOHOL, & DRINKING BEHAVIOR

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Genome wide association studies (GWAS) hold much promise in identifying novel genes related to alcohol response. Yet, one limitation that has left this potential unfulfilled is a consistent lack of replication in follow-up studies. Therefore, the goal of this study was to perform a GWAS to identify a SNP related to neurobiological response to alcohol-related cues and then examine, in a separate second sample, if this SNP also related to subjective alcohol response and self-reported drinking behavior. An initial genome wide analysis suggested an association between a SNP of the ferrochelatase gene (FECH; rs1790611) and cue-elicited BOLD response in the insula and striatum. In a second sample, one hundred and ninety-three heavy drinkers were genotyped for the FECH SNP (AA = 38, AG = 91, GG = 64). Subjects participated in a screening session in which they reported recent drinking history using a Timeline Follow-Back interview and in two laboratory sessions in which they consumed a high dose of alcohol (0.8g/kg) or a placebo beverage and completed various subjective measures. In order to compare acute response to alcohol across several measures, an exploratory factor analysis was performed to create a composite index of positive-like subjective effects. A comparison of these factor scores between genotypes indicated a significant difference in alcohol response at 60-minutes after the initiation of beverage consumption (i.e. peak BrAC), with GG ($p=0.01$) and AG ($p<0.05$) subjects reporting greater positive effects than AA. Additionally, AA individuals reported significantly more drinks per drinking day ($p<0.05$) and more drinks per binge drinking episode ($p<0.05$) than those with the AG genotype. In sum, this study identified a novel association between FECH and alcohol-related neurobiological response and successfully replicated these results on the subjective and behavioral level. Importantly, these results provide additional support for cue-elicited BOLD response as a useful intermediate phenotype to identify genes related to alcohol response. It is at this point unclear as to how ferrochelatase, an enzyme involved in heme synthesis, is biologically involved in response to alcohol and future studies should strive to characterize this relationship on a molecular basis.

0657

DOPAMINERGIC GENETIC ASSOCIATIONS WITH IMPULSIVE DECISION-MAKING IN PROBLEM DRINKERS

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Impulsivity has been implicated in both the development and maintenance of substance use disorders. However the mechanisms underlying the link between impulsivity and substance use are complex and not fully understood. Impulsive decision-making, a dimension of impulsivity routinely measured by the Delay Discounting Task (DDT), has been repeatedly associated with alcohol use disorders. In addition, dopaminergic neurotransmission is thought to play a role in impulsive behavior; hence this study examines two functional dopaminergic candidate genes: (a) the dopamine receptor 2 (DRD2) gene Taq1 polymorphism, and (b) the dopamine transporter (DAT) SCL6A3, both of which have been previously associated with impulsivity and problem drinking. The study aim was to test whether dopaminergic candidate genes mediate the association between impulsive decision-making and alcohol use/problems. Structural equation modeling was used to test two models in which DRD2/Taq1 and DAT were entered, respectively, as mediators of the relationship between impulsive decision-making (DDT performance) and alcohol use and alcohol-related problems. Participants were 209 (47 females; all Caucasian) non-treatment seeking adult problem drinkers (72% alcohol dependent). Both models were found to fit the data well (DRD2/Taq 1: χ^2=453.027, RMSEA=.016; DAT: χ^2=420.212, RMSEA=.042) and revealed significant paths between both candidate genes and impulsive decision-making in this sample (DRD2/Taq 1: β=.156; DAT: β=.134). However, neither genotype nor impulsive decision-making were found to directly predict alcohol use or alcohol-related problems. Due to the heavy drinking inclusionary criteria of the sample, it is likely that the homogeneity in alcohol use and alcohol-related problems reduced statistical power to detect associations between impulsivity and alcohol outcomes. Nevertheless, these results suggest that both candidate genes are associated with impulsive decision-making in problem drinkers, a plausible mechanism of risk for alcoholism. Future studies using a non-drinking comparison group will help elucidate the role of impulsivity, and its genetic determinants, as a risk marker for alcoholism.

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0658

CRFR1 GENE POLYMORPHISM IS ASSOCIATED WITH HEAVY DRINKING ONSET IN ALCOHOL-DEPENDENT SUBJECTS

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This study aims at exploring the association of corticotrophin-releasing factor receptor 1, *CRFR1*, single nucleotide polymorphism (SNP), rs1876831, with heavy alcohol use onset and personality traits in alcohol-dependent subjects. Alcohol-dependent subjects (fulfilled DSM-IV criteria for alcohol dependence) were recruited during a five-day in-patient detoxification treatment. Patients suffered from major psychiatric or personality disorders were excluded apart from depression and anxiety due to their high prevalence among alcohol abusers. History of alcohol use and abusive experiences (sexual and physical) was collected during a private interview. Personality traits were measured by the NEO PI-R. DNA was extracted from venous blood; genotyping of rs1876831 was done by PCR-RFLP. This study included 192 subjects (114 male and 78 female; mean age=42.7 years). Male subjects started heavy drinking significantly earlier than female subjects (t test p=0.027; 25.3 vs 28.8 years). Two-way ANOVA revealed significant main effect of abusive experience (p=0.033) and rs1876831 A allele carrier status (p=0.004) on heavy drinking onset age in male subjects: those who had been abused and those who carry the A allele started heavy drinking earlier. However for female subjects, significant interaction between abusive experience and rs1876831 was detected (p=0.035): A allele carriers started drinking earlier than non-carrier in the abused group but later in the non-abused group. Neuroticism differed only between genders (p<0.001) but not affected by abusive experience nor rs1876831 A allele carrier status. *CRFR1* rs1896831 A allele may contribute to early heavy drinking behaviour in alcohol-dependent subjects. Gender and abusive experience are important determinant of such a contribution. Neurotic personality trait differed by gender, but not by experience of abuse and rs1876831 A allele carrier status.

0659

INTERACTION BETWEEN OPRK1 AND PDYN GENES AND CUMULATIVE LIFE STRESS IN RISK OF ALCOHOL DEPENDENCE

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Chronic stress and cumulative adversity are linked to alcohol dependence. Animal and human studies have demonstrated that interactions of stress and kappa opioid receptor gene (OPRK1) and its peptide, prodynorphin (PDYN) significantly increase alcohol drinking and other addictive behavior. Our goal is to investigate whether or not genetic variants on OPRK1 and PDYN interact with cumulative life stress in increasing vulnerability of developing alcohol dependence,. We recruited 979 subjects including and experimental group of 187 individuals with alcohol dependence (AD) and, 67 healthy control (HC), and 725 subjects from a community sample (CS). We assessed Childhood Trauma Questionnaire (CTQ) and Perceived Stress Scale (PSS) for subjects. Cumulative adversity interview (CAI) and alcohol drinking survey were conducted to assess cumulative life stress and drinking behavior for CS group. Each subject was genotyped for 32 SNPs on OPRK1 and 15 SNPs on PDYN. Generalized linear model was applied to analyze associations of each stress variable, SNP, and alcohol dependence. All analyses were adjusted for gender, age and race. We found that alcohol drinking is highly correlated with CAI score (p=0.00005). The SNP rs 7832417 on OPRK1 was significantly associated with total CAI score (FDR p=0.03). There were no significant CAI score and SNP interaction on alcohol drinking behavior. However, in our experimental sample (AD and HC), we found that significant interactive effects of three SNPs (rs7832417 on OPRK1 and rs2235751, rs6045868 on PDYN) with CTQ and PSS and risk of alcohol dependence (FDR ps <0.02). Three SNPs were significant associated with CTQ and PSS scores in entire sample population (p's<0.03). In summary, our results suggest that genetic variants on OPRK1 and PDYN increase vulnerability of stress, and further interact with traumatic events in the development of alcohol dependence (supported by R01-AA013892; UL1-DE019586; PL1-DA024859, APA/Merck early Career Award).

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INFLUENCE OF SEROTONIN (5-HT) RECEPTOR POLYMORPHISMS ON THE SUBJECTIVE RESPONSE TO ALCOHOL IN NON-DEPENDENT DRINKERS: PRELIMINARY FINDINGS

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Previous studies have shown that functional polymorphisms in genes encoding 5-HT receptors may influence alcohol addiction vulnerability. The 5HT3 receptor is potentiated by alcohol and mediates excitatory 5-HT transmission that modulates dopamine release in mesolimbic circuits in rodents. The 5-HT3 antagonist ondansetron has also been shown to modulate the response to alcohol and has been evaluated as a potential treatment for alcoholism. This study investigated the influence of 5-HT3 A/B receptor polymorphisms on the acute subjective response to intravenous (IV) alcohol in non-dependent drinkers.

Data for this analysis was obtained from two studies in which healthy male and female non-dependent drinkers (n=42) received an IV alcohol infusion to a target breath alcohol level of 0.08% and placebo in separate sessions. Subjective response was measured repeatedly using the Drug Effects Questionnaire (DEQ). The peak response on measures of ''feeling drug effects'', ''high'', ''intoxicated'', ''like drug effects'' and ''want more drug'' were compared by treatment and genotypes for common 5-HT3A/B receptor variants (rs2276302, rs1176744 and rs3758987).

Preliminary results indicated a significant effect of treatment (alcohol vs. placebo) on subjective measures of alcohol effects. There was a significant genotype X treatment X gender interaction for the measure of ''high'' for both rs1176744 (p=0.032) and rs3758987 (p=0.033). Females carrying the variant form of both genes reported significantly greater feelings of ''high'' compared to males. The rs1176744 polymorphism has been shown to increase 5HT3 receptor sensitivity, and may be involved in modulating mesolimbic dopamine release resulting in greater subjective responses following acute alcohol exposure.

These preliminary results are consistent with reports implicating the role of 5-HT3 receptors in alcoholism vulnerability and response to treatment in alcoholism. Further studies examining the influence of 5-HT on objective measures of alcohol response are critical in evaluating the role of serotonin in the pharmacological effects of alcohol. In addition, this study exemplifies the need for quantitative endophenotypes in genetic studies of alcohol pharmacology and alcoholism.

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WITHDRAWN.

0662

KAPPA-OPIOID MECHANISMS IN THE 2 BOTTLE-CHOICE ETHANOL INTAKE PARADIGM
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The effective clinical use of non-selective opioid antagonists to treat alcoholism and concordant results of opioid antagonists in preclinical studies demonstrates an important role for the endogenous opioids in regulating the rewarding value of ethanol (EtOH). Previously published data indicate the critical involvement of mu- and delta-opioid receptors; however, the role of Kappa-opioid receptors (KORs) is still somewhat unclear. Pharmacological studies using antagonists indicate that alterations in the function of KORs can both contribute to and diminish EtOH reward. Here, using global and region specific KOR deletion, we investigated the role of kappa-opioid mechanisms in the expression of preference for EtOH using a 2 bottle choice paradigm.
Methods: To globally ablate KORs, we crossed mice with floxed KORs with EIIa-Cre mice (mice expressing Cre on a ubiquitous promoter). For selective ablation of KORs in dopamine transporter (DAT) containing neurons, we crossed our floxed KOR mice to (DAT)-Cre mice (mice expression Cre on the DAT promoter). Singly housed female mice were given access to tap water through two sipper tubes for 4 days (acclimation). During the choice phase of the experiment, one of the two water bottles was replaced with a bottle containing EtOH in increasing concentrations (3%, 6% and 10%, 15% v/v).
Results: EIIa KO (global knock-out) mice demonstrated a significantly lower preference for EtOH (6, 10 & 15%) compared to WT littermates. Similarly, DAT-Cre+ (DA neuron knock-out) mice also expressed a lower preference compared to their littermates that lacked Cre.
Conclusions: Data from KOR knock-out mice suggest that KOR activation contributes to the rewarding value of EtOH. The lower EtOH preference observed in DAT-Cre+ (region specific KO) mice partially accounts for the difference detected in global KO mice. This suggests that EtOH preference is mediated at least in part by regions expressing DAT, such as the VTA. These findings contribute to the growing evidence that KORs play a role in regulating EtOH intake.

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THE ROLE OF OPIOID PEPTIDES IN ETHANOL REWARD
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Substantial evidence has implicated the endogenous opioid system in alcohol reward. However, the role of each component of this system in alcohol reward remains largely unclear. In this study, using the conditioned place preference (CPP) paradigm as an animal model of reward, we determined whether ethanol-induced CPP would be altered in mice lacking the mu opioid receptor compared to their wild-type controls. Given that β-endorphin and enkephalin have high affinity for the mu opioid receptor, we also examined whether genetic deletion of one or both of these peptides would alter the development of ethanol-induced CPP. Mice were tested for baseline place preference on day 1 and were conditioned with ethanol (2 g/kg) in their initially non-preferred chamber for 3 consecutive days. They were then tested under a drug-free state for postconditioning place preference on day 5. On each test day, mice were placed in the neutral chamber and allowed to freely explore the conditioning chambers through this smaller central chamber. The amount of time that mice spent in each chamber was recorded. Mu opioid receptor knockout mice were able to acquire CPP; however, this response was significantly attenuated in comparison to their wild-type littermates/controls. Deletion of β-endorphin alone had only a modest, although not significant, effect while deletion of the proenkephalin gene failed to alter the acquisition of ethanol-induced CPP. On the other hand, the absence of both β-endorphin and enkephalins completely abolished the CPP response. These findings provide clear evidence illustrating that ethanol induces its rewarding action via the mu opioid receptor involving a joint action of β-endorphin and enkephalin.

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DIFFERENTIAL ROLES OF DOPAMINE D2 RECEPTOR ISOFORMS IN ALCOHOL CONSUMPTION AND THE ACTION OF OTHER ADDICTIVE DRUGS
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Individual differences in dopamine D2 receptor (D2R) expression in the brain are thought to influence motivation and reinforcement for ethanol and other rewards. D2R exists in two isoforms, D2 long (D2LR) and D2 short (D2SR), produced by alternative splicing of the same gene. The relative contributions of D2LR versus D2SR to consumption of ethanol and the actions of other abused drugs are not known. Genetic engineering was used to produce a line of knockout (KO) mice that lack D2LR, but still express functional D2SR (D2L KO mice). The purposes of the study are to investigate the role of two D2R isoforms in ethanol drinking and in the action of other addictive drugs such as cocaine and morphine.
D2L KO and wild-type (WT) mice of both sexes were tested for intake of 20% ethanol, 10% sugar water and plain tap water using established drinking-in-the-dark (DID) procedures. D2L KO mice drank significantly more ethanol than WT in both sexes. KO mice drank more sugar water than WT in females but not in males. The D2 antagonist eticlopride dose-dependently decreased ethanol intake in female mice of both genotypes. Results suggest that over-representation of D2SR contributes to increased intake of ethanol in the KO mice. In another series of experiments, mice of both genotypes were tested in conditioned place preference (CPP) to morphine and cocaine. In contrast to WT mice, D2L KO mice did not develop a place preference to morphine. Both KO and WT showed similar CPP responses to cocaine. Results suggest that D2L is important for the rewarding aspects of morphine, but is not essential for cocaine-induced rewards. Taken together, these studies reveal that D2LR and D2SR contribute differentially to the consumption of alcohol and the action of other addictive substances/drugs such as sugar and morphine. Our findings suggest that the up-regulation of DSR or increased ratio of D2SR to D2LR plays a significant role in excessive alcohol drinking in mice. On the other hand, the presence of D2LR is critical for the expression of morphine-induced rewards. These studies enhance our understanding of the neurobiological basis underlying alcohol-drinking behavior and may facilitate the development of novel therapeutic agents for alleviating heavy drinking.

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ALTERED STRIATAL DOPAMINE NEUROTRANSMISSION IN MICE WITH LOW ENDOGENOUS BDNF FOLLOWING DRINKING-IN-THE-DARK ETHANOL EXPOSURE

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Behavioral studies suggest brain-derived neurotrophic factor (BDNF) has a protective role in the caudate-putamen (CPu) to regulate the reinforcing effects of ethanol. Recently, we demonstrated attenuated extracellular dopamine increases in the CPu following acute ethanol in $BDNF^{+/-}$ mice. In the present study, we measured the effects of repeated ethanol exposure on dopamine transmission using a drinking-in-the-dark procedure to further elucidate the mechanism through which BDNF modulates drinking behavior. The increase in ethanol consumption following 7 days of daily limited access to a 15% ethanol solution was 50% greater in $BDNF^{+/-}$ mice compared to wildtype mice. Assessment of dopamine dynamics in the CPu using in vivo microdialysis and in vitro voltammetry revealed that ethanol drinking did not alter extracellular dopamine levels or the extent of electrically-stimulated dopamine release and uptake in wildtype mice. Alternatively, ethanol exposure in $BDNF^{+/-}$ mice resulted in elevated baseline dialysate dopamine levels that corresponded with enhanced electrically-evoked dopamine release, with no difference in uptake rate, compared to control mice. Extracellular dopamine increases following an acute injection of ethanol (2 g/kg) was significantly attenuated in ethanol-exposed wildtype mice (6.5-fold) and completely abolished in $BDNF^{+/-}$ mice compared to controls. Preliminary evidence suggests the lack of dopamine response following ethanol challenge in drinking mice may be related to enhanced dopamine D3, but not D2, autoreceptor functionality. Together, these findings indicate drinking-in-the-dark exposure alters the sensitivity of the nigrostriatal pathway to ethanol and supports the growing evidence that BDNF is an integral component in the regulation of ethanol intake.

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BDNFVAL68MET POLYMORPHISM PROMOTES COMPULSIVE ETHANOL DRINKING IN MICE

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A single nucleotide polymorphism G196A in the human brain-derived neurotrophic factor (BDNF) gene results in amino acid substitution of $Valine^{66}$ (Val) by $Methionine^{66}$ (Met) in the pro-region of BDNF. This substitution leads to a deficit in neuronal activity-dependent release of BDNF[1]. In humans, Met^{66}BDNF contributes to the severity of several psychiatric disorders including alcoholism[2-3]. We previously reported that BDNF is part of a protective homeostatic pathway that gates the level of ethanol consumption in rodents[4-5]. We therefore hypothesized that the Met allele of *BNDF* reduces the protective role of the growth factor. We generated homozygous knock-in mice carrying the *MetBDNF* allele on a C57Bl/6J background (Met^{68}BDNF), and tested whether this polymorphism promotes excessive ethanol drinking. We found that the Met^{68}BDNF mice exhibited a higher level of voluntary ethanol intake (20%v/v) compared to wild type mice (WT) in a 2-bottle choice paradigm, which was not due to differences in the kinetics of ethanol metabolism in the two genotypes. Met^{68}BDNF mice also consumed a higher level of ethanol solution (10% or 20%) that was adulterated with quinine (0.1–0.3g/l) than WT mice, suggesting that the Met^{68}BDNF displayed compulsive ethanol intake and continued to drink more ethanol despite negative consequence. On the other hand, the two genotypes did not differ in general compulsivity as measured by T-Maze or quinine palatability. Furthermore, Met^{68}BDNF and WT mice consumed the same amount of a saccharin solution (0.03%w/v) even when the saccharin solution was adulterated by quinine (0.1–0.3g/l), revealing that the compulsive drinking of the Met^{68}BDNF mice is specific to ethanol and is not due to a general increase of motivation to drink an appetitive solution. Together, our results suggest that the *MetBDNF* allele increases the risk for developing ethanol abuse disorders by promoting the compulsive intake.

1. Egan et al 2003 *Cell*.
2. Rybakowski 2008 *Pharmacogenomics*.
3. Matsushita et al 2004 *ACER*.
4. Jeanblanc et al 2009 & 2006 *J. Neurosci*
5. McGough et al 2004 *J. Neurosci*.

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PHARMACOLOGICAL AND GENETIC DISSECTION OF THE ROLE OF GABA RECEPTORS CONTAINING RHO1 OR RHO2 SUBUNITS IN BEHAVIORAL EFFECTS OF ETHANOL

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GABA receptors can be formed from rho1,2 or 3 subunits (previously called GABAC receptors). Receptors formed from rho1 are inhibited by low concentrations of ethanol (Mihic, Harris, 1996) and family-based association analyses have linked the rho1,2 subunit genes on chromosome 6q14–16 with alcohol dependence (Xuei et al., 2010). The ethanol sensitivity of rho2 subunits is not known and we expressed human rho2 in Xenopus oocytes and found that, similar to rho1, the function is inhibited by ethanol (30–50 mM). We previously showed that genetic deletion of the rho1 subunit in mice produced a longer duration of ethanol-induced loss of righting reflex (LORR) and faster recovery from ethanol-induced motor incoordination (RMI) (Blednov et al., RSA 2011). Because rho2 null mutant mice are not available, we used rho antagonists with selectivity for rho1 or rho2 to confirm the role of rho1 in these alcohol behaviors and to explore the role of rho2. We used two mixed rho1/rho2 antagonists - (S)-ACPBPA (''Rho1'' selective) and (R)-ACPBPA (''Rho2'' selective) (Chebib et al., 2009). In wild type mice of both sexes ''Rho1'' antagonist increased duration of LORR and accelerated RMI. In wild-type mice, the ''Rho2'' antagonist did not change the RMI in either sex and did not change the duration of LORR in female mice but slightly reduced the duration of LORR. In rho1 knockout (-/-) mice of both sexes the ''Rho1'' antagonist did not change the RMI and did not change the duration of LORR in null female mice but reduced it in male mice. In contrast, ''Rho2'' antagonist significantly reduced the duration of LORR and slowed the motor recovery in null mutant mice of both sexes. Overall, administration of the ''Rho1'' antagonist to wild type mice mimicked the changes in ethanol behaviors observed in rho1 null mutant mice and did not produce these effects in mice lacking rho1. In contrast, the ''Rho2'' antagonist did not change alcohol actions in wild type mice but produced behavioral effects in mice lacking rho1 that were the opposite of the effects from deleting (or inhibiting) rho1. These results indicate that the rho1 subunit has a predominant role in two behavioral effects of ethanol, but a role of rho2 may be revealed when rho1 is deleted. Supported by NIH/NIAAA INIA Consortium (AA U01 13520 - INIA Project; AA06399).

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EVALUATION OF ETHANOL RESPONSES IN S296A A1 GLYR KNOCKIN MICE

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Accumulating evidence has suggested that strychnine-sensitive glycine receptors (GlyRs) are one of the primary targets of alcohol action in the nervous system. Ethanol can allosterically potentiate glycine-activated current (I_{Gly}) in various native neurons and in heterologous cell lines expressing recombinant α1 subunit-containing GlyRs. Although the precise molecular mechanism of ethanol-induced allosteric modulation of GlyRs remains elusive, a number of residues in the transmembrane (TM) domains of the α1 GlyR are found to be critical for the sensitivity of GlyRs to ethanol-induced potentiation. One of them is the serine residue at 296 in the TM3. A previous study has shown that the S296A mutation can reduce the magnitude of ethanol potentiation of the α1 GlyR expressed in HEK 293 cells (Yevenes et al, *J. Biol. Chem.* 285(39): 30203–3021, 2010). To determine if S296 contributes to ethanol-induced behaviors, we constructed S296A knockin mice by gene targeting. There were no significant differences in body weight, food consumption, locomotor activity, startle response and rotarod performance between homozygous S296A mice and their wild type littermates. We next compared genotypes following acute ethanol exposure. Ethanol (1.2 g/kg, i.p.) significantly reduced the time to fall from a rotarod, body temperature, and locomotor activity in wild type mice. Parallel experiments in homozygous knockin mice indicate that these ethanol-induced changes were similar in compared to wild type littermates. Further examination of responses to ethanol in the S296 mice is in progress. Supported by the NIAAA intramural research program and AA017875.

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ALCOHOL PHENOTYPE OF MICE WITH POINT MUTATIONS OF MGLUR5 AFFECTING THE PHOSPHORYLATION OF THE HOMER BINDING SITE

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The mGluR5 subtype of Group1 metabotropic glutamate receptors and its interactions with Homer scaffolding proteins are critical for regulating various aspects of alcohol reward in rodents, including alcohol intake and reinforcement. Recently, a transgenic mouse was developed with T1123/S1126-AA point mutations within the Homer binding domain on mGluR5 that prevents the phosphorylation of the binding domain and reduces mGluR5-Homer coupling by 50%. Here, we characterized the alcohol behavioral phenotype of these TS mutant mice, hypothesizing that akin to mGluR5 or Homer2 knock-out mice, TS mutant animals would exhibit lower indices of alcohol reward/reinforcement, compared to wild-type (WT) controls. Contrary to our hypothesis, TS mutants exhibited a shift upwards in the dose-response function for alcohol intake in the home cage under continuous access, relative to WT animals and mice heterozygous for the mutation (HET) exhibited an intermediate phenotype in this paradigm. However, when assessed for binge alcohol drinking under either Scheduled High Alcohol Consumption or Drinking-in-the-Dark procedures, genotypic differences in alcohol drinking were not apparent. Interestingly, TS mutants exhibited a shift to the right in the dose-response function for an alcohol-conditioned place-preference (1–3 g/kg), suggesting reduced sensitivity to the rewarding properties of the drug. However, in a pilot study using operant procedures, TS mutants (n=4) exhibited WT-levels of alcohol-reinforced lever-pressing (5–30%), although the TS mice tended to consume less alcohol at the 30% concentration, compared to WT animals. These data indicate clearly that mutations of the T1123/S1126 sites on mGluR5 produce an alcohol behavioral phenotype that can be distinguished from that produced by the constitutive deletion of either *mGluR5* or *Homer2* and further study is required in order to understand the psychobiological processes contributing to the elevated intake exhibited by mutant mice under free-access drinking conditions.

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NMDA NR1 (F639A) KNOCK-IN MICE DISPLAY SELECTIVE ALTERATIONS IN THEIR RESPONSE TO ACUTE ETHANOL

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Ethanol's inhibition of glutamatergic N-Methyl-D-Aspartate receptors (NMDARs) is thought to be important in mediating some of the behavioral actions of ethanol. NMDARs are calcium-permeable, glutamate-activated ion channels that are assembled from NR1 and NR2 subunits. Previous studies in our laboratory identified a phenylalanine residue (F) at position 639 in the NR1 subunit that regulates much of the receptor's sensitivity to ethanol. Based on this knowledge, we generated a knock-in mouse where F639 was replaced by an alanine and used these animals in a series of behavioral and electrophysiological studies. Mice homozygous for the F639A allele died at post-natal day one while F639A heterozygous mice were viable and bred normally. No major differences in NR1 or NR2B expression were observed between F639A Het and WT mice in tissue isolated from medial prefrontal cortex, dorsal striatum, hippocampus, amygdala or nucleus accumbens. The kinetics of evoked NMDA EPSCs did not differ between F639A and WT mice and both groups showed similar currents during bath application of NMDA. However, as expected, ethanol had significantly less effect on NMDA-mediated EPSCs in F639A mice as compared to WT. F639A Het and WT mice did not differ in loss of righting reflex or sleep time following a 4.0 g/kg acute dose of ethanol. Both groups of mice also had similar rates of ethanol clearance as measured by changes in blood ethanol concentration following an acute dose of ethanol. In WT mice, low doses of ethanol enhanced spontaneous locomotor activity while higher doses inhibited activity. F639A Het mice showed no increase in locomotor activity at the low doses of ethanol and a blunted response to the high dose. In the elevated zero maze used to test anxiety, ethanol (1.25 g/kg; i.p.) significantly increased time spent in the open arm in WT mice but not F639A Het mice. In drinking studies, F639A Het mice consumed significantly less ethanol compared to WT mice in the 2 hr-limited access paradigm, but drank more when ethanol was available for 24 hrs every other day. The changes in ethanol drinking in F639A mice were not due to a change in taste reactivity as preference for saccharin, sucrose or quinine solutions was not different between genotypes. The results from these ongoing studies suggest that certain behavioral actions of ethanol are mediated via inhibition of NMDA receptors.

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THE ROLE OF β4 NICOTINIC ACETYLCHOLINE RECEPTOR IN ETHANOL-MEDIATED BEHAVIOR

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Neuronal nicotinic acetylcholine receptors (nAChRs) have been well established to play an important role in ethanol-mediated behaviors. Recent human genetic studies have implicated gene variants in the β4 nAChR subunit in the development of alcohol dependence. The β4 nAChRs are predominantly found in the habenula region of the brain. Inhibition of habenular neurons has been shown to excite dopamine neurons in the mid brain and vice versa. In this study we characterized ethanol drinking behavior in β4+/+ and β4-/- mice using an adapted Drinking-in-the Dark (DID) paradigm, which has been shown to induce high ethanol consumption in mice. Briefly, male β4+/+ and β4-/- mice were given access to one bottle of 20% ethanol and one bottle of water for a four-hour period, Monday to Friday, for thirty exposure days. Bottles were weighed at 2 and 4 hours after presentation. The preference of ethanol over water was calculated at both time points. We found the β4+/+ mice to have increased basal ethanol intake compared to β4-/- mice at two hours. However, the water intake was significantly increased in β4-/- compared to β4+/+ mice. The β4+/+ mice had an increased preference for ethanol to water at two hours compared with β4-/- mice. At the four hour time point, we found no genotypic difference in ethanol intake or preference, although the water intake remained higher in β4-/- compared to β4+/+mice. β4 subunit is mainly associated with α3 subunit in forming the α3β4* nAChR subtype in the brain. We have recently shown PF-4575180, a partial agonist at α3β4 nAChRs, was effective in reducing ethanol consumption and self-administration. While the partial agonist activity will permit some activation, PF-4575180 could strongly inhibit α3β4 nAChRs having a potent IC_{50} value of 0.1μM. Together our data suggests that the deletion of β4* nAChRs or inhibition of α3β4 nAChRs can effectively modulate ethanol drinking behavior. We can postulate this is an effect of habenular neuron inhibition, which can lead to increase in dopamine release in the mid brain leading to a decrease in ethanol consumption. Thus, the β4 nAChR subunit appears to play an important role for ethanol-mediated behaviors and can be an important pharmaco-therapeutic target for alcohol use disorders.

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THE CHRNB4 GENE DOES NOT MODULATE ETHANOL BEHAVIORS

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Alcohol (ethanol) and nicotine are widely used psychoactive substances and the co-use of these drugs has been demonstrated in the literature. Data from both human and animal studies has provided evidence that genetic correlations exist among ethanol and nicotine behaviors, providing evidence of shared genetic influence and possibly common neurochemical mechanisms underlying these traits. Nicotine has actions at nicotinic acetylcholine receptors in the brain and recent evidence suggests that alcohol may act through these receptors as well. The *Chrnb4* gene is located on mouse chromosome 9 in a cluster with two other nicotinic receptor subunits (*Chrna5* and *Chrna3*). Human genetic studies have provided evidence that variation in this gene cluster is associated early alcohol initiation and the level of response to alcohol, both thought to be early indications of alcohol use disorders. More recently, pharmacologic studies in animal models have implicated the α3β4 nicotinic acetylcholine receptor in alcohol consumption. In the current experiments we examined the hypothesis that the *Chrnb4* gene influences alcohol behaviors in a mouse model. To this end we tested mice lacking the *Chrnb4* gene using three different behavioral tasks that measure the response to an acute injection of ethanol. Additionally, we challenged mice with ethanol to determine if the *Chrnb4* gene influenced ethanol metabolism. Mice lacking the *Chrnb4* gene on a C57BL/6 background were bred at the Institute for Behavioral Genetics animal facility and used for the current experiments. Wildtype, heterozygous and knockout mice of both sexes were tested for ethanol-induced ataxia using the balance beam and dowel tests. Ethanol-induced sedation was measured using the Loss of Righting Reflex (LORR) paradigm. There were no significant differences between *Chrnb4* knockout mice and wildtype mice for any behavior tested, nor were there genotypic differences in ethanol metabolism. These data provide no evidence for a role of *Chrnb4* in ethanol behaviors, although this study is limited to the behaviors tested which are all measures of response to acute injection. Future work examining other ethanol behaviors such as consumption may more clearly define the role of this receptor subunit in ethanol behaviors.

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INVOLVEMENT OF HYPERSENSITIVE α6 SUBUNIT CONTAINING NEURONAL NICOTINIC ACETYLCHOLINE RECEPTORS IN MODULATING ALCOHOL INTAKE AND PREFERENCE

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Alcohol and nicotine are often abused together. Evidence is emerging that neuronal nicotinic acetylcholine receptors (nAChRs) in the mesolimbic dopamine system are involved in mediating the reinforcing effects of alcohol. Twelve mammalian neuronal nAChR subunits exist (α2-10 and β2-4), which can form a variety of nAChR subtypes with varying biophysical properties. Identifying the relevant nAChR subunits involved in alcohol reward may aid in uncovering potential therapeutic targets for the treatment of alcohol use disorders (AUDs). Midbrain dopamine (DA) neurons express high levels of nAChRs containing the α6 subunit, and α6* (* indicates that other subunits may be present in the pentameric receptor) nAChRs have been shown to modulate dopamine transmission, implicating their potential involvement in reward-related behaviors. The goal of the current study was to assess the involvement of the α6 subunit in alcohol intake and preference. We used transgenic mice expressing mutant (“L9’S”) hypersensitive α6 nAChR subunits, which can be activated by concentrations of endogenous ACh or ectopic nicotine that are 10 to 100-fold lower than concentrations required to activate WT α6* nAChRs. α6 L9’S mice were compared to their wildtype (WT) littermates for alcohol intake and preference behavior. Male and female mice were exposed to a 24 hr 2-bottle choice (alcohol vs. water) procedure with increasing concentrations of alcohol (3%, 6%, 10% and 20%; 4 days for each concentration) for a total of 16 days. Results indicate that α6 L9’S mice show increased alcohol intake compared to WT littermates in an alcohol concentration-dependent manner; α6 L9’S mice showed significantly higher alcohol intake on days 3 and 4 of the 3% and 6% alcohol concentrations. No sex differences were seen. Higher intake at low alcohol concentrations in α6 L9’S mice may reflect enhanced DA transmission in response to alcohol, implicating α6* nAChR involvement in modulating alcohol intake. To further study α6* nAChRs in modulating alcohol intake, experiments are currently underway to assess the role of these receptors in alcohol-conditioned place preference and an alternative alcohol drinking model, “drinking in the dark.” Supported by AA016843 and DA030396.

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MODULATION OF ALCOHOL REWARD VIA ACTIVATION OF NICOTINIC ACETYLCHOLINE RECEPTORS CONTAINING THE A4 SUBUNIT

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Similar to all drugs of abuse, ethanol activates the mesocorticolimbic dopamine reward pathway resulting in a release of dopamine (DA) in the nucleus accumbens, a phenomenon critical for drug reinforcement. Neuronal nicotinic acetylcholine receptors (nAChRs), ligand gated cation channels activated by the endogenous neurotransmitter, acetylcholine, have been implicated as therapeutic targets to reduce alcohol consumption. However, whether nAChRs are inherently critical for the rewarding properties of alcohol is unknown. Previously, we determined that the full nAChR agonist nicotine or the partial agonist, varenicline targets high affinity nAChRs containing the α4 subunit (α4* nAChRs) to reduce binge drinking. To test the hypothesis that α4* nAChR expression and function can modulate alcohol reward, we measured alcohol conditioned place preference in mice that did not express α4* nAChRs (α4 KO mice), wild-type (WT) mice, and mice that express a single point mutation rendering α4* nAChRs 50-fold more sensitive to agonist (Leu9’Ala mice). Ethanol conditioned a significant place preference in WT animals compared to saline. However, the time spent in the ethanol paired chamber was significantly reduced in α4, KO mice, suggesting a critical role for α4* nAChRs in alcohol reward. Conversely, a low, sub-rewarding dose of alcohol was sufficient to condition a place preference in Leu9’Ala mice; whereas the low dose had no effect in WT animals. To test the hypothesis that α4* nAChRs expression was critical for ethanol-induced activation of DAergic neurons within the ventral tegmental area (VTA), mice were injected with alcohol and c-Fos expression was measured as a marker for neuronal activation. In WT mice, a rewarding dose of alcohol produced a significant increase in the number of c-Fos immunopositive, tyrosine hydroxylase-immunopositive neurons compared to a saline injection indicating that alcohol activated these neurons. In α4 KO mice, alcohol injection did not significantly increase activation of VTA DAergic neurons compared to a saline injection. Finally, a sub-rewarding dose of alcohol had little effect on VTA DAergic neurons in WT mice; whereas this low dose significantly increased VTA DAergic neuron activation in Leu9’Ala mice. Together, our data indicate that α4* nAChR activation is involved in acute alcohol reward and that increased α4* nAChR agonist sensitivity can modulate the rewarding properties of the drug.

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P2X4 KNOCK OUT MICE DISPLAY SEX DIFFERENCES IN ALCOHOL INTAKE AND BEHAVIORAL RESPONSES

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P2X receptors (P2XRs) are a family of cation-permeable ligand-gated ion channels activated by synaptically released extracellular ATP. Of the P2XR subtypes, P2X4 is the most abundant subtype expressed in the CNS and to date is the most ethanol sensitive when measured in recombinant expression systems. A recent *in vivo* study identified the *p2rx4* gene as a candidate gene linked to alcohol intake and/or preference. Collectively, these findings led us to hypothesize that P2X4Rs play an important role in regulating alcohol intake, but direct evidence is lacking. The current study tests this hypothesis by investigating the role of P2X4Rs in alcohol intake using an intermittent limited access model that results in high levels of alcohol consumed in 4 hours that mimics “binge-like” drinking in humans. Adult male and female mice lacking the *p2rx4* gene (KO) and wild-type (WT) littermate controls were utilized. We found that P2X4 KO male and female mice drank significantly more 10% ethanol compared to WT littermate controls. Interestingly, the increase in alcohol intake persisted for the duration of testing (4 weeks, every other day) in the female KOs (KO = 5.73 g/kg ± 0.07; WT = 5.21 g/kg ± 0.08) while the effect was transient in male KO mice (only on 1st 10E exposure; KO = 5.16 g/kg ± 0.75; WT = 3.05 g/kg + 0.17). In addition, the duration of loss of righting reflex, produced by systemic administration of 3.6 g/kg ethanol, was significantly increased by 37% in male KOs and decreased by 33% in female KO mice, versus respective WT controls. Taken together, the data provide the first direct evidence that P2X4Rs play a key role in modulating high alcohol consumption and behavioral responses to ethanol, and that these responses appear to be sex dependent. Future studies aimed at delineating the sex-specific role P2X4Rs play in regulating ethanol intake and the specific neural pathways involved will provide insight related to targets for the development of novel therapeutics for the treatment of alcohol use disorders in males and females.
Support: NIH F31AA018926 (LRW), Tourette Syndrome Assoc and USC Zumberge Grant (MB), AA016981 and Dept of Veterans Affairs (DAF), AA03972 (RLA), AA13992 and INIA [Pilot project AA013517 (DLD)], USC School of Pharmacy.

2. MOLECULAR / CELL BIOLOGY C.N.S

a. Epigenetics 33–48/676–691

0676

WHOLE TRANSCRITOME AND METHYLOME SEQUENCING IN THE ALCOHOL POST-DEPENDENT RAT MODEL

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Background: Emerging evidence suggests that epigenetic alterations, including DNA methylation are important mechanisms underlying the long-term neuroadaptations observed in drug addiction. Furthermore, we previously found that increased methylation in the brain induced by injection of L-methionine (0.5g/kg, i.p) increases alcohol self-administration, similar to what is seen in our alcohol post-dependent rat model. In turn, intracerebroventricular infusion of RG-108 (DNMT inhibitor) significantly decreases alcohol consumption in the alcohol post-dependent rat, but not in the control rats. Thus, the aim of this study is to investigate the molecular mechanisms underlying the role of DNA hypermethylation in increased alcohol consumption.
Using next generation sequencing, we measured whole transcriptome and methylome in the medial prefrontal cortex (mPFC) to analyze the global regulation patterns associated with alcohol dependence.
Methods: Total RNA was run through the whole transcriptome sequencing protocol (n = 4/group). The methylated DNA fragments were captured with MBD2b/MBD3L1 heterodimer and sequenced following the DNA Chip sequencing protocol (Illumina®). Log2 transformation and normalization of the raw data using the Limma package from Bioconductor was used. WT and DNA Chip sequence reads were mapped to rat genomic sequences (UCSC rn4) using Bowtie.
Results: Whole transcriptome and DNA sequencing generated a total of 30 million and 22 million reads, respectively. 783 genes were found to be differentially regulated within our data set. 473 of the 783 genes were significantly down regulated. Ingenuity® analysis shows that most of the down regulated genes are involved in synaptic plasticity, calcium release and regulation of gene transcription. DNA methylation, induced by chronic alcohol exposure, may account for the significant decrease in gene expression in the mPFC. Preliminary analysis of the DNA Chip sequencing data shows 78 significant differences in methylation levels between the control and post-dependent rats and 5 of these differences are located in intronic region of genes that are found to be differentially expressed in the RNA sequencing.
Discussion: Our results show a significant alteration of mRNA expression in the mPFC following a history of alcohol dependence. DNA Chip sequencing data currently being analyzed will help us better understand the effect DNA methylation has on gene expression regulation induced by alcohol exposure.

0677

WITHDRAWN.

0678

FETAL ALCOHOL ALTERS THE HISTONE MARKS H3K4ME3 AND H3K9ME2 ALONG THE PROOPIOMELANOCORTIN GENE IN THE ARCUATE AREA OF THE HYPOTHALAMUS

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Hypothalamic proopiomelanocortin (POMC) neurons, one of the major regulators of the hypothalamic-pituitary-adrenal (HPA) axis, immune functions and energy homeostasis, are particularly vulnerable to the effects of fetal alcohol exposure. This vulnerability is manifested by hypermethylation of POMC gene promoter with a deficit in *POMC* gene expression and a decrease in protein levels of its derived opioid peptide β-endorphin. We previously demonstrated that fetal alcohol exposure significantly decreased the protein levels of the activation mark H3K4me3 and increased the protein levels of the repressive mark H3K9me2 in β-endorphin-producing POMC neurons. In this study, we specifically investigated if this deficit in gene expression and β-endorphin peptide production is also mediated by modulation of histone marks such as H3K4me3 and H3K9me2 along *POMC* gene in fetal alcohol exposed offspring. The spatial distribution of histone marks along a gene body plays a crucial role in transcriptional regulation and gene expression. We found by chromatin immunoprecipitation assay (ChIP) that fetal alcohol exposure from gestational days GD7-GD21 decreased in exposed male and female adult rats the occupancy of H3K4me3 along Exon 3 of *POMC* gene. Although the level of H3K9me2 was higher in alcohol exposed rats compared to controls, the occupancy of this mark was low and did not change significantly along Exon 3 or along POMC gene promoter in control and treated rats. Interestingly, the occupancy of the mutually exclusive histone marks H3K4me3 and H3K9me2 changed in opposite direction as expected along Exon 3 of *POMC* gene. Overall, this study shows a distinctive spatial distribution of H3K4me3 and H3K9me2 along *POMC* gene that reflects the modulation of POMC chromatin landscape in response to prenatal alcohol exposure. The reduction of H3K4me3 along Exon 3 of *POMC* gene could modulate the efficiency of Exon 3 splicing. This could be one of the causes of the decrease in generation of functional POMC transcripts and in production of functional β-endorphin peptides from hypothalamic *POMC* gene. (Supported by NIAAA grants R21 AA016695 and R37 AA0875715)

0679

ADOLESCENT, BUT NOT ADULT, BINGE DRINKING MODULATES MIR-590-3P EXPRESSION IN BRAIN

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Adolescent drinkers have a 4-fold higher risk for developing alcoholism, compared to those who start drinking in adulthood. Although the difference in risk is well documented, the mechanisms that underlie the preferential adolescent susceptibility are not understood. MicroRNAs (miRNAs) are a class of non-coding RNAs that coordinate gene-translation networks and are important regulators of development and maturation. Specific brain miRNAs may be selectively vulnerable to ethanol during adolescence, increasing the risk for subsequent addiction. Using an F1 FVB/NJ x C57BL6/J mouse model of high ''Drinking In Dark'' binge consumption, we tested the hypothesis that ethanol insult would drive brain miRNA expression in an age-dependent manner. Adolescent (P30) or adult (P70) F1 mice were given 4 hr/day access to 20% ethanol for 4 days beginning 3 hrs after dark. Brain tissue was harvested on day 4 after the final binge episode. MiRNA expression was assessed using an Exiqon high throughput qRT-PCR screen in an Age x Treatment design (n=5/group). Expression was normalized across 40 runs with interplate controls, and between subjects with internal control genes. Two-way ANOVAs were completed with significance set at a Benjamini Hochberg false discovery rate (FDR) q-value of <0.05 or <0.1, with post-hoc t-tests at p<0.05. The analysis of 540 mouse miRNA genes showed that, at FDR q<0.05, 11 brain miRNAs were altered in the transition from adolescence to adulthood. However, only one, miR-530-3p (ANOVA, q<0.005) was induced by ethanol in the adolescent (3.84 ± 0.52, p=0.009) but not the adult brain (0.55 ± 0.22, p=0.26). When FDR stringency was reduced to q<0.1, 157 suggestive changes were identified. Again, developmental changes predominated with 127 miRNAs showing age divergence in expression. However, 42 miRNAs met the criterion for an ethanol response with only 7 showing an interaction with age. Ethanol generally increased miRNA expression in brain, with very few miRNAs showing a decrease, suggesting that ethanol consumption is likely to repress translation of gene networks controlled by these miRNAs during the critical adolescent period. Our results further suggest that miR-590-3p, with a recently implicated role in neurodegeneration, may drive a portion of the increased risk of alcoholism among binge drinking adolescents. The mechanism of how this might occur remains to be elucidated. (Supported by NIAAA grants U01AA13475 (SEB) and R01AA013440 (RCM) and SPAARC.)

0680

EFFECTS OF ACUTE ETHANOL EXPOSURE ON MICRORNA PROFILING IN THE AMYGDALA OF RATS

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Regulation of gene expression by microRNA (miRNA) is an important epigenetic mechanism that has been shown to be involved in synaptic plasticity. We and others have shown that acute ethanol produced anxiolytic effects in rats. However, it is unknown if acute ethanol exposure alters miRNA expression profiling in the amygdala. In this study we examined the effects of acute ethanol exposure on the expression profiling of several microRNAs in the amygdala. Adult male Sprague Dawley rats were intraperitoneally injected with ethanol (1g/kg) or n-saline and one hour after the injection, rats were subjected to anxiety-like behavioral measurements using the light-dark box exploration test (LDB). It was found that acute ethanol exposure produced anxiolytic effects in rats. Immediately after the behavioral measures, the amygdala tissues were collected for the miRNA studies. Total RNA from the amygdala was isolated and complete miRNA profiling on rat amygdala tissue of n-saline and ethanol treated rats was performed using hybridization to a microRNA microarray chip, which utilizes the current Sanger miRBase Release 18. The experiment was analyzed using Student's t-test and statistically significant (p<0.05) changes in the expression of several microRNAs were observed in the amygdala due to acute ethanol exposure. We chose miRNA-494 as it showed the most robust down-regulation following acute ethanol exposure for further confirmation. Using quantitative real-time PCR we found significant down-regulation of mature miRNA-494 levels in the amygdala by acute ethanol, as observed in the miRNA profiling microarray. Interestingly, predicted targets of miRNA-494 include several genes that are involved in signaling pathways and synaptic plasticity. These results indicate that acute ethanol induced reduction in miRNA-494 levels in the amygdala may be involved in the molecular mechanisms associated with the anxiolytic effects of ethanol (Supported by NIH-NIAAA and VA Grants to SCP).

0681

EPIGENETIC CHANGES DURING ABSTINENCE: IMPORTANCE OF HISTONE DEACETYLATION

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Persistent alterations in brain gene expression have been proposed to underlie the risk for relapse in the recovering alcoholic. An important mechanism for long-term regulation of gene expression is through epigenetic chromatin modifications. We have previously identified epigenetic changes during abstinence in a mouse model of the low response to alcohol (ethanol, EtOH) endophenotype, the Withdrawal Seizure Resistant (WSR) selected mouse line. Notably, these changes in gene expression are absent in the high response to alcohol group (Withdrawal Seizure Prone, or WSP). WSR and WSP mice were exposed to intoxicating doses of EtOH vapor for 72 hours and then left abstinent for 21 days. In prefrontal cortex (PFC), gene expression profiling and bioinformatics identified 'histone deacetylase complex' as an overrepresented Gene Ontology (GO) category in the class of genes with highly dimorphic expression between the WSR and WSR mice during abstinence. We then employed quantitative PCR profiling using an array containing 84 genes involved in chromatin modification. Sixteen genes were significantly regulated in WSR samples and 12 genes were identified in WSP mice, only one gene showed significantly changed expression in both WSP and WSR PFC during abstinence (*Rps6ka5*). However, the direction of change was opposite (down in WSR, up in WSP), further supporting a strongly divergent pattern of gene expression during abstinence between these models. In addition, Class II histone deacetylase HDAC4 showed significant up-regulation in WSR mice while HDAC2 was regulated in WSP mice. HDAC4 immunohistochemistry in the PFC of abstinent WSR mice confirmed the up-regulated expression (1.34 fold, p=0.039), with increased staining density per cell compared to control mice indicating that increased expression of HDAC4 is primarily a result of increased expression in cells already expressing HDAC4. Modulation of histone acetylation is an important regulator of chromatin accessibility, with decreased histone acetylation as a result of increased histone deactylase activity resulting in decreased transcription at targeted loci. Thus, induction of HDAC4 would lead to decreased expression of HDAC4 targeted genes only in the low-response (WSR) group. The use of specific HDAC inhibitors to modulate the long-lasting gene expression changes observed during abstinence targeted to the low-response to alcohol individuals may have therapeutic effects.

0682

BINGE DRINKING OF ETHANOL IS CONTROLLED BY THE LEVEL OF CHROMATIN CONDENSATION

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Epigenetic mechanisms regulate gene expression by controlling the accessibility of DNA to the transcriptional machinery within the chromatin structure via DNA and histone methylation and acetylation. Specifically, histone acetylation induces a release of chromatin condensation, which increases gene expression. In contrast, DNA or histone methylation leads to the tight packaging of chromatin, resulting in repression of gene expression. These epigenetic mechanisms have been reported to play a role in drug and ethanol effects[1-3]. Here, we set out to determine whether altering the chromatin structure modifies the level of "binge-like" ethanol consumption in mice. To do so, we examined the actions of several agents that change the level of chromatin condensation on ethanol intake. We tested histone deacetylase (HDAC) inhibitors and a methyltranferase inhibitor (5-Azacytidine), that promote the relaxed form of chromatin, as well as a DNA methylation enhancer (methionine), which promotes chromatin condensation.

We used a behavioral paradigm that we previously shown to result in "binge-like" ethanol drinking in mice[4]. Specifically, C57BL/6J mice were housed in a reverse dark cycle. Two hours after the start of the dark cycle, mice had access to a solution of 10% or 20% ethanol (v/v) or saccharine (0.03%, w/v) for 4 hours every other day. We found that systemic administration of pan-HDAC inhibitors, Trichostatin A and suberoylanilide hydroxamic acid (SAHA), the HDAC class I inhibitor, MS-275, as well as the methyltranferase inhibitor, reduced binge-drinking of ethanol. Conversely, enhancement of DNA methylation promoted binge ethanol intake. We further found that these agents did not alter saccharin intake. Together, our findings suggest that the level of chromatin condensation plays a significant role in the mechanisms underlying the maintenance of ethanol intake, but does not change the motivation to drink an appetitive solution such as saccharin. Finally, our study further highlights the use of the FDA-approved drug SAHA (Vorinostat), and MS-275, which is currently in phase II clinical trials, as promising new drug candidates to treat alcohol use and abuse disorders.

1. Maze & Nestler 2011 Ann N Y Acad Sci
2. Pandey et al 2008 J.Neurosci.
3. Sakharkar et al 2011 ACER.
4. Neasta et al 2010 PNAS.

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0683

EFFECTS OF HISTONE DEACETYLASES INHIBITOR ON AMYGDALOID SYNAPTIC PLASTICITY MEASURES IN RATS DURING ALCOHOL DEPENDENCE

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Histone deacetylases (HDAC) induced histone modifications play an important role in synaptic plasticity associated with learning and memory. We recently reported that treatment with the HDAC inhibitor, trichostatin A (TSA) prevented the development of anxiety-like behaviors and corrected deficits in histone acetylation (H3-K9) in the central (CeA) and medial nucleus of amygdala (MeA) of rats. Here, we examined the effects of TSA treatment on synaptic plasticity measures [dendritic spine density (DSD) and levels of brain-derived neurotrophic factor and its target, activity regulated cytoskeleton-associated (Arc) protein] in the amygdaloid structures during ethanol withdrawal after chronic ethanol exposure in rats. Male adult Sprague Dawley rats were pair fed with Lieber-DeCarli control or ethanol diets. Ethanol diet-fed rats were gradually introduced to Lieber-Decarli diet containing ethanol and then maintained on ethanol diet containing 9%(v/v) ethanol for 15 days. Ethanol diet-fed rats were withdrawn for 0 and 24h. Both control and ethanol-withdrawn rats were treated with TSA (2 mg/kg; IP) or vehicle. Two hours after the injections of TSA, brains were processed for either Golgi-Cox staining to measure DSD or Arc and BDNF expression. We found that ethanol withdrawal produced significant reductions in DSD and protein levels of BDNF and mRNA and protein levels of Arc in the CeA and MeA, but not in basolateral amygdala (BLA) of rats. Interestingly, TSA treatment corrected the deficits in BDNF protein levels, Arc mRNA and protein levels, and DSD in the CeA and MeA of rats. We reported earlier that ethanol withdrawal produced an increase in HDAC activity and a decrease in histone acetylation (H3-K9&H4-K8) in the amygdaloid structures of rats. Taken together, these results suggest that HDAC-induced chromatin remodeling may be involved in the regulation of BDNF and Arc expression, and related DSD thereby altering synaptic plasticity during alcohol dependence

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0684

EFFECTS OF VARIOUS DOSES OF ETHANOL EXPOSURE ON HDAC AND DNMT ACTIVITIES IN THE EXTENDED AMYGDALA OF ADOLESCENT RATS

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Binge drinking is very common in teenagers and this can lead to abnormal brain maturation and behaviors. Epigenetic modifications, such as histone deacetylases (HDAC)-induced histone deacetylation and DNA methyltransferases (DNMT)-induced DNA methylation has been shown to regulate gene transcription and synaptic plasticity related to several behaviors. We examined the effects of various doses of ethanol on anxiety-like behaviors and HDAC and DNMT activities in amygdala and bed nucleus of stria terminalis (BNST) of adolescent rats (PND 31–34). We injected adolescent rats with ethanol (1, 2, 2.25, 2.5, and 3 g/kg IP) and measured anxiety-like behaviors one hour after injection using the light/dark box (LDB) exploration test. Immediately after behavioral measures, brains were collected and amygdala and BNST were used for the measurement of HDAC and DNMT activities in the nuclear and cytosolic fractions. It was found that ethanol exposure (1g/kg) was not able to produce an anxiolytic response or inhibit nuclear HDAC or DNMT activity in the amygdala. However, a lower dose of ethanol (1g/kg) was able to inhibit DNMT activity in the BNST. HDAC activity in the cytosolic fraction of amygdala or nuclear and cytosolic fraction of BNST was not modulated by any doses of ethanol exposure in the adolescent rats. Higher doses of ethanol (2, 2.25, 2.5, and 3.0 g/kg) were able to inhibit nuclear HDAC and DNMT activity in the amygdala and only DNMT activity in the BNST. We found that ethanol 2.0 or 2.25 g/kg produced anxiolytic effects in adolescent rats. However, higher doses of ethanol (2.5 and 3.0 g/kg) produced sedative effects as demonstrated by decreased total ambulations in LDB test. These results suggest that adolescent rats were less sensitive to the anxiolytic effects of ethanol, as 1g/kg ethanol did not produce anxiolytic effects. Furthermore, DNMT activity was inhibited both in BNST and amygdala, while nuclear HDAC activity was inhibited in amygdala by acute ethanol in adolescent rats. The inhibitory effects of ethanol on DNMT in BNST and amygdala and on HDAC in the amygdala of adolescent rats may produce a negative impact on brain maturation and psychiatric disorders such as anxiety and alcoholism at adulthood

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0685

HISTONE DEACETYLASES (HDAC) EXPRESSION PROFILING IN THE AMYGDALA DURING CHRONIC ETHANOL EXPOSURE AND WITHDRAWAL IN RATS

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Amygdaloid chromatin remodeling has shown to be an important mechanism that may be involved in the anxiolytic and anxiogenic effects of alcohol exposure and withdrawal, respectively. We have shown earlier that the anxiety-like behaviors during withdrawal after chronic alcohol treatment were associated with an increase in class I and II histone deacetylases (HDAC) activity in the amygdala of rats. However, it is unknown how ethanol treatment and withdrawal regulates the expression of various HDAC isoforms. In this study, we examined the expression profiling of various HDAC isoforms in the amygdala of rats during chronic ethanol exposure and withdrawal. Male adult Sprague Dawley rats were pair fed with Lieber-DeCarli control or ethanol diets. Ethanol diet-fed rats were gradually introduced to Lieber-Decarli diet containing ethanol and then maintained on ethanol diet containing 9%(v/v) ethanol for 15 days. Ethanol diet-fed rats were withdrawn for 0 and 24h. Control rats were fed with the control liquid diet. The rats were perfused and brains were used to measure protein and mRNA levels using gold immunolabeling and in-situ RT-PCR procedure, respectively. It was found that protein and mRNA levels of HDAC2 and HDAC3 isoforms were significantly increased in central (CeA) and medial nucleus of amygdala (MeA), but not in the basolateral amygdala (BLA) during ethanol withdrawal after chronic ethanol exposure. The chronic ethanol exposure and withdrawal had no effects on protein and mRNA levels of other HDACs (HDAC1, HDAC4, HDAC5 and HDAC6) in the CeA, MeA, or BLA of rats. These results suggest that only HDAC2 and HDAC3 among the HDAC family may be involved in decreasing histone acetylation(H3 &H4) in the CeA and MeA during ethanol withdrawal, as previously reported by us. Furthermore increased HDAC activity in the amygdala during ethanol withdrawal could be related to increased expression of HDAC2 and HDAC3 and these HDAC isoforms may be crucial in the pathophysiology of alcoholism
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0686

BINGE-LIKE ETHANOL CONSUMPTION SUPPRESSES DIMETHYLATION OF H3K9 SELECTIVELY IN THE NUCLEUS ACCUMBENS, BUT NOT THE AMYGDALA OR VENTRAL TEGMENTAL AREA

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A growing body of literature has implicated aberrant changes in gene expression induced by drugs of abuse as possible mechanisms for long-term neuroplastic changes that likely contribute to the transition to dependence. Posttranslational histone modifications, such as histone acetylation or methylation, can alter the extent to which downstream genes are expressed or repressed. Recently, administration of cocaine (acute, chronic and self-administered) has been shown to suppress the activity of histone methyltransferases, G9a and G9a-like protein (GLP), in the nucleus accumbens (NAc), resulting in decreased dimethylation of histone 3 lysine 9 (H3K9me2) and the activation of numerous genes involved in dendritic plasticity. The investigation of the role of histone modifications in response to administration of ethanol (EtOH) has focused mainly on histone acetylation, which has been implicated in the regulation of acute responses to EtOH, development of tolerance, and withdrawal. Data examining the impact of EtOH on histone methylation, however, are limited to in vitro preparations. Because regular binge EtOH consumption (i.e., drinking associated with BECs >80mg/dl) increases the risk for developing dependence, possibly via epigenetic mechanisms, the present study sought to determine the impact of binge-like (BL) EtOH consumption on H3K9me2 activity using 4-day drinking-in-the-dark (DID) procedures. On days 1–3, 3 hr into the dark cycle, C57BL/6J mice were given access to either water or 20% EtOH for 2 hr, and 4 hr on day 4 (BL drinking test). All EtOH drinking mice achieved BECs >100mg/dl during the BL drinking test. Immediately following the BL drinking test, brain tissue was collected and Western blots were performed on brain areas known to modulate EtOH intake (the NAc, ventral tegmental area [VTA], and amygdala [Amyg]) to determine changes in H3K9me2 expression. Densitometric analysis (using ImageJ, NIH) revealed a significant decrease in H3K9me2 in the NAc after BL EtOH consumption compared to water controls. No differences were found in H3K9me2 in the Amyg or the VTA. These results are consistent with the results with cocaine, and implicate a role for the suppression of H3K9me2 in modulating neurobiological responses to BL EtOH consumption. Theoretically, epigenetic modifications to histones induced by BL EtOH drinking may provide a novel mechanism by which BL EtOH intake increases the risk of dependence. (Supported by NIH grants AA013573 and AA015148).

0687

EPIGENETIC MODIFICATIONS ARE INVOLVED IN THE REGULATION OF ALCOHOL DRINKING BEHAVIOR

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Repeated alcohol-exposure and withdrawal is known to increase significantly subsequent voluntary ethanol intake in C57BL/6 mice. Chronic ethanol consumption-induced long-lasting adaptations of NR2B gene expression are considered to underlie behavioral phenotypes associated with alcohol drinking. Recently, we demonstrated that chronic intermittent ethanol (CIE) exposure and removal produced epigenetic modifications in the NR2B gene promoter. This suggests that such epigenetic regulation of the NR2B gene may be associated with animal drinking behavior. The present study investigated the impact of epigenetic regulation of NR2B gene expression on mice drinking behavior. To establish a CIE treatment model, male C57BL/6 mice were exposed to an alcohol inhalation chamber for 10h ethanol/14h room air exposure over a 10-day period. Changes in alcohol drinking behavior were measured using a two bottle choice design. Repeated exposure and withdrawal to ethanol increased subsequent ethanol consumption in these mice. The increase was prevented by systemic injection of an NR2B receptor subunit selective antagonist, ifenprodil, 30 min before exposure to the vapor chamber each day. The result suggests that the NR2B subunit is involved in the regulation of alcohol consumption. Furthermore, to investigate the role of epigenetic modifications in the development of alcohol drinking behavior, instead of exposing animals to the vapor chamber, 5-azacytidine (5'AZA), a DNA methyltransferase inhibitor, or Trichostatin-A (TSA), a histone deacetylase inhibitor, were chronically administrated to C57BL/6 mice for 7 days. TSA (2.5 μg/g BW, i.p.) -treated mice significantly increased ethanol intake relative to saline-treated mice. However, this was not seen after systemic administration of 5'AZA (2μg/g BW, i.p.). In order to determine of this was due to the inability of this compound to pass the blood brain barrier, we administrated it intracerebroventricularly (10μ/μl). Now, 5'AZA also significantly increased ethanol intake. Moreover, the increase was prevented by systemic injection of a methyl donor, *S*-adenosyl-*L*-methionine (100 or 300mg/kg BW, daily i.p.). Taken together, these results suggest that epigenetic modifications are involved in regulating alcohol drinking behavior.
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EFFECT OF DIFFERENT HISTONE DEACETYLASE INHIBITORS ON ALCOHOL DRINKING BY NON-DEPENDENT AND DEPENDENT RATS

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The development of effective treatments for alcohol dependence is a high public health priority. Alcohol dependence is reliant upon both genetic and environmental factors and occurs over time, requiring neuronal adaptations. Emerging evidence suggests that epigenetic alterations, including DNA methylation and histone modifications, are important mechanisms underlying alcohol addiction. Indeed, recent studies provided evidence suggesting the importance of chromatin remodeling in controlling gene transcription and revealed its possible implication in cocaine addiction and in alcohol withdrawal-induced anxiety (Pandey et al., 2008; Romieu et al., 2008).
In the present work we have investigated the effects of different histone deacetylase inhibitors (HDACi) on diverse components of ethanol addiction. We studied the efficacy of HDACi on excessive ethanol consumption in dependent Wistar rats using the operant ethanol self-administration paradigm. Dependence has been induced in rats by chronic and intermittent ethanol exposure to ethanol vapors (Simon O'Brien et al., 2011). We also assessed the effects of HDACi in others rodents model such as intermittent 20% ethanol intake and alcohol deprivation effect. Behavioral data show that HDACi can reduce and/or prevent different behavioral effects of alcohol. To further investigate the role of brain chromatin remodeling caused by histone modifications, we studied the expression of histone acetylation and HDAC activity in these models. Our results confirm that behavioral effects of HDACi are partly due to epigenetic mechanisms. These results suggest that HDACi might be an interesting target in the development of new treatments in alcoholism.
Pandey, S.C., Ugale, R., Zhang, H., Tang, L. & Prakash, A. (2008) Brain chromatin remodeling: a novel mechanism of alcoholism. J Neurosci, 28, 3729–3737.
Romieu, P., Host, L., Gobaille, S., Sandner, G., Aunis, D. & Zwiller, J. (2008) Histone deacetylase inhibitors decrease cocaine but not sucrose self-administration in rats. J Neurosci, 28, 9342–9348.
Simon O'Brien, E., Legastelois, R., Houchi, H., Vilpoux, C., Alaux-Cantin, S., Pierrefiche, O., Andre, E. & Naassila, M. (2011) Fluoxetine, desipramine, and the dual antidepressant milnacipran reduce alcohol self-administration and/or relapse in dependent rats. Neuropsychopharmacology, 36, 1518–1530.

0689

EPIGENETIC MODIFICATIONS IN THE WAKE-PROMOTING BASAL FOREBRAIN MAY CONTRIBUTE TO INSOMNIA DURING ETHANOL WITHDRAWAL

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Background: Sleep disturbances including insomnia are amongst the most profound and protracted symptoms of ethanol withdrawal. Moreover, insomnia during ethanol withdrawal predicts relapse to alcoholism. Recently, we have demonstrated that ethanol withdrawal-induced insomnia is due to reduction in the expression of genes involved in adenosine release and transmission resulting into increased activation of wake-promoting neurons in the cholinergic basal forebrain (BF). Histone acetylation plays a key role in the regulation of gene expression. Increased histone acetylation enhances the gene expression and vice-versa. Does chronic ethanol exposure reduce histone acetylation in the BF? To address this issue, we performed two experiments on male Sprague-Dawley rats.
Methods: In *Experiment 1*, ethanol dependency was induced by Majchrowicz's chronic binge drinking protocol. The controls (water-treated) and experimental (ethanol-treated) rats were euthanized on the withdrawal day i.e. 12 hr after the last dose of ethanol when insomnia-like symptoms begins to peak. The brain was removed, blocked and the BF region was sectioned and processed for acetylated histone immunohistochemistry. In *Experiment 2,* animals were stereotaxically implanted with sleep recording electrodes along with bilateral guide cannulas targeted towards the BF. Following post-operative recovery and habituation, rats were made ethanol dependent as mentioned above. On withdrawal day, at light onset, the animals were randomly divided into two groups. Group 1 animals were bilaterally microinjected with trichostatin (TSA; 10 nmol/1μL/each side), a histone deacetylase inhibitor, into the BF. Group 2 animals were bilaterally microinjected with the vehicle (10% DMSO/1 uL/each side). Subsequently, undisturbed sleep-wakefulness was continuously recorded for 24 hr.
Results: *Experiment 1* showed that there was a significant reduction ($p<0.05$; N=5) in the number of cells with acetylated histones in the BF region of ethanol dependent rats as compared to the controls (N=5). *Experiment 2* is underway. However, our initial results suggest that TSA treatment caused a profound reduction in the wakefulness with a concomitant increase in the sleep in ethanol dependent rats as compared to vehicle (N=2/group).
Conclusion: These initial results suggest that epigenetic mechanisms may have a pivotal role in causing insomnia observed during ethanol withdrawal.

0690

ASSESSMENT OF POST-TRANSLATIONAL HISTONE MODIFICATIONS FOLLOWING ETHANOL-INDUCED LOCOMOTOR SENSITIZATION IN DBA/2J MICE

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Chromatin modifications have been implicated as potential mechanisms contributing to the neuroplastic changes underlying drug and alcohol dependence. Post-translational histone modifications, including histone acetylation and methylation, have been prime targets of study. Recent evidence has implicated histone acetylation in the modulation of neurobiological responses to ethanol, but histone methylation (specifically histone dimethylation) has not been well characterized. DBA/2J mice develop robust behavioral sensitization to the locomotor stimulant effects of ethanol; neuroadaptations underlying this phenomenon are thought to occur within the mesolimbic dopaminergic pathway, and accumulating evidence suggests that chromatin remodeling may be involved. Here we examined the expression of histone modifications in key brain regions following the induction of ethanol-induced locomotor sensitization. Following habituation to testing chambers, forty-five male DBA/2J mice received a test injection (i.p.) of isotonic saline or 2.0 g/kg dose of ethanol immediately before being placed into an open-field activity chamber. This was followed by 10 days of saline (control and non-sensitized groups) or 2.5 g/kg ethanol (sensitized group) injections in the home cage. On the final test day, mice again received injections of saline or a 2.0 g/kg dose of ethanol immediately before being placed in the activity chamber. Forty-eight hours after the final injections, brain tissue was collected and Western blot procedures using anti-histone (lysine 9) acetylation (H3K9ac) and dimethylation (H3K9me2) antibodies were performed on brain areas previously implicated in locomotor sensitization. Relative to mice in the control and non-sensitized ethanol groups, mice in the sensitized ethanol group displayed a significantly augmented locomotor response to ethanol on the final test day. Analysis of Western blot data revealed that sensitized mice showed greater H3K9ac expression within the nucleus accumbens relative to saline treated mice; no significant differences in H3K9me2 protein expression were detected within this region. These results suggest histone modifications may play a role in ethanol-induced locomotor sensitization. Further analysis will determine if histone acetylation and/or dimethylation in other target regions may also play a role in this phenomenon. (Supported by NIH grants AA013573, AA015148, and AA019839).

0691

PRENATAL ALCOHOL EXPOSURE DISRUPTS EPIGENETIC MACHINERY INVOLVED IN HIPPOCAMPAL NEUROGENESIS RESULTING IN LEARNING AND MEMORY DEFICITS

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An average of 12% of women still consume ethanol during pregnancy despite alcohol's known teratogenicity. (Floyd et al. 2009) The myriad of cognitive deficits, including reduced fetal and adult neurogenesis resulting from alcohol exposure, have been well characterized. (Gil-Mohapel et al. 2011; Uban et al. 2010) Adult neurogenesis is thought to play a vital role in hippocampal-dependent modes of learning and memory and is quite sensitive to extrinsic factors including alcohol. (Shors et al. 2011) We have shown deficits in adult neurogenesis and hippocampal-dependent behavioral tasks after prenatal alcohol exposure (PAE) in mice. (Choi et al. 2005) Our exposure model involves voluntary drinking four hours per day throughout pregnancy resulting in average BEC of 68.5 ± 9.2 mg/dl after two hours drinking, increasing to 88.3 ± 11.5 mg/dl after four hours of drinking. (Brady et al. 2011) New data collected from our lab show deficits in context discrimination after this moderate exposure paradigm. While the link between PAE and learning and memory deficits is clear, the mechanism remains elusive. We hypothesize that this mechanism is epigenetic in nature and that PAE disrupts epigenetic machinery necessary for appropriately timed DNA methylation and histone modifications regulating neurogenesis in the hippocampus. Here, we show that the mRNA levels of several genes involved in epigenetic regulation, including histone demethylases and methyltransferases, are aberrant in hippocampi derived from PAE PD35 mice. For example, the fold regulation in histone 3 lysine demethlyases ranges from −1.32 to −1.67 with significance as low as 0.01 for some genes. Our preliminary protein data qualitatively shows changes in DNMT1, DNMT3a, and DNMT3b concentrations in PAE PD35 mice. These DNA methyltransferases play a key role in the timing, maintenance, and differentiation of neural progenitor cells in fetal neurogenesis (Sun et al. 2011); however, no studies have shown their role in adult neurogenesis with prenatal alcohol exposure. While studies have looked at the overall effects of alcohol on methyl-donor synthesis in the DNA methylation story (Zhou et al. 2011), our study is the first to look at the DNA methylation machinery itself for aberrant expression in the hippocampi of mice prenatally exposed to alcohol. [supported by: NIH-NIAAA T32A0A1412707 (CRT); NIH-NIAAA R01AA017449 (AMA); NIH-NIAAA F31AA020434 (MLB); NIH-NIAAA R03AA020101 (KKC)]

3. PHARMACOLOGY C.N.S.

a. Neurotransmitters **49–64/692–707**

0692

RELATIVE LOCATION OF $GABA_A$ RECEPTORS TRANSMEMBRANE AMINO ACIDS CRITICAL FOR ALCOHOL ACTION PROBED BY CYSTEINE SUBSTITUTION AND CROSSLINKING

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The $GABA_A$ receptor is a likely target for alcohols and volatile anesthetics. The transmembrane regions (TMs) 1, 2 and 3 provide at least one amino acid each that line a putative alcohol and volatile anesthetic binding site. However, the relative position of these amino acids is still uncertain, as the pocket they line could be located between or within receptor subunits. Introducing cysteines in TM locations (including some that are key to alcohol modulation), we tested the proximity of cysteine pairs by applying reducing (dithiothreitol, DTT) and oxidizing (Cu^{++}:phenanthroline) agents that may break or form disulfide bridges between cysteines that are close enough. The disruption or formation of disulfide bridges usually alters GABA-induced currents through the receptor. Wild-type and cysteine-mutant α1 and β2 $GABA_A$ receptor subunits were expressed along with wild-type g2 in *Xenopus laevis* oocytes. A cysteine located in either α1 TM1 [α1 (L232C)] or β2 TM2 [β2 (N265C)] was paired with a cysteine in different positions along β2 TM3. EC_{50} GABA-induced currents were recorded before and after application of DTT (2 mM) or Cu^{++}:phenanthroline (100:200 μM). Three pairs of cysteines appeared to crosslink. We will test alcohol and volatile anesthetics in $GABA_A$ receptors containing these cysteine combinations and a few others, after application of reducing or oxidizing agents. Our hypothesis is, if the cysteines that crosslink are located in the drug binding site, the drug's effect will be decreased. The results will be used to inform structural models based on recent high-resolution structures of related channels. Supported by the Waggoner Center for Alcohol and Addiction Research and the National Institute of Alcohol Abuse and Alcoholism, NIH (AA06399).

0693

REGIONAL PHARMACOLOGY OF $GABA_A$ RECEPTORS IN HUMAN ALCOHOLIC BRAIN

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The binding of [3H]flunitrazepam, [3H]flumazenil ([3H]Ro15-1788) and [3H]Ro15-4513, and the effects on this of unlabelled GABA and zolpidem, was used to assess the affinity, density, and pharmacology of sub-types of g-aminobutyrate type A (GABAA) receptors in five informative brain regions (Hippocampus; caudate; and inferior frontal, anterior cingulate and occipital cortices) obtained at autopsy from six alcoholic cases and 6 matched controls. The data for each radioligand were best fitted by a single-site non-cooperative binding model. Neither the patients' age nor the post-mortem interval was significantly correlated with the affinity or density of any binding site. The affinity of [3H]flunitrazepam did not differ between brain regions and case groups, but the other two ligands showed some variation. The affinities of GABA and zolpidem for the modulation of [3H]Ro15-4513 binding were markedly lower in hippocampus and caudate than in the cortical regions studied, whereas the slopes of these binding isotherms were distinctively different in occipital cortex. These variations in binding may inform the interpretation of PET data obtained from live imaging studies of human subjects

0694

ACTIVATION OF $GABA_A$ RECEPTORS AND INHIBITION OF NEUROSTEROID SYNTHESIS HAVE SEPARABLE ESTROUS-DEPENDENT EFFECTS ON BINGE DRINKING IN FEMALE MICE

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GABAA receptors containing δ-subunit proteins (δ-GABAAR) are particularly sensitive to low/moderate concentrations of alcohol, within the range relevant to the beginning stages of binge intoxication (BrEC's $\sim$80mg/dL or 17mM). These δ-GABAAR are also sensitive to neurosteroids, such as the neuroactive metabolite of progesterone, allopregnanalone(ALLO). This sensitivity may underlie the increased expression of these receptors during the diestrus phase of the female rodent estrous cycle, when progesterone synthesis reaches a nadir. We have previously reported that the ability to modulate binge drinking by selective activation of δ-GABAAR (with the high affinity agonist, gaboxadol) is dependent upon estrous phase (Melón et al., SfN 2010). The present series of experiments were designed to further clarify the estrous-dependent effects of activation of δ-GABAAR on binge drinking. Given the interaction between the δ-GABAAR and ALLO, as well as alcohol's effects on ALLO synthesis, we were also interested in demonstrating the effect that inhibition of neurosteroid synthesis would have on gaboxadol's estrous-dependent reduction of binge drinking. Using the Drinking-in-the-Dark (DID) binge model, regularly cycling females were given daily access to alcohol (20%v/v) for 2hours each day. Vaginal cytology was assessed after each drinking session to track estrous status. In experiment 1, animals were administered gaboxadol prior to their 8th day of access. In experiment 2, these methods were repeated, but mice received vehicle or finasteride (FIN) 22hr prior to their 8th day of access. Results from experiment 1 demonstrated that diestrus females were insensitive to the significant gaboxadol-induced decrease in binge drinking observed for proestrus, estrus and metestrus females. In experiment 2, vehicle and FIN treated diestrus females exhibited gaboxadol-induced reduction of their binge drinking, perhaps a result of habituation to the injection procedure. Surprisingly, FIN pretreatment significantly reduced binge drinking for estrus females. These studies suggest that ovarian-linked changes to extrasynaptic GABAA R and to neurosteroid activity may be important factors in the binge consumption of alcohol. Future studies will further explore the role that acute stress during diestrus may play in inhibiting the effects of δ-GABAA R activation on binge drinking. This work was supported by NIH grants AA016789 (SLB) and AA07462 (LCM), and the Indiana Alcohol Research Center.

0695

THE ROLE OF EXTRASYNAPTIC $GABA_A$ RECEPTORS IN THE ALCOHOL CONSUMPTION BEHAVIOR OF MICE SELECTIVELY BRED FOR HIGH ALCOHOL PREFEREENCE DRINKING

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Extrasynaptic $GABA_A$ receptors appear to be a target for the actions of alcohol at relatively low concentrations. Pharmacological studies in rodents using the selective agonist Gaboxadol (THIP) have found both promotional and inhibitory effects on alcohol consumption. The goal of this study was to determine the role of extrasynaptic $GABA_A$ receptors in the alcohol consumption of a second replicate of selectively bred High Alcohol-Preferring (HAP-2) mice. We hypothesized that chronic alcohol consumption in HAP-2 mice would be significantly reduced following systemic THIP administration. Naïve male and female HAP-2 mice were established on continuous access 2-bottle choice drinking for tap water or a 10% ethanol solution for 5 weeks before testing. Estrous status was also monitored in females due to the finding that the subunit composition of extrasynaptic $GABA_A$ receptors can be altered by progesterone levels, perhaps altering sensitivity to THIP. On test day, mice received systemic administration of THIP (0, 2, 4, or 8 mg/kg; i.p. injection) at the onset of the dark cycle. Due to THIP's short half-life (under 2 hours), hourly fluid intake was recorded for 2 hours post-injection at which point blood samples were collected from the retro-orbital sinus. THIP was found to significantly reduce alcohol intake ($p < .001$), although this effect was stronger in females. No effect of THIP on water intake was detected. For attained BEC values, no main effect of dose was found; however, females reached overall lower BECs ($p < .05$). Furthermore, no significant effects of estrous status were detected for alcohol consumption (p=.68) or BEC values (p=.25). However, the estrous status effect on BECs likely did not reach significance due to very small group sizes (n = 3–6); a statistical trend (p=.25) is apparent for a dose-dependent effect on BEC in non-estrous stages (metestrus and diestrus) which may become significant with larger group sizes. Even though some effects likely did not reach significance due to a lack of statistical power, the observed overall main effect of dose on alcohol consumption provides evidence that THIP acts in some capacity to reduce alcohol consumption in HAP-2 mice, implicating extrasynaptic $GABA_A$ receptors in the HAP-2 high alcohol consumption phenotype. Current efforts are aimed at increasing dose and estrous status group sizes.

0696

ADOLESCENT C57BL/6J MICE SHOW REDUCED SENSITIVITY TO THE NR2B-NMDA RECEPTOR ANTAGONIST IFENPRODIL, AS COMPARED TO ADULT MICE

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Adolescence is a developmental period marked by heightened risk taking, including binge-like patterns of ethanol intake. However, the neurobiological substrates underlying heightened binge drinking during adolescence remain elusive. Previous research from our laboratory has highlighted the importance of metabotropic glutamatergic signaling pathways to ethanol intake in both adolescent and adult mice, but less is known about the contribution of ionotropic glutamate receptors to binge-like ethanol intake. Therefore, using an intermittent limited-access procedure that reliably produces high levels of intake and blood alcohol concentrations over 80 mg/dl, we examined the contribution of the NMDA, AMPA and kainate receptors to binge-like ethanol intake in adolescent (4–6 wks) and adult (10–12 wks) C57BL/6J male mice. Briefly, mice were given access to a 20% v/v ethanol solution for 4 h/day, every other day. After 1 week of baseline intake, mice were administered vehicle, an NMDA receptor antagonist (ifenprodil, which targets NR2B-containing NMDA receptors) or a non-NMDA receptor antagonist (NBQX) prior to the limited-access session, and the effect on ethanol intake was recorded. Ifenprodil (30 mg/kg) significantly reduced ethanol intake in adult mice during early stages of the limited-access session (first 2 hrs). Although a reduction in the onset of binge-like ethanol drinking was observed in adult mice, this same dose also produced a pronounced locomotor deficit, supporting a nonspecific, sedative-like mechanism for the reduction in intake. In contrast, ifenprodil was without effect on either ethanol intake or locomotor activity in adolescent mice. Rather, a higher dose of ifenprodil (50 mg/kg) was required to see any alteration in motor activity in adolescents, supporting an age difference in sensitivity to this NR2B-specific NMDA receptor antagonist. The non-NMDA receptor antagonist NBQX, which targets both AMPA and kainate receptors, did not affect ethanol intake in either age group. These results support a developmental regulation of the expression of the NR2B subunit of the NMDA receptor, which may, in part, contribute to altered ethanol responding in adolescents. However, the lack of a specific regulation of ethanol drinking in either age group suggests that neither the NR2B-containing NMDA receptors or the AMPA/kainate receptors specifically regulate limited-access, or binge-like, ethanol intake. Supported by AA011605, AA016629, AA014983, and AA007573.

0697

ALCOHOL WITHDRAWAL ACTIVATES GABAERGIC NEURONS IN THE PREFRONTAL CORTEX AND PREDICTS COGNITIVE IMPAIRMENT AND ESCALATION OF ALCOHOL INTAKE

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Chronic-intermittent access to alcohol leads to the escalation of alcohol intake, similar to binge drinking in humans. Converging lines of evidence suggest that impairment of prefrontal cortex (PFC) cognitive function and overactivation of the central nucleus of the amygdala (CeA) are key factors that lead to excessive drinking in dependence. However, the role of the PFC and CeA in the escalation of alcohol intake in rats with a history of binge drinking without dependence is currently unknown. To address this issue, we examined Fos and GAD_{67} expression in the PFC and CeA and evaluated working memory and anxiety-like behavior in rats given continuous (24 h/day, 7 days/week) or intermittent (3 days/week) access to alcohol (20% v/v) using a two-bottle choice paradigm. The results showed that abstinence from alcohol in rats with a history of escalation of alcohol intake specifically recruits g-aminobutyric acid (GABA)-ergic (GAD_{67}+) neurons in the PFC and produces working memory impairments associated with excessive alcohol drinking during acute (24–72 h), but not protracted (16–68 days), abstinence. Abstinence from alcohol only slightly increased the number of Fos+ neurons in the CeA (10-fold lower than in the PFC) and was not associated with increased anxiety-like behavior. These results demonstrate that recruitment of a subset of GABAergic neurons in the PFC, but not CeA, during withdrawal is a key mechanism that leads to impaired executive control over motivated behavior, and suggest that the dysregulation of this component of the PFC may be an early index of neuroadaptation in alcohol dependence.

0698

ALLOPREGNANOLONE IMMUNOHISTOCHEMICAL STAINING IS REGIONALLY ALTERED DURING WITHDRAWAL FROM CHRONIC INTERMITTENT ETHANOL EXPOSURE IN C57BL/6J MICE

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The GABAergic neuroactive steroid allopregnanolone ((3alpha,5alpha)-3-hydroxypregnan-20-one) has been studied during ethanol withdrawal in humans, rats and mice. Previous work has shown that acute ethanol (2g/kg) did not alter serum levels of GABAergic neuroactive steroids in male C57BL/6J mice. Immunohistochemical detection of allopregnanolone allows brain region specific analysis of the effects of chronic intermittent ethanol (CIE) exposure and withdrawal. Given CIE exposure increases subsequent voluntary ethanol drinking, we examined brain regions known to influence this behavior. Adult male C57BL/6J mice were exposed to the CIE model of ethanol dependence. Briefly, after establishing stable baseline drinking using a limited access (2 hr/day) 2-bottle choice (15% ethanol vs. water) paradigm, mice received four cycles of chronic intermittent exposure (16 hr/day x 4 days) to ethanol vapor (EtOH group) or air (CTL group) in inhalation chambers. Exposure cycles 1–3 were followed by a week of daily limited access drinking. All mice were sacrificed and perfused at 8 hr following the final exposure cycle. Free floating brain sections (40 microns; 3–4 sections/region) were immunostained and analyzed for each animal. Data were transformed and expressed as a percent of CTL and compared to the values for the EtOH group. Withdrawal from CIE exposure (8 hr) produced region-specific effects on immunohistochemical detection of allopregnanolone levels across limbic brain regions. We observed significant increases in cellular allopregnanolone-like immunoreactivity in the prefrontal cortex, ventral tegmental area and the lateral amygdala. There was a trend for increased immunoreactivity in the nucleus accumbens and the medial division of the central nucleus of the amygdala. Ethanol-exposed mice showed ~2.5-fold increase in corticosterone levels. These data suggest that specific adaptations in GABAergic neurosteroids may be present in regions of brain that mediate anxiety, stress and drinking responses related to ethanol dependence. The present data are consistent with previous studies, which showed the peak of ethanol withdrawal at the 8 hr time point is characterized by elevated plasma corticosterone levels. Alterations in neurosteroid levels may have functional consequences that mediate behavioral adaptations to ethanol.

0699

ETHANOL ACTIONS IN C57BL/6J EXPOSED TO SOCIAL ISOLATION: EFFECTS ON HIPPOCAMPAL PLASTICITY AND ROLE OF NEURACTIVE STEROIDS

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Ethanol (EtOH) has been show to impair long-term potentiation (LTP) in the rodent hippocampus, an effect prevented by the 5α-reductase inhibitor finasteride, suggesting an involvement of locally released neurosteroids such as 3α,5α-THP (ALLOP). In animals exposed to prolonged stress such as social isolation (SI), an array of behavioral and neurophysiological changes, including altered EtOH sensitivity and plasticity of the GABAergic transmission were observed in comparison with group-housed control (GH) animals. In the present work we further examined the effects of SI on EtOH sensitivity and synaptic plasticity in dentate gyrus and CA1 synapses. C57BL/6J mice were subjected to SI for 6 weeks starting at PND 21 and compared to GH. Extracellular and single cell recordings of field excitatory postsynaptic potentials (fEPSPs) and GABA-mediated currents, respectively, were performed in hippocampal slices from both SI and GH mice. LTP induced in the CA1 region was significantly reduced in SI mice compared with GH animals. EtOH (40 mM) significantly reduced LTP only in SI but not in GH animals, and this effect was abolished by co-application of 1 μM finasteride. Current-clamp analysis performed in CA1 and DG neurons revealed a decrease in action potential (AP) frequency and an increase in the intensity of injected current required to evoke APs in SI mice compared with GH mice, suggesting a decrease in neuronal excitability associated with SI. In order to understand whether these effects were dependent on the reduction of ALLOP associated with SI, we treated SI mice with daily injections of progesterone (5 mg/Kg, s.c.). Such treatment reversed the decrease in neuronal excitability and LTP associated with SI in both DG and CA1 neurons suggesting that these changes might induced by the persistent decrease of circulating steroids during prolonged SI in mice.
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0700

GABAERGIC ACTIONS MEDIATE OPPOSITE ETHANOL EFFECTS ON DOPAMINERGIC NEURONS IN THE ANTERIOR AND POSTERIOR VENTRAL TEGMENTAL AREA

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It is known that posterior ventral tegmental area (p-VTA) differs from anterior VTA (a-VTA) in that rats learn to self-administer ethanol into p-VTA, but not into a-VTA. Since activation of VTA dopaminergic neurons by ethanol is a cellular mechanism underlying the reinforcement of ethanol consumption, we hypothesized that ethanol may exert different effects on dopaminergic neurons in p-VTA and a-VTA. In patch-clamp recordings in midbrain slices from young rats (P22–32), we detected no difference in electrophysiological properties between p-VTA and a-VTA dopaminergic neurons. However, acute exposure to ethanol (21–86 mM) stimulated p-VTA dopaminergic neurons but suppressed a-VTA dopaminergic neurons. Conversely, ethanol (> 21 mM) dose-dependently reduced the frequency of spontaneous GABAergic inhibitory postsynaptic currents (sIPSCs), generated by inhibitory neuronal firing but not the miniature IPSCs in p-VTA dopaminergic neurons. By contrast, ethanol increased frequency and amplitude of both sIPSCs and miniature IPSCs in a-VTA dopaminergic neurons. All these effects of ethanol were abolished by a $GABA_A$ receptor antagonist. There was a strong negative correlation between ethanol-evoked modulation of sIPSCs and neuronal firing in VTA dopaminergic neurons. These results indicate that GABAergic inputs play an important role in ethanol's actions in VTA. The differential effects of ethanol on sIPSCs and neuronal firing in p-VTA and a-VTA could be the basis for ethanol reinforcement via p-VTA.

0701

IN VIVO VOLTAMMETRIC MONITORING OF EVOKED DOPAMINE RELEASE IN PREFRONTAL CORTEX: EFFECT OF ACUTE ALCOHOL

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Dopamine modulates activity of the neurons in prefrontal cortex (PFC) and participates in top-down regulation of behavior, and the effect of alcohol on prefrontal dopamine release is not well understood. While dopamine release can be evoked by electrical stimulation of the ventral tegmental area (VTA), there are complications in its measurement. First, dopamine is indistinguishable from norepinephrine by using fast scan cyclic voltammetry (FSCV). Second, the VTA is anatomically close to the ventral noradrenergic bundle (VNB) that carries noradrenergic input to the PFC. Thus, it is difficult to separate dopamine from norepinephrine release. The current study was conducted to optimize the stimulation placement to evoke dopamine rather than norepinephrine release based on a depth analysis, and next to evaluate the effect of alcohol on dopamine release evoked by electrical stimulation of VTA neurons. Male Sprague-Dawley rats were anaesthetized with urethane. A bipolar stimulating electrode was placed above VNB/VTA, a carbon-fiber microelectrode was placed into the ipsilateral PFC, and a Ag/AgCl reference was placed in the contralateral cortex. Catecholamine overflow was detected with FSCV in response to electrical stimulation in the midbrain (60 Hz, 24 pulses, 120–125 μA).
Experiment 1: Catecholamine overflow was monitored in the PFC while the electrical stimulation was delivered at different depths (−5.0 to −9.4 mm). Electrical stimulation was delivered at 200-μm increments. Evoked catecholamine release reached a first maximum (1.2±0.2 nA) at the depth of −7.4 mm (VNB) and a second maximum (2.0±0.6 nA) at the depth of −8.6 mm (VTA). Thus, we could anatomically differentiate catecholamine release due to VNB and VTA.
Experiment 2: Presumed PFC dopamine release was evoked by VTA stimulation every 5 min in 2 rats. Dopamine signals were assessed at baseline, after saline and after alcohol (3 g/kg, i.p.). Basal evoked dopamine release was 1.6±0.04 nA. Saline did not influence the dopamine signals (1.5±0.1 nA), while alcohol decreased the signal to 25% below saline levels to 1.2±0.3 nA. Thus, these preliminary data suggest that alcohol modestly decreases electrically-evoked dopamine release in the PFC similar to its actions in the striatum.
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0702

CONDITIONED ODOR CUES ASSOCIATED WITH THE ACCESS TO OR THE ABSENCE OF ALCOHOL DIFFERENTIALLY MODULATE DOPMAMINE EFFLUX IN THE NUCLEUS ACCUMBENS SHELL

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Conditioned drug cues play a large role in drug craving and represent a key factor in drug relapse. Recent data from our laboratory show that odor cues that signal access to or the absence of alcohol differentially alter cFos expression within the nucleus accumbens shell (AcbSh). Given that dopaminergic activity within the AcbSh has been tied to the reinforcing properties of alcohol the current research sought to evaluate dopamine (DA) levels in the AcbSh while animals were exposed to odors that had been previously associated with alcohol access (CS^+), the absence of alcohol (CS^-), or possessed no predictive relationship in regard to alcohol access (CS^0). The current study utilized alcohol-preferring (P) rats that had previously undergone odor training and testing in a two lever operant chamber, (alcohol (15% v/v) on one lever; water on the second lever; CS^0 presented in neutral environment). Rats were randomly divided into three groups (CS^+, CS^-, CS^0 exposure) and underwent stereotaxic surgery to implant a guide cannula aimed at the AcbSh. Following one week of recovery, rats received a three day habituation period to the microdialysis chambers. At the conclusion of the habituation period, microdialysis probes were inserted into the AcbSh and animals underwent microdialysis testing 24 hrs later. After the collection of 3 baseline samples, odor stimulus presentation occurred for 3 samples with an additional 5 samples collected following odor presentation. Samples were analyzed using high-pressure liquid chromatography with electrochemical detection. The data show that the CS^0 did not significantly alter DA levels throughout microdialysis testing. Rats exposed to the CS^+ exhibited a significant increase in DA levels within the AcbSh (66% above baseline) whereas animals exposed to the CS^- exhibited a significant decrease in DA levels (33% below baseline). DA levels in the CS^+ and CS^- groups did not significantly differ from baseline levels over the final 5 samples. The current data show a divergent dopaminergic response within the AcbSh in regard to stimuli predictive of access to alcohol. Thus, DA release within the AcbSh may represent an underlying neurological mechanism contributing to the salience of conditioned drug cues associated with alcohol abuse and alcoholism. Paradigms that are similar to the current study may be useful in the development of novel pharmacotherapeutic interventions for use in populations with a high relapse rates.

0703

SEROTONIN-3 (5-HT_3) RECEPTORS WITHIN THE POSTERIOR VENTRAL TEGMENTAL AREA (P-VTA) MEDIATE ALCOHOL-SEEKING BEHAVIOR

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Previous studies indicated that 5-HT_3 receptors are involved in mediating the local reinforcing actions of ethanol (EtOH) within the p-VTA, and in regulating oral EtOH self-administraion. Another study demonstrated that activation of 5-HT_3 receptors within the p-VTA produces reinforcing effects. The objective of the current study was to test the hypothesis that 5-HT_3 receptors within the posterior VTA are involved in mediating alcohol-seeking behavior by examining the effects of microinjecting the 5-HT_3 agonist, (m-chlorophenyl)-biguanide (CPBG), or the 5-HT_3 antagonist, Zacopride, into the p-VTA while measuring EtOH-seeking behavior in the Pavlovian Spontaneous Recovery (PSR) test. Adult female alcohol-preferring (P) rats were trained in 2-lever operant chambers to self-administer 15% EtOH (v/v) and water on a concurrent fixed-ratio 5-fixed-ratio 1 (FR5-FR1) schedule of reinforcement in daily 1-hour sessions. After 10 weeks of concurrent access to EtOH and water, P rats underwent 7 extinction sessions (EtOH and water withheld), followed by 2 weeks in their home cages without access to EtOH or operant sessions. In the 2nd week of the home cage phase, rats were bilaterally implanted with guide cannulae aimed at the p-VTA; rats were allowed 7 days to recover before PSR testing. P rats [n = 4–5] were microinjected bilaterally with CPBG (0, 1 or 10 uM) into the p-VTA and then returned to the operant chambers in the absence of EtOH and water to undergo PSR testing. The vehicle treated groups significantly increased responding on the EtOH lever compared to extinction baselines ($p < 0.05$) in the 1st test session. One uM CPBG significantly enhance responding on the EtOH lever compared to vehicle control (63 ± 10 vs 130 ± 5 responses). In contrast, 10 uM CPBG significantly reduced responding on the EtOH lever to 16 ± 3, which was below extinction levels (35 ± 6 responses), suggesting that CPBG may be acting at other sites that prevent expression of EtOH-seeking behavior. Microinjection of Zacopride (100 and 200 uM; n=5–7) prevented responding on the EtOH lever compared to vehicle levels (25 ± 5 and 12 ± 3 responses with Zacopride vs 66 ± 8 responses with aCSF). Overall, the results suggest that 5HT_3 receptors in the p-VTA are involved in regulating EtOH-seeking behavior in P rats. (AA07611, AA07462, AA10721).

0704

DOPAMINE D1- RECEPTORS ARE REQUIRED FOR CONTEXT-INDUCED RENEWAL OF PAVLOVIAN CONDITIONED ALCOHOL-SEEKING IN RATS

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Rationale: Environmental contexts associated with drug intake can induce craving in humans, but the neuronal mechanisms underlying this effect remain unknown. *Objective* We used an animal model to test the hypothesis that dopamine neurotransmission at D1-receptors was required for context-induced renewal of Pavlovian conditioned alcohol-seeking in rats.
Methods: Male, Long-Evans rats learned to discriminate between two 10-sec auditory stimuli (white noise and clicker). One stimulus (CS+) was paired with 15% ethanol (EtOH, 0.2 ml per CS+, 3.2 ml per session) and the second (CS-) was presented without EtOH. Each CS was randomly presented 16 times during a single session 54-min session, according to independent variable-time 67-sec schedules. Port-entries into the fluid receptacle where EtOH was delivered were measured before, during and after each CS. Pavlovian discrimination training occurred in operant conditioning chambers to which distinctive contextual stimuli were added to form a specific environment (Context A). Following 19 training sessions, behaviour was extinguished in a different environmental context (Context B; 8 sessions) by presenting both cues without EtOH. At test, rats were injected with saline (1 ml/kg, s.c.) or a dopamine D1-receptor antagonist, SCH 23390 (10 μg/kg, s.c.) and placed into the prior training context (Context A) where the cues were presented without EtOH. In a control study, different rats (n=11) learned to lever press for 10% sucrose (0.1 ml per press) on an FR1 schedule during 6 daily 30 min sessions. Using a within-subjects design, rats received either saline (1 ml/kg, s.c.) or SCH 23390 (10 μg/kg, s.c.) before a test of sucrose seeking under extinction conditions.
Results: Across Pavlovian discrimination training rats developed higher response levels to the EtOH-predictive CS+, compared with the CS-. Across extinction in Context B, port entries during the CS+ responses gradually decreased. At test, placement into Context A triggered a significant increase in CS + responses for saline pre-treated rats, but not for rats infused with SCH 23390. There was no difference in sucrose-seeking between rats infused with saline or SCH23390.
Conclusion: These findings suggest a critical role of dopamine acting at D1 receptors in the renewal of Pavlovian-conditioned alcohol-seeking.

0705

EFFECTS OF CNQX, SCH23390 AND TETRODOTOXIN IN THE POSTERIOR VENTRAL TEGMENTAL AREA ON ETHANOL- AND SUCROSE-SEEKING AND DRINKING

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Background: The ventral tegmental area (VTA) is a pivotal relay site within the brain's reinforcement circuit that has been shown to play a role in ethanol-motivated behaviors. The primary dopamine projections within this system originate in the VTA and innervate several areas including the nucleus accumbens (NAc) and prefrontal cortex (PFC), and the PFC has afferent glutamate projections to the VTA and the NAc. The following studies utilized two different operant paradigms, one focusing on reinforcer-seeking and one on reinforcer drinking, (both with an ethanol and a sucrose reinforcer solution) to elucidate regulation of these behaviors by the posterior VTA, and the specific roles of dopamine and glutamate in this region.
Methods: The present experiments assessed the effects of microinjections of the glutamate (AMPA/kainate) antagonist CNQX and the dopamine D1-like antagonist SCH23390 in the posterior VTA, as well as transient chemical inactivation of this region using tetrodotoxin (TTX). In four separate experiments, (two Dopamine, two Glutamate, both with TTX) male Long Evans rats (n=6–10 group) were trained to complete a single response requirement that resulted in access to 10% ethanol or 2% sucrose for a 20-min drinking period. Results: Prior to drug/TTX microinjections, ethanol-reinforced subjects were consuming ~0.45–0.65 g/kg ethanol and making ~50 responses during intermittent non-reinforced (extinction) aCSF sessions (Sucrose Groups had similar baseline response levels). Overall, TTX inactivation of the VTA consistently and significantly ($p<.01$-$.05$) decreased reinforcer-seeking [for both ethanol (by 68–80%) and sucrose (by 76–79%)] but NOT intake in all experiments. CNQX also significantly ($p<.01$) and dose-dependently decreased ethanol-seeking (by up to 53%), with no effect on sucrose-seeking or reinforcer intake. SCH23390 had no effects on reinforcer-seeking, and very moderately decreased intake of both ethanol and sucrose. Discussion: Using this behavioral model, rats consume ethanol in "pharmacologically relevant" binges, and distinct assessment of seeking responses versus drinking behavior is possible. Inactivation of the posterior VTA implicated this region in reinforcer-seeking as opposed to reinforcer intake. Overall, the present findings provide support for the importance of posterior VTA glutamate activity specifically in ethanol-seeking behavior in animals consuming pharmacologically relevant amounts of ethanol.

0706

ENDOCANNABINOIDS AND FEAR-RELATED BEHAVIOR IN MICE SELECTIVELY BRED FOR HIGH OR LOW ALCOHOL PREFERENCE

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Alcohol-naïve mice selectively bred for high alcohol preference (HAP) show greater fear potentiated startle (FPS), a model for anxiety and fear-related disorders such as post-traumatic stress disorder (PTSD), compared to their counterparts bred for low alcohol preference (LAP). The endocannabinoid system (ECS) modulates anxiety-related and alcohol drinking behaviors and has been identified as a promising target for pharmacotherapies to treat anxiety disorders and alcoholism. The purpose of this study was to determine whether brain region specific levels of the endocannabinoids, anandamide (AEA) and *sn*-2 arachidonylglycerol (2-AG), are associated with genetic propensity toward alcohol drinking and fear-related behavior in HAP1 and LAP1 mice. Naïve male and female HAP1 and LAP1 mice were randomly assigned to a fear-conditioned (paired light+shock), shock control (unpaired light+shock), or no shock control (light only) group. Twenty–four hrs after conditioning procedures, all mice received an FPS test after which the prefrontal cortex (PFC), amygdala (AMG), and hippocampus (HIPP) were rapidly dissected. Tissue levels of AEA and 2-AG were analyzed using mass spectrometry. HAP1 males showed greater FPS than LAP1 males but no line difference in FPS was seen in females. Significant line x sex x conditioning group interactions were found for AEA in the HIPP and 2-AG in the AMG. In the HIPP, LAP1 females had greater AEA than HAP1 females in the no shock control groups; HAP1 fear-conditioned females had greater AEA than HAP1 female control groups (both shock and no shock). In the AMG, LAP1 females had greater 2-AG than HAP1 females in the fear-conditioned groups. These results show that fear-conditioning elevates AEA in the HIPP to a greater extent in HAP1 than LAP1 females and elevates 2-AG in the AMG of LAP1 but not HAP1 females. Results from the current study suggest line differences in FPS that are sex-specific; however, the absence of a line difference in FPS in female mice is not consistent with our prior work in the HAP1 and LAP1 lines. Overall, these findings suggest line- and sex-dependent differences in endocannabinoid levels within specific brain regions before and after fear-conditioning which could be related to line/sex differences in FPS. Additional work in this animal model may facilitate the identification of pharmacotherapies that target the ECS for the treatment of anxiety disorders and alcoholism. Supported by AA019529.

0707

THE REDUCTION OF ALCOHOL CONSUMPTION BY MEMANTINE IS MEDIATED VIA A BDNF-DEPENDENT MECHANISM

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Despite the increasing number of studies in the alcohol field only few medications are efficient and available to control alcohol (EtOH) consumption. Recent studies show that the glutamate is one of the neurotransmitter most involved in addiction. Among the different pharmacological agents acting on the glutamatergic system, memantine, a partial antagonist of the NMDA receptors, might be a potential candidate to treat alcoholism. Indeed, memantine induces expression of BDNF in several brain regions implicated in addiction such as the striatum and the prefrontal cortex). We previously showed that BDNF within the striatum is part of a homeostatic pathway regulating EtOH consumption.
The aims of this work were to study the effects of systemic injections of memantine on EtOH self-administration in rats and then to test our hypothesis stating that the memantine effect on EtOH consumption is mediated *via* the BDNF signalling pathway.
We found that memantine decreases EtOH self-administration and motivation to consume EtOH 6 hrs and 30 hrs post-injection (but not glucose self-administration). Moreover, we found that inhibition of the BDNF receptor TrkB by intracerebroventricular micro-infusion of K252a 2 hours after the memantine injection (but not 26 hrs after) totally blocks the decrease induced by memantine suggesting that the early memantine effect on EtOH consumption is mediated by the BDNF signalling pathway. Real-time PCR experiments conducted with prefrontal cortex samples show that BDNF expression is indeed increased 4 hrs post-memantine injection, however it is decreased at 26 hrs post-injection. Interestingly, 26 hrs after the injection of memantine, expression of the genes coding for NPY and for TH, known to be involved in the regulation of EtOH consumption, is increased in the prefrontal cortex.
This study provides evidences that memantine specifically decreases EtOH self-administration and motivation to consume EtOH for at least 30 hrs and that the early effect of memantine (6 hrs) is BDNF –dependent whereas the delayed effect (30 hrs) is BDNF-independent and might be NPY and dopamine-dependent.

4. PHYSIOLOGY C.N.S.

a. Electrophysiology 65–80/708-723

0708

ALCOHOL ENHANCES $GABA_A$ INHIBITION OF CEREBELLAR GRANULE CELLS IN LOW PREFERRING DBA/2J MICE BUT SUPPRSSESS $GABA_A$ INHIBITION IN HIGH PREFERRING C57BL/6J MICE

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In humans, low cerebellar sensitivity to alcohol is associated with high risk for alcohol abuse, but the cellular mechanisms underlying such differential sensitivity are unclear. We recorded from cerebellar granule cells (GCs) in slices from high- and low-alcohol preferring C57BL/6J (B6) and DBA/2J (D2) mice to test the hypothesis that low sensitivity to alcohol-induced enhancement of $GABA_A$ inhibition corresponds to high alcohol preference. Contrary to previously published data in Sprague Dawley rats (SDRs) showing that alcohol consistently enhances tonic $GABA_A$ inhibition in GCs, a significant proportion of D2 and B6 GCs (35% and 38%, respectively) were unresponsive to EtOH (up to 52mM). Furthermore, of the cells that responded to EtOH, we detected both enhancement and suppression of tonic $GABA_A$ inhibition. The distribution of response type varied as a function of preference phenotype, with enhancement and suppression of tonic $GABA_A$ inhibition being significantly greater in D2 and B6 mice respectively. The average amplitude of these antipodal responses across all cells resulted in a net increase in GC tonic $GABA_A$ inhibition in D2s but a net decrease in B6s. In parallel studies in GCs from low drinking SDRs, we determined that the enhancement of tonic $GABA_A$ inhibition is mediated by inhibition of nitric oxide synthase (NOS), since blocking NOS prevented enhancement by EtOH. Although direct inhibition of NOS also caused an increase in $GABA_A$ inhibition in B6 GCs, the magnitude of the enhancement was significantly less than in SDRs. Immunocytochemistry confirmed reduced expression levels of NOS in the GC layer of B6 mice relative to SDRs. Thus, the lack of enhancement of tonic $GABA_A$ inhibition by EtOH in the majority of B6 GCs results from reduced expression of NOS. In B6 GCs that showed EtOH-induced suppression of tonic $GABA_A$ inhibition, there was no change in sIPSC frequency, and the suppression was not blocked by TTX. Thus, suppression of tonic $GABA_A$ inhibition in B6 GCs may be due to direct actions of EtOH on extrasynaptic $GABA_A$ receptors that mediate tonic inhibition. Together, our study identifies antipodal actions of EtOH on GC tonic inhibition: enhancement mediated by inhibition of NOS, and direct inhibition of extrasynaptic $GABA_A$ receptors. The differential expression of these two opposing mechanisms may be a cellular mechanism underlying differential sensitivity of the cerebellum to EtOH, an important risk factor for alcohol abuse in humans.

0709

ETHANOL AND BARBITURATE INCREASE NEURAL OSCILLATIONS IN CEREBELLUM
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Our goal is to examine how ethanol affects cerebellar motor function. Neural oscillations have been suggested to be important in movement control. Cerebellar neural oscillations have been suggested to be important in movement modulation, particularly in movement anticipation. Since ethanol (2g/Kg, ip) does not always eliminate motor activity while barbiturate anesthesia (Pentobarbital 60mg/Kg, ip) always does, we have compared the effect of ethanol and barbiturate anesthesia on neural oscillations in the rat cerebellum. Since it is thought that a major function of the Golgi cells is to dynamically gate the transmission of mossy fiber information to the granule cells at the input stage of the cerebellar cortex, we have sampled granule cells and Golgi cells. By the dynamic nature in cerebellar movement coordination, a major function of the Purkinje cells is thought to be the coding of temporal information for motor control as the output of the cerebellar cortex. We have therefore also sampled Purkinje cells. We first examined the temporal discharge characteristics of neuronal spike trains from the anterior lobe of conscious, unrestrained rats. We focused on the effect of ethanol and pentobarbital on the discharge rate, the distribution of inter-spike-intervals, the autocorrelogram, and the power spectrum from the fast Fourier transform (FFT) analysis. Our results showed that (1) the temporal characteristics of spike trains for Golgi cells and Purkinje cells were distinctively different by every one of the above temporal measures in the three behavioral states (awake, ethanol, or barbiturate), thereby providing a reliable multi-dimensional, on-line identification of putative cell types. (2) Purkinje cells transmitted the bulk of their information in the awake state within a bandwidth of 0–30 Hz. Although Golgi cells typically discharged at a lower rate than Purkinje cells, Golgi cells appeared to transmit information over a broader bandwidth of 0–100 Hz. (3) Ethanol and barbiturate increased the discharge rates of Golgi cells and Purkinje cells by shifting the power distribution toward a higher frequency accompanied by an increasing tendency for neural oscillations at that frequency. (4) Golgi cell oscillations have been suggested to be linked to experimental cerebellar ataxia. Our observations, however, suggest that cerebellar neural oscillations are likely to be pathological and not a part of normal movement modulation mechanisms of the cerebellum.

0710

ALCOHOL AND OPIOID MODULATION OF GABAERGIC TRANSMISSION IN DOPAMINERGIC CELLS IN THE PERIAQUEDUCTAL GRAY (VPAG)
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The ventral periaquaductal gray (vPAG), a region strongly implicated in negative affective disorder and ethanol withdrawal, is interesting due to its cell type heterogeneity, including a sub-population of dopamine neurons. Several studies have shown that dopamine neurons in the vPAG are required for opioid-mediated antinociception and locomotor sensitization. However, to date, there have been no studies of how drugs of abuse can alter these neurons. Our initial studies focused on the ability of acute alcohol to modulate functions in these neurons. We found, surprisingly, that acute ethanol had no impact on GABAergic transmission. This finding suggests that the dopamine neurons located in the PAG are differentially altered by alcohol when compared to dopamine neurons in the ventral tegmental area. Ongoing studies in the lab are examining the impact of chronic alcohol vapor exposure. Previous studies have found that alcohol exposure leads to an upregulation of dynorphin, the endogenous kappa opioid receptor (KOR) agonist, in the PAG. KORs have been linked to anxiety, depression and withdrawal, thus we hypothesize that upregulation of this system in the PAG may play a role in the negative affective state during alcohol withdrawal. We first sought to evaluate how this might impact dopamine neuron functions in the PAG. We found that activation of KOR lead to a reduction of GABAergic transmission in the PAG, similar to what was observed in previous studies in the BNST. We next examined the signaling mechanisms of KOR activation-induced attenuation of GABAergic input. Upon KOR activation, several downstream signaling pathways, including the ERK1/2 and MAPK p38 pathways, are activated. Studies have suggested a link between both the rewarding properties and withdrawal of alcohol to ERK signaling in other brain regions. Preliminary data in miniature inhibitory postsynaptic currents (mIPSC) frequency and amplitude suggests that KOR activation-induced attenuation of GABAergic input on the vPAG dopamine neurons are mediated via the ERK1/2 pathway, but not the p38 pathway. Ongoing studies investigate the effects of chronic ethanol exposure on kappa opioid functions by using ethanol vapor chambers. Selective recording from eGFP+ neurons of these transgenic mice will enable understanding of the role of vPAG dopamine neurons in drug abuse, abstinence, craving, relapse, and series of behaviors.

0711

ACUTE ETHANOL EFFECTS ON ENDOCANNABINOID-MEDIATED PLASTICITY OF DORSOLATERAL STRIATUM INHIBITORY MICROCIRCUITRY
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The purpose of this study is to elucidate the circuit dynamics underlying ethanol-induced disinhibition of the dorsolateral striatum, a basal ganglia substructure necessary for habit learning. The principal cell type of the striatum is the medium spiny neuron (MSN). These GABAergic neurons project to downstream basal ganglia sites via the direct and indirect pathways. MSN output is inhibited by GABAergic innervation arising from other MSNs and from striatal fast-spiking interneurons (FSIs). When direct and indirect pathway MSNs are voltage clamped at a depolarized ''up state'' these cells express a form of endocannabinoid-mediated long-term depression (eCB-LTD) selectively of the GABAergic input arising from MSN collaterals. However, when direct, but not indirect, pathway MSNs are clamped at a hyperpolarized ''down state'' these cells express a different form of eCB-LTD that involves both MSN and FSI inputs. Here, we hypothesize that ethanol interacts with this inhibitory microcircuit eCB signaling system to enhance the disinhibition of the direct pathway, a neural circuit operation thought to encode action reinforcement. To test this, we examine acute ethanol effects on FSI-MSN and MSN-MSN GABAergic transmission, and on up and down state forms of eCB-LTD using whole-cell patch clamp electrophysiological recordings combined with optogenetics in the adult mouse striatal slice preparation. Bath application of ethanol (50 mM) depresses both MSN-MSN and FSI-MSN GABAergic transmission evoked by selective light-induced activation of channelrhodopsin that is virally expressed in presynaptic MSNs or FSIs. We also find that in the presence of ethanol, up state eCB-LTD is completely lost, but down state eCB-LTD is preserved. We conclude that ethanol disinhibits dorsolateral striatum MSNs, and that further disinhibition of the direct pathway may occur through selective retention of the down state form of eCB-LTD. These results may provide mechanistic insight into the reinforcing properties of ethanol.

0712

ETHANOL INTERACTIONS WITH NICOTINIC RECEPTORS IN BRAINSTEM CHOLINERGIC CENTERS
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A. The goal of this study was to investigate the role of brain alpha7* nicotinic receptors (alpha7* nAChRs) in ethanol induced motor impairment.
B. We tested the effect of bath applied ethanol on alpha7* nAChR mediated currents using whole cell patch clamp recording in tissue slices including a brainstem cholinergic center, the lateral dorsal tegmental nucleus (LDTg) from adult rats. Ethanol induced motor impairment was tested using the accelerating rotarod.
C. Bath application of ethanol at low, physiologically relevant levels (1–10 mM) caused a profound reduction in the magnitude of the alpha7* nAChR responses. Interestingly, the inhibitory effect of ethanol on alpha7* nAChRs was blocked by either the PKA inhibitor H89 or the adenylate cyclase inhibitor SQ22536 (introduced via the recording electrode solution). Bath application of PKA activators potentiated LDTg alpha7* nAChR currents, while inhibitors suppressed these currents. Bath application of the alpha7* nAChR positive allosteric modulator PNU120596, which interferes with alpha7* nAChR desensitization, eliminated the modulatory effects of ethanol on alpha7* nAChRs. Thus, ethanol may inhibit alpha7* nAChRs by enhancing desensitization through inhibition of the PKA pathway. Nicotine increased the frequency of miniature EPSCs in the mediodorsal thalamus, a brain region involved in motor control that receives extensive cholinergic input from the LDTg. This presynaptic effect of nicotine was significantly reduced either by MLA or 10 mM ethanol. Finally, using an accelerating rotarod to assess motor performance, we found that intra-cerebroventricular injection of PNU120596 reduced the motor impairment with systemic ethanol administration.
D. These findings suggest that the motor impairment by ethanol is mediated, at least partially by a reduction in alpha7* nAChR-mediated excitation.

0713

BLOCKADE OF PRESYNAPTIC BK CHANNELS OCCLUDES ETHANOL-INDUCED ENHANCEMENT OF GABAERGIC TRANSMISSION IN THE RAT CENTRAL NUCLEUS OF THE AMYGDALA

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The large conductance Ca^{++} and voltage-dependent BK potassium channel is modulated by ethanol and is involved in acute tolerance to ethanol effects (Martin et al., PNAS 105:17543, 2008). In the present study we examined the role of presynaptic BK channels in modulating ethanol actions on inhibitory synaptic transmission mediated via $GABA_A$ receptors in the rat central nucleus of the amygdala. In the presence of TTX (1.0 μM), CGP55845 (1.0 μM) and kynurenic acid (3 mM), we isolated miniature spontaneous post-synaptic inhibitory currents (mIPSCs) from neurons within the central nucleus using whole-cell voltage clamp techniques and analyzed their response to selective BK channel antagonists and ethanol. Bath application of the selective BK channel blockers paxilline (10 μM, n=7) or iberitoxin (200 nM, n=3) for 10 minutes significantly increased the frequency of mIPSCs, respectively (K-S test, $p<0.001$). Similarly, 50 mM ethanol (n=5) also enhanced mIPSC frequency (K-S test, $p<0.001$). Increases in mIPSC frequency by selective BK channel antagonists or ethanol were not accompanied with changes in amplitude of mIPSCs. Furthermore, following bath application of selective BK channel blockers for 10 min, ethanol (50 mM, n=7) failed to further increase mIPSC frequency (KS test, $p>0.05$). The present results suggest that presynaptic BK channels could serve the loci of action for modulating neurotransmitter release and that blockade of presynaptic BK channels occludes the effect of ethanol on inhibitory synaptic transmission in the amygdala, a critical brain region involved in alcohol abuse and addiction.
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0714

TARGET SPECIFIC EFFECTS OF NEUROPEPTIDE SYSTEMS IN THE CENTRAL AMYGDALA

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Endogenous neuropeptides likely play a role in mediating ethanol dependence, including opioid peptides and the stress-related peptide, corticotropin releasing factor (CRF). However, these neuropeptides and their receptors localize heterogeneously, in some case exclusively, in subpopulations of neurons and may affect neuronal excitability in opposing ways. Therefore, in this study we examined the sensitivity of the mu opioid and CRF systems in subpopulations of central amygdala (CeA) neurons projecting to specific extrinsic target areas en route to understanding ethanol effect in the specific pathway. We used whole cell patch recording techniques in brain slices from Sprague Dawley rats 5 days after injection of a retrograde tracer (Neuro-dil) into either the bed nucleus of the stria terminalis (BNST) or the locus coeruleus (LC). To study isolated inhibitory synaptic neurotransmission as well as membrane effects on target specific CeA neurons, we used K^+-containing internal pipette solutions while pharmacologically blocking excitatory neurotransmission. Among 14 CeA neurons targeting BNST, the mu opioid receptor agonist DAMGO (1 μM) hyperpolarized 9 neurons (64%) while CRF (100 nM) depolarized 6 neurons (42%); 4 neurons showed sensitivity to both. In 7 of 9 neurons, the postsynaptic effect of DAMGO was accompanied by a decrease in spontaneous GABAergic synaptic events, suggesting that afferents to these neurons are also DAMGO sensitive. Of those 7 neurons, 5 showed a CRF-induced *increase* in the frequency of spontaneous synaptic events. In contrast among 5 of 5 neurons projecting to the LC were insensitive to DAMGO, while 4 of 5 were depolarized by CRF (80%) without any change in the frequencies of inhibitory neurotransmission. These results confirm that the heterogeneity between and within subpopulations of CeA neurons projecting to specific target regions. However, 2 of 2 cells from each group showed ethanol (40 mM) enhancement of evoked IPSC amplitude. Our data suggest that BNST-projecting CeA neurons are relatively more sensitive to postsynaptic DAMGO effects, while LC-projecting CeA neurons may be exclusively sensitive to postsynaptic CRF effects, though these cells may not differ in ethanol sensitivity. Further exploration of these effects may facilitate our understanding of acute ethanol actions and the subsequent plastic changes in CeA neural networks underlying ethanol dependence.
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0715

PKA MODULATES PHYSIOLOGICAL CHANGES IN $GABA_A$ RECEPTORS ASSOCIATED WITH ETHANOL EXPOSURE IN CULTURED CEREBRAL CORTICAL NEURONS

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Ethanol elicits bidirectional changes in $GABA_A$ receptor surface expression, causing a decrease in $GABA_A$ alpha 1 subunits and an increase in $GABA_A$ alpha 4 subunits. These changes are likely mediated largely by activation of various second messenger pathways, including protein kinase C (PKC) and protein kinase A (PKA). While PKC activation decreases alpha 1 and increases alpha 4 subunit surface expression, biochemical data suggest that PKA contradicts these changes. This study sought to investigate the functional consequences of PKA activation by ethanol with electrophysiological recording in primary cultures of cerebral cortical neurons prepared from rat pups on postnatal 0-1 and maintained in culture for at least 17 days. Cells were exposed to ethanol (50 mM) for one hour ± PKA activators and inhibitors. Ethanol decreased zolpidem responses in the presence of 1 μM GABA (−20%, $p<0.05$), which was exacerbated by the addition of Rp-cAMP (−45%, $P<0.01$). In addition, the PKA activator Sp-cAMP increased (+41%, $p<0.05$) zolpidem responses with1 μM GABA, suggesting adaptations in $GABA_A$ a1 subunit receptors. Next, we examined the effects of ethanol and PKA modulators on mIPSC kinetics. No effects of ethanol or PKA modulators alone were observed. However, in the presence of zolpidem, an increase mIPSC decay τ2 and decay 90-37 was observed after Sp-cAMP exposure, consistent with an increase in synaptic alpha 1 subunits. Interestingly, Ro15-4513 (1 μM) also increased the decay τ2 of mIPSCs in ethanol-exposed cells, and this effect was also prevented by Rp-cAMP, suggesting adaptations of multiple a subunit receptors in the cells. The results support the hypothesis that PKA modulates ethanol-induced changes in $GABA_A$ receptor expression. PKA activation may ameliorate some of the changes in receptor expression induced by ethanol, and may represent an important target for development of drugs involved in the treatment of alcoholism.

0716

L-TYPE VOLTAGE-GATED CALCIUM CHANNEL FUNCTION IN RAT CA3 HIPPOCAMPAL PYRAMIDAL NEURONS FOLLOWING 3^{RD} TRIMESTER ETHANOL EXPOSURE

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Alcohol consumption during pregnancy can dose-dependently result in varying degrees of neurobehavioral deficits that are collectively termed fetal alcohol spectrum disorders (FASD). Animal models of FASD have shown deficits in learning and memory that may be related to hippocampal damage. Repeated ethanol exposure of rats during the first few days of the neonatal period (a model of the 3^{rd} trimester of human pregnancy) was shown to abolish GABAergic long-term potentiation in CA3 hippocampal pyramidal neurons. We hypothesize that this is a consequence of a reduction in dendritic BDNF release due to inhibition of L-type voltage gated Ca^{2+} channels (L-VGCCs). To test this hypothesis, rat pups and mother were exposed to air or vaporized ethanol for 4 hours/day between post-natal (P) days 2–12. Pups were sacrificed at P6, P8, P13, and P15. Pup peak serum alcohol concentration was approximately 60 mM. The ethanol exposed pups gained weight slightly slower and, by P15, weighed significantly less than the air exposed control pups. Coronal brain slices were prepared using standard procedures, and hippocampal CA3 pyramidal neurons were visualized under infrared-differential interference microscopy. Using whole-cell patch-clamp electrophysiology, Ba^{2+} currents were evoked by stepping the membrane potential from −70 mV to 0 mV. Ba^{2+} currents were recorded in the absence and presence of verapamil (100 μM), an L-VGCC blocker. The L-VGCC component was assessed by subtracting the peak amplitude of the Ba^{2+} currents in the presence of verapamil from baseline Ba^{2+} currents. At P6, but not later time points, the ethanol treated animals had significantly smaller cell capacitance (air = 104.2 ± 5.62 pF; ethanol = 81.13 ± 7.41 pF; $p<0.05$ by unpaired t-test) and membrane resistance (air = 157.9 ± 27.4 M§Ù; ethanol = 81.13 ± 7.41 M§Ù; $p<0.05$ by unpaired t-test) (n=8). In the absence of verapamil, current densities were significantly greater at P15 when compared to P6 (P6 = 20.91 ± 2.06; P15 = 35.82 ± 4.06 pA/pF, $p<0.05$ by unpaired t-test; n = 8). No effect of ethanol treatment was detected on this developmental change. Preliminary data suggest that the L-VGCC component of these currents is reduced at P8, but not other time points, in the ethanol exposed animals. Studies are underway to further characterize the effect of 3^{rd} trimester ethanol exposure on L-VGCCs.
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0717

A NOVEL ALCOHOL-SENSITIVE SITE IN THE M3 DOMAIN OF THE NMDA RECEPTOR GLUN2A SUBUNIT

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Accumulating studies have demonstrated that the N-methyl-D-aspartate receptor is one of the most important targets of ethanol in the central nervous system. Previous studies from this laboratory have found that one position in the third (F637) and two positions in the fourth (M823 and A825) membrane-associated (M) domains of the N-methyl-D-aspartate receptor GluN2A subunit modulate alcohol action and ion channel gating. Using site-directed mutagenesis and whole-cell patch-clamp recording, we have found an additional position in M3 of the GluN2A subunit, F636, which significantly influences ethanol sensitivity and functionally interacts with F637. Tryptophan substitution at F636 significantly decreased the ethanol IC_{50}, decreased both peak and steady-state glutamate EC_{50}, and altered agonist deactivation and apparent desensitization. There was a significant correlation between steady-state:peak current ratio, a measure of desensitization, and ethanol IC_{50} values for a series of mutants at this site, raising the possibility that changes in ethanol sensitivity may be secondary to changes in desensitization. Mutant cycle analysis revealed a significant interaction between F636 and F637 in regulating ethanol sensitivity. Our results suggest that F636 in the M3 domain of the GluN2A subunit not only influences channel gating and agonist potency, but also plays an important role in mediating the action of ethanol. These studies were supported by grants R01 AA015203-01A1 and AA015203-06A1 from the NIAAA to R.W.P.

0718

A SITE OF ALCOHOL ACTION AT THE NMDA RECEPTOR M3-M4 DOMAIN INTERFACE

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The N-methyl-D-aspartate (NMDA) glutamate receptor is a major target of ethanol in the brain. Previous studies have identified positions in the third and fourth membrane-associated (M) domains of the NMDA receptor GluN1 and GluN2A subunits that influence alcohol sensitivity. The structural model of the NMDA receptor, predicted from the structure of the related GluA2 subunit, indicates a close apposition of the alcohol-sensitive positions in M3 and M4 between the two subunit types. We investigated possible interactions between the M3 and M4 domain positions of the two subunit types affecting the ethanol sensitivity of the receptor by using dual substitution mutants. In an initial screen of single-substitution mutants, we found that a position in both subunits adjacent to one previously identified, GluN1(G638) and GluN2A(F636), can strongly regulate ethanol sensitivity. Significant interactions affecting ethanol inhibition were observed at four pairs of positions in GluN1/GluN2A: G638/M823, F639/L824, M818/F636, and L819/F637. Two of these interactions involve a position in M4 of both subunits, GluN1(M818) and GluN2A(L824), that does not by itself alter ethanol sensitivity, and one of the previously identified positions affecting ethanol sensitivity, GluN2A(A825), did not appear to interact with any other position tested. These results also indicate a shift by one position of the predicted alignment of the GluN1 M4 domain. These findings have allowed for the refinement of the NMDA receptor M domain structure, and support the existence of four sites of alcohol action on the NMDA receptor at the M3-M4 domain intersubunit interfaces. These studies were supported by grants R01 AA015203-01A1 and AA015203-06A1 from the NIAAA to R.W.P.

0719

A ROLE FOR TLR4 AND IL-1RI IN ETHANOL EFFECTS ON GABAERGIC TRANSMISSION AND ETHANOL DRINKING IN THE MOUSE

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A growing body of evidence indicates that neuroinflammation is involved in enhanced alcohol consumption and contributes to the progression to alcoholism. Several inflammatory signaling pathways have been shown to play a role in increased ethanol drinking and dependence. We have focused on two such pathways, TLR4 (toll-like receptor 4) and IL-1 (interleukin-1), and examined effects of their activations on GABAergic transmission in the central amygdala (CeA). GABAergic transmission is augmented by ethanol in CeA and is hypothesized to be a crucial mediator of ethanol drinking. Therefore, we superfused lipopolysacharide (LPS) or IL-1β to activate TLR4 and IL-1RI receptors, respectively, and performed intracellular recording of GABAergic IPSPs with sharp electrodes in murine brain slices. Our previous studies showed that acute superfusion of LPS (25 mg/ml) increased (by 42%), whereas IL-1 β (50 ng/ml) superfusion decreased (by 22%), IPSP amplitudes in CeA neurons. The ethanol augmentation of $GABA_A$-IPSPs is markedly diminished by knocking out CD14 (an essential accessory protein for TLR4 activation by LPS). Conversely, acute pre-application of LPS potentiates ethanol effects (by 25%) on CeA GABAergic transmission in control mice, and restores ethanol effects in CD14KO mice. Acute activation of the IL-1 pathway diminished IPSPs and prevented ethanol potentiation (93% of control) of GABAergic transmission in CeA. The opposite effects of IL-1 β on GABAergic transmission in the CeA compared to LPS and ethanol may suggest a negative feedback of acute IL-1 β in the CeA. In support of this construct, our preliminary data from behavioral studies indicate that IL-1RI plays a role in negative regulation of EtOH drinking in mice, suggesting that increased activation of IL-1R decreases EtOH drinking. Thus, our data support the hypothesis of immune mechanisms underlying ethanol effects and drinking.

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0720

ETHANOL-MEDIATED FACILITATION OF AMPA RECEPTOR FUNCTION IN THE DORSOMEDIAL STRIATUM: IMPLICATIONS FOR ALCOHOL DRINKING BEHAVIOR

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We previously found that acute ex vivo or repeated cycles of in vivo ethanol exposure and withdrawal produces a long?]lasting increase in the activity of NR2B-containg NMDA receptors (NMDARs) in the dorsomedial striatum (DMS) of rats [1, 2]. Activation of NMDARs is required for the induction of long-term potentiation (LTP) of AMPA receptor (AMPAR)-mediated synaptic response (AMPAR-LTP) in the DMS [3]. We therefore examined whether the ethanol-mediated upregulation of NMDAR activity alters the induction of AMPAR-LTP. We found that ex vivo acute exposure of striatal slices to, and withdrawal from, ethanol facilitates the induction of AMPAR-LTP in DMS neurons, which is abolished by inhibition of NR2B-containing NMDARs. We also found that repeated systemic administration of ethanol causes an NR2B-NMDAR-dependent facilitation of AMPAR-LTP in the DMS. LTP triggers the insertion of AMPAR subunits to the synaptic membrane [4]. In line with this concept, we found that repeated systemic administration of ethanol as well as excessive ethanol consumption produce a long-lasting increase in synaptic localization of the GluR1 and GluR2 subunits of AMPARs in the DMS. Importantly, we report that inhibition of AMPARs in the DMS attenuates operant self-administration of ethanol, but not of sucrose. Together, our data suggest that aberrant synaptic plasticity in the DMS induced by repeated cycles of ethanol exposure and withdrawal contributes to the molecular mechanisms underlying the development and/or maintenance of excessive ethanol consumption.

1. Wang et al. 2007 J Neurosci.
2. Wang et al. 2010 J Neurosci.
3. Partridge et al. 2000 J Neurophysiol.
4. Malinow et al. 2002 Annu Rev Neurosci.

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0721

ACUTE ETHANOL DISRUPTS NEURON EXCITABILITY IN THE ORBITOFRONTAL CORTEX THROUGH A GLYCINE RECEPTOR MECHANISM

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In humans, stroke or trauma-induced damage to the orbitofrontal cortex (OFC) often results in poor judgment and behavioral inflexibility. Human alcoholics exhibit similar cognitive deficits including impaired behavioral inhibition and self-control suggesting that OFC neurons are susceptible to alcohol-induced damage or dysfunction. Our lab has modeled OFC mediated cognitive deficits in mice and this work reveals reduced behavioral flexibility during a reversal learning discrimination task in alcohol dependent mice (Badanich et al, 2011). Despite these intriguing findings, the cellular actions of alcohol on OFC neuron function are largely unknown. To address this issue, whole-cell patch clamp electrophysiology was used to determine the effects of ethanol (EtOH) on OFC neurons isolated from adult C57 mice. In alcohol naïve mice, bath application of EtOH (11–66 mM) decreased action potential firing induced by direct current injection and caused a small but concentration-dependent decrease in input resistance. Both of these effects recovered during washout of the EtOH containing solution and were prevented by adding the $GABA_A$ receptor antagonist picrotoxin to the bath. EtOH (11–66 mM) did not alter the amplitude of stimulus-evoked GABA IPSCs or the amplitude or frequency of spontaneous GABA IPSCs suggesting that synaptic GABA events are not involved in the ethanol inhibition of spike firing. However, during voltage-clamp recordings, the holding current was increased during ethanol application suggesting an enhanced GABA-mediated tonic current that may reduce OFC neuron excitability. The competitive $GABA_A$ antagonist bicuculline did not completely block the EtOH-induced increase in holding current while the less selective inhibitor picrotoxin did. As picrotoxin also blocks glycine receptors, the more selective glycine antagonist strychnine was tested. Strychnine prevented both the EtOH-mediated increase in holding current and the EtOH-mediated decrease in action potential firing. These findings show that OFC neurons in adult mice express strychnine-sensitive glycine receptors that mediate inhibition of OFC neuron excitability during acute exposure to ethanol. This inhibition may trigger neuroadaptive mechanisms that are revealed following chronic exposure to ethanol and may contribute to the impairment of OFC-dependent behaviors in alcohol-dependent individuals. Supported by F32 AA019610 (KAB) and the P50 AA010761 (JJW).

0722

TYROSINE TO PHENYLALANINE SUBSTITUTIONS IN THE NR2B C-TERMINUS DOES NOT ALTER ETHANOL INHIBITION OF RECOMBINANT NMDA RECEPTORS

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N-methyl-D-aspartate receptors (NMDARs) are ion channels activated by the neurotransmitter glutamate and are highly expressed in neurons. These calcium-permeable receptors are critical for excitatory synaptic signaling and alteration of NMDA receptor function by drugs or disease is associated with impaired perception, cognition and learning. Previous studies from this laboratory and others demonstrated that ethanol inhibits NMDA receptor currents at concentrations associated with many of the behavioral effects of ethanol including intoxication. Numerous mechanisms have been suggested to account for how ethanol inhibits NMDA receptors but experimental data has ruled out direct actions of ethanol on the agonist binding site, channel permeation pathway and most of the known modulatory sites on the receptor. Recently, findings in the literature have suggested that ethanol, via activation of intracellular tyrosine phosphatases, leads to dephosphorylation of key tyrosine residues in the C-terminus of NR2B subunits resulting in diminished channel function. Whether such receptors show reduced sensitivity to acute ethanol is unknown. In this study, we directly tested this hypothesis by engineering NMDA receptor mutants in which phenylalanine replaced tyrosine at three different sites (Y1252, Y1336, Y1472) on the NR2B subunit. These mutants were then transiently expressed in human embryonic kidney (HEK) cells and whole-cell patch clamp electrophysiology was used to record glutamate-activated currents in the absence and presence of ethanol (10–600mM). NMDAR transfected cells showed robust glutamate-activated inward currents with no change in the steady-state to peak ratio between wild-type and Y-F mutants. Current amplitudes were also similar for wild-type, Y1472F and the triple mutant but were slightly reduced in cells expressing the Y1252 and Y1336 mutants. Ethanol inhibited all receptors and analysis of the dose-response curves showed no significant difference in ethanol IC_{50} values between wild-type receptors and Y1252F, Y1336F, Y1472F or triple Y-F mutants. These findings suggest that ethanol inhibition of channel function in NR2B containing NMDA receptors is unlikely to involve dephosphorylation of C-terminal tyrosine residues. Supported by R37 AA009986.

0723

THE EFFECT OF ALCOHOL ON THE VOR IN XENOPUS LAEVIS TADPOLES

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Alcohol ingestion has been shown to disrupt the normal functioning of the vestibulo-ocular reflex (VOR). To investigate the effects of alcohol on the VOR, we examined the change in extraocular motor discharge before, during and after administration of various concentrations of ethanol in a semi-intact preparation of *Xenopus laevis* tadpoles. Recordings were made while the *in vitro* preparation was rotated sinusoidally on a two-axis turn-table to naturally activate the vestibular system. A signifcant increase in neuronal firing during alcohol administration through the bath solution occurred at low amplitudes and/or frequencies. This increase persisted even after alcohol washout, suggesting that the effect is due to a modulation of the signal transduction and/or transmission in the labyrinth. However, an effect on central nervous processing can not be excluded. Future studies exploring a more localized application will reveal more site-specific effects of alcohol administration on VOR peformance.

0724

PHYSIOLOGICAL ETHANOL DEPENDENCE IN DROSOPHILA LARVAE

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Chronic ethanol consumption can cause adaptive physiological responses that produce functional tolerance in the presence of ethanol and withdrawal symptoms when ethanol is withheld. We have developed a model of physiological ethanol dependence in the *Drosophila melanogaster* model system. We demonstrate that ethanol withdrawal negatively effects the performance of larvae in an associative learning assay. Drosophila larvae were reared on ethanol-containing food until the 3rd instar developmental stage. Some larvae were then removed from ethanol for a withdrawal period while others continued to consume ethanol. Larvae were then trained in a heat shock olfactory conditioning paradigm in which an aversive heat stimulus was paired with an attractive odorant. Reduced attraction to the odorant indicated that conditioning (learning) had occurred. Surprisingly, larvae receiving the chronic ethanol treatment learned equally as well as larvae reared in the absence of ethanol. Conversely, a six-hour period of withdrawal from ethanol significantly reduced levels of learning. This reduction could be rescued by a one-hour reintroduction of ethanol. Interestingly, when the ethanol-treated larvae were removed from the drug and allowed to mature into adult flies, we still observed a withdrawal phenotype. Using electrophysiological recordings of the giant fiber pathway, we observed that flies that were treated with ethanol during the larval stages were significantly more susceptible to induced seizures. By combining the unique and unusual genetic toolbox available in Drosophila with our behavioral and electrophysiological assays, this model will be invaluable for unearthing the genetic underpinnings of ethanol dependence and withdrawal. We have already identified a synaptic protein without which, the aforementioned withdrawal phenotypes are not observed. In short, we have shown that Drosophila larvae can adapt to chronic ethanol exposure to the point that performance in a learning paradigm suffers when ethanol is not present. Additionally, this ethanol withdrawal survives metamorphosis and can be seen in the form of a reduced seizure threshold in adult flies.

0725

STIMULUS CONTROL OF ETHANOL'S EFFECTS UPON EARLY RESPIRATION PATTERNS

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Preclinical and human studies systematically indicate fetal depression of respiration rates as a function of maternal ethanol exposure. In a variety of experimental studies it has been observed that rat perinates are capable of associating different conditioned stimuli with unconditioned autonomic and motivational effects of the drug. As indicated by prior research, central nervous system maturation patterns of infant rats [postnatal days (PDs) 3–9] are homologous to those observed during the third trimester in human fetuses. In this study we sequentially (PDs 3, 5, 7) evaluated respiration rates in freely behaving unrestrained pups by whole body flow through plethysmography. The research was conducted in order to determine the net effects of a relatively high ethanol dose (3.0 g/kg, i.g.) upon neonatal respiration as well as the possibility that the magnitude of this autonomic response is regulated by stimuli that predict ethanol's effects. Hence, pups either received vehicle or 3.0 g-kg ethanol. These doses were preceded by no specific treatment or intraperitoneal administrations of vehicle or a 1.0 g/kg dose that in itself is not sufficient to alter respiration rates. At PD 9 all subjects were evaluated after being exposed to the stimuli that potentially signalled the effects of intragastric vehicle or the high ethanol dose. As expected, 3.0 g/kg ethanol resulted in all ages in a marked level of suppression of breathing frequencies. Of major importance was the observation that at PD9, stimuli that signalled the effects of this high ethanol dose generated isodirectional respiratory frequencies as those observed with 3.0 g/kg ethanol. This effect was particularly relevant when pups were re-exposed to a small ethanol dose (1 g/kg) and to a lesser extent, when exposed to i.p. administration of vehicle. No particular effects were observed in those pups in which no specific treatment preceded ethanol intoxication. These results strongly suggest that respiration depression originally generated by a high ethanol dose is reinstated by stimuli that are paired with such a dose. In light of the association existing between fetal alcohol exposure and sudden infant death syndrome, it is important to indicate that marked depressions in neonatal breathing patterns are likely to be elicited by stimuli originally associated with detrimental autonomic effects of relatively high ethanol doses experienced during early development.

0726

NEONATAL DEPRESSION OF RESPIRATION FREQUENCY AS A FUNCTION OF PRE- AND POSTNATAL EXPOSURE TO MODERATE ETHANOL DOSES AND ALCOHOL-RELATED SENSORY CUES

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Human and animal studies indicate a substantial depression of fetal respiration rates as a function of maternal ethanol intoxication. This effect seems to be linked with a variety of factors; among others hypoxia due to vasoconstriction of blood vessels in the umbilical cord, hypercanea, direct action of the drug upon neural systems controlling fetal breathing and suppression of fetal activity. In a variety of preclinical studies, we have observed that rat fetuses sense ethanol-related sensory cues when the drug accumulates in the amniotic fluid. In addition, the near term fetus also exhibits pavlovian conditioning when these cues are contigous with different unconditioned effects of the drug such as maternal hypothermia. The hypothesis under analysis in the present study is linked to the possibility of establishing early conditioned respiration responses as a function of the explicit association between ethanol odor sensed in utero in contiguity with depressed respiratory frequency. In this study we also examined whether prenatal exposure to the drug either results in infantile sensitization or tolerance in terms of respiration frequencies when the developing organism experiences different ethanol doses. Pregnant dams (gestational days 17–20) received a daily intragastric administration of 2.0 g/kg ethanol or water (vehicle). At postnatal day 7, infants either received i.g. administration of vehicle, 0.5, 1.0 or 2.0 g/kg ethanol. Respiration rates were evaluated in freely behaving unrestrained pups by whole body flow through plethysmography. These evaluations took place under the presence or absence of ethanol odor. As expected, relatively high ethanol doses resulted in depressed respiration rates. Pertinent ANOVAs and post-hoc comparisons also indicated that pups prenatally exposed to ethanol exhibit marked sensitization to the depressant effects of the drug particularly when ethanol odor was present. These results strongly suggest that prenatal ethanol experience results in conditioned respiration patterns that may endanger the physiological wellbeing of the infant when re-exposed to ethanol sensory cues or the combination of these cues and the process of ethanol intoxication.

0727

EXERCISE DOES NOT AFFECT MORRIS WATER MAZE ACQUISITION NOR ETHANOL-INDUCED COGNITIVE IMPAIRMENTS IN ADULT MALE RATS

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Exercise promotes hippocampal plasticity and improves hippocampal dependent memories in both humans (Chaddock et al., 2010, Erickson et al., 2011) and rats (Gomes da Silva et al., 2010, van Praag et al., 1999). In this study, we attempted to replicate these findings, as well as investigate the potential neuroprotective effects of exercise against ethanol-induced spatial memory impairments.

Six adult male Sprague-Dawley rats (PD 90) were subjected to a 20-day regimen of daily physical exercise, which was increased so that rats were running at 25 m/min for 60 minutes for the last 14 days of exercise training. Time spent on the treadmill was matched in the 6 sedentary control group. Following exercise training, all rats received 4 trials per day for five consecutive days in the Morris Water Maze (MWM) beginning on PD 110. Maximum trial time was limited to 45 seconds and animals were allowed to remain on the platform for 10 seconds after all trials.

On day six, an ethanol challenge was administered. Animals in the sedentary and exercise groups were randomly assigned to receive an acute i.p. injection of 2.0 g/kg 10% w/v ethanol or equivalent volume of saline. Spatial memory was tested in the MWM 30 minutes following administration, and animals received 4 trials. Tail blood was collected after the final trial from animals receiving ethanol to assess plasma blood ethanol concentrations (BECs).

Exercise training had no effect on latency during MWM acquisition compared to sedentary controls ($F = 0.12$, n.s.), which is contrary to most published data. Agreeing with published data, exercise did not alter swim speed ($F = 0.45$, n.s.). Additionally, exercise did not have a neuroprotective effect against ethanol-induced spatial memory impairments, as ethanol increased latency ($F = 18.20$, $p < 0.01$) and path length ($F = 12.15$, $p < 0.01$) to the escape platform regardless of activity level. Ethanol administration also increased percentage of time spent in thigmotaxis ($F = 59.80$, $p < 0.001$.), and exercise training exacerbated this effect ($F = 6.39$, $p < 0.05$). Exercise did not alter BEC levels after the ethanol challenge ($t = 0.99$, n.s.). The current results demonstrate that the effect of exercise on hippocampal dependent learning is complex and does not alter ethanol induced spatial memory impairments but can alter search strategies in the water maze.

0728

ACQUISITION OF ETHANOL DISCRIMINATION IN ADOLESCENT AND ADULT RATS USING A PAVLOVIAN CONDITIONED APPROACH PARADIGM

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Adolescents and adults vary in sensitivity to many effects of ethanol (EtOH), although it is unknown whether they also differ in their perception of EtOH's subjective cues. Standard 2-lever drug discrimination procedures used to examine interoceptive effects of EtOH require extensive training and are not easily adaptable to adolescents due to the short span of this ontogenetic period. The present study characterized acquisition of EtOH discrimination in food-restricted adolescent and adult male Sprague Dawley rats using a Pavlovian conditioned approach discrimination procedure previously shown to be acquired rapidly in adult rats (e.g., Reichel et al., 2007). EtOH at 1 of 3 training doses (0.75, 1 and 1.25 g/kg, ip) and 1 of 2 time points (5 or 30 min post-injection) served as either a positive (POS) or negative (NOS) occasion setter. Twice daily acquisition sessions (1 EtOH and 1 saline [SAL], with order counterbalanced) were conducted 5 hrs apart. Each 20-min operant session consisted of 8 15-s presentations of 2 cue lights located on either side of a dipper delivering chocolate Boost. For POS-trained rats, the cue lights reliably predicted 5-s presentations of chocolate Boost during EtOH but not SAL sessions, with the opposite contingencies used for NOS-trained rats. Of the 149 animals trained, 91% of adults and 89% of adolescents met discrimination criterion within the 10-day training period. Although adults met discrimination criterion on average slightly sooner (6.4 days) than adolescents (7.4 days), analysis of first trial data for each session revealed no age differences in acquisition. Adolescents met criterion more slowly at 0.75 g/kg than at the higher training doses, whereas training dose did not influence acquisition among adults. When elevation scores representing differences in head entries into the Boost reward delivery area during vs. before the cue presentation were examined, separation of elevation scores between EtOH and SAL sessions occurred slightly faster for POS-trained than NOS-trained rats, an effect that was dependent on time point for adolescents but not adults. Overall, these data suggest that the Pavlovian discrimination model is appropriate for comparing contributors to the subjective effects of EtOH in adolescent and adult subjects, given that the task is acquired rapidly, with both ages performing similarly by the end of training.

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0729

DOPAMINE D1 BUT NOT D2 RECEPTOR BLOCKADE IMPAIRS THE DEVELOPMENT OF ETHANOL-CONDITIONED PLACE PREFERENCE

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Dopaminergic transmission has been implicated in ethanol reward and involvement of dopamine D1 and D2 receptors has been examined using various pharmacological and genetic manipulations. However, studies assessing the consequences of systemic blockade of these receptors on the development of a place preference induced by ethanol remain largely absent from the literature. In the present experiments, we used systemic administration of selective dopamine receptor antagonists to examine the roles of D1 and D2 receptors in the acquisition of ethanol-induced conditioned place preference (CPP) in adult male DBA/2J mice. All experiments used an unbiased place conditioning procedure. Testing occurred 24 hrs after the first two conditioning sessions and again after another two sessions, so that mice received four conditioning sessions in total. In experiments 1 and 2, antagonists selective for D2 (raclopride, 0–1.2 mg/kg) and D1 (SCH-23390, 0–0.3 mg/kg) receptors were administered before conditioning sessions, where ethanol (2 g/kg) was paired with a distinctive tactile floor cue. While antagonism of D2 receptors produced no effect, D1 receptor blockade impaired ethanol-CPP acquisition. In experiment 3, we determined these impairments were not due to aversive properties of SCH-23390 (0.3 mg/kg) by demonstrating the inability of this drug to produce a conditioned place aversion (CPA). Experiment 4 examined the effect of SCH-23390 on the development of a CPA produced by post-trial ethanol (2 g/kg) injection. Ethanol-CPA was not impaired by SCH-23390, suggesting that reductions in ethanol-CPP acquisition were likely not due to general learning or memory impairments produced by the drug. Overall, these findings suggest that D1 receptor function is specific to the rewarding and not aversive motivational effects of ethanol. Supported by NIH-NIAAA grant AA07702.

0730

PHARMACOLOGICAL SILENCING OF THE BLA BLOCKS ENHANCEMENT, BUT NOT REDUCTION, OF ETHANOL-SEEKING INDUCED BY CONDITIONED CUES

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Our lab has demonstrated that CS+ conditioned odor cue can induce the expression of c-fos in the basolateral amygdala (BLA) during alcohol-seeking, whereas CS neutral (CS^0) or CS- conditioned odor cue did not alter the expression of c-fos in BLA. The objective of the current study was to determine if inactivating the BLA with a baclofen+muscimol mixture would alter the effects of 3 conditioned odor cues on Pavlovian Spontaneous Recovery (PSR), a measure of alcohol-seeking behavior. Adult female alcohol-preferring (P) rats were trained in 2-lever operant chambers to self-administer 15% EtOH (v/v) and water on a concurrent fixed-ratio 5-fixed-ratio 1 (FR5-FR1) schedule of reinforcement in daily 1-hour sessions. EtOH exposure for a 10-week period was paired with the presence of an odor (CS+). Rats were then exposed to 7 consecutive extinction sessions (no water or EtOH), which were paired with a 2^{nd} odor (CS-). From day 58 to 77 (overlapping both EtOH self-administration and extinction), rats were exposed to a 3^{rd} odor in a novel environment (CS neutral or CS^0). After extinction training, rats were maintained in their home cages for two weeks. In the 2^{nd} week of the home cage phase, rats were bilaterally implanted with guide cannulae aimed at the BLA; rats were allowed 7 days to recover before PSR testing. P rats [n = 6] were microinjected bilaterally with baclofen (0.3 nmol) + muscimol (0.03 nmol)/ 0.3 ul and then returned to the operant chambers in the absence of EtOH and water to undergo PSR testing. Rats were randomly assigned to 3 groups (CS+, CS-, or CS^0), which received the corresponding odor for PSR sessions. P rats that were exposed to CS^0 responded significantly more on the EtOH lever in the PSR test compared to extinction baseline (37 ± 7 vs. 62 ± 6 responses/session). Compared to the CS^0, CS+ increased responses on the EtOH lever (135 ± 7), whereas CS- reduced EtOH lever responses (17 ± 4). Microinjection of baclofen + muscimol mixture into BLA significantly ($p < 0.05$) reduced CS^+ EtOH responses in the 1^{st} PSR session compared to aCSF (72± 5 vs 135 ± 7). However, the baclofen + muscimol mixture did not have any effect on CS^0 or CS- EtOH responses compared to vehicle. Overall, the data suggest that the BLA is involved in the conditioned excitation (CS+) of EtOH-seeking behavior in P rats but not in the suppression (conditioned inhibition; CS-) or induction (CS^0) of EtOH-seeking behavior. (Supported in part by AA07611, AA07462, AA10721)

0731

ERASURE OF ETHANOL-RELATED MEMORIES BY MTORC1 INHIBITION: USING MEMORY PLASTICITY TO PREVENT ETHANOL RELAPSE

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Relapse to ethanol (EtOH) abuse is typically caused by retrieval of EtOH-associated memories. Memory reconsolidation is a process in which memories are temporarily destabilized upon their retrieval/reactivation, and then undergo re-stabilization in order to persist. During reconsolidation, the reactivated memory is labile to manipulations such as inhibition of protein translation, offering an opportunity to interfere with unwanted memories. Activation of the kinase mammalian target of rapamycin complex 1 (mTORC1) is required for dendritic translation of a subset of proteins, and is implicated in synaptic plasticity, learning and memory processes. We recently reported that EtOH administration and consumption activates the mTORC1 pathway in the nucleus accumbens and that inhibition of this pathway reduces EtOH seeking and consumption in rodents. Here, we tested whether reconsolidation of EtOH-associated memories requires activation of the mTORC1 signaling pathway, and whether these memories can be disrupted by inhibition of this pathway. We found that reactivation of EtOH-related memories led to the activation of mTORC1, measured by an increase in the phosphorylation of the mTORC1 substrates 4E-BP and S6 kinase, as well as the S6K substrate S6, in the medial prefrontal cortex and central amygdala. Next, we tested whether mTORC1 inhibition during memory reconsolidation interferes with subsequent EtOH seeking/intake. To do so, rats were first trained to self-administer a 20% EtOH solution. After achieving stable baseline EtOH consumption, rats underwent 10 days of abstinence. On the 11th day, the EtOH-associated memory was reactivated by re-exposure to the self-administration context and/or taste/odor cue, and EtOH seeking and intake were measured on subsequent days. We found that systemic administration of the mTORC1 inhibitor rapamycin immediately after memory reactivation produced a long-lasting reducion in EtOH seeking and intake that was detected 24 hrs, 48 hrs or even 14 days later. Importantly, EtOH seeking was not affected by rapamycin when the memory was not reactivated, or when rapamycin was administered 5 hrs after memory reactivation. The latter suggests that memories are destabilized and can be disruption only shortly after their reactivation. Together, our findings suggest that inhibition of the mTORC1 pathway can be used to erase EtOH-related memories and thus be used as a valuable strategy to reduce relapse.

0732

PKMZETA EXPRESSION FOLLOWING CHRONIC INTERMITTENT ETHANOL EXPOSURE AND CONDITIONED TASTE AVERSION PROCEDURES

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Substantial evidence indicates that drugs of abuse co-opt synaptic plasticity and influence brain circuits critical for reward and aversion. Recent studies have shown that the persistence of long-term potentiation (LTP), a basic component of learning and memory, requires the constitutive activity of the atypical protein kinase C isoform M zeta (PKMzeta), which has been shown to play a role in fear conditioning, spatial memory, conditioned taste aversion, and maintenance of morphine-associated drug reward. In the first study mice received 4 weekly cycles of chronic intermittent ethanol (CIE) exposure (16 hr/d for 4d) of ethanol vapor (EtOH group) or air (CTL group) in inhalation chambers, with each exposure cycle alternating with a weekend of home cage rest. After the fourth cycle, fresh tissue punches were taken from the amygdala, nucleus accumbens, hippocampus, ventral tegmental area, and prefrontal cortex to quantify PKMzeta expression by western blot analysis. PKMzeta levels were not altered by CIE in any brain region. In separate groups of mice undergoing a similar CIE exposure, mice were trained in a conditioned taste aversion procedure (CTA) with the conditioned stimulus (CS) being a 30 min access to a saccharin solution (1% w/v). Following each exposure to the CS, mice were immediately injected with ethanol (2 g/kg) or saline. After testing ethanol and saline-injected mice for CTA, tissue was collected and analyzed for PKMzeta. CTL mice injected with ethanol following saccharin intake showed a substantial aversion ($p<0.05$) to saccharin the next day while aversion in CIE exposed mice was attenuated, consistent with tolerance. Relative to saline-conditioned animals, CTL mice injected with 2 g/kg Etoh showed an 18% reduction in PKMzeta levels in the basolateral amygdala, while CIE mice showed a greater decrease in expression (61% reduction). Ongoing studies are continuing to examine PKMzeta in learned aversions in EtOH and CTL mice. Supported by R37AA009986 (JJW), AA10761 (CTS, WCG) and AA018036 (WCG).

0733

ETHANOL SELF-ADMINISTRATION IN RELATION TO GO/NO-GO PERFORMANCE WITH VARYING STIMULUS CONDITIONS

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Impulsivity has been linked to alcohol abuse. Further, it has been suggested that cognitive and physiological challenges may affect individuals' regulation of behavior. The current study tested the hypothesis that a cognitive challenge would alter the regulation of drinking. Female cynomolgus monkeys (*Macaca fascicularis*, n = 3) were trained to self-administer ethanol and to perform a go/no-go task to measure impulsivity. In the go/no-go task, monkeys were reinforced with banana pellets (which comprise their meals) during two types of trials: 1) responding during go trials, and 2) omitting a response during no-go trials. The monkeys performed this task for their meals three times per day every 2 hours. The time that the monkeys were required to inhibit responding to receive a banana pellet was manipulated. Specifically, the total duration of no-go stimuli presented during each session was systematically varied (0 s, 30 s and 150 s) by manipulating their number and duration. Two monkeys drank doses of ethanol resulting in measurable blood-ethanol concentration prior to the third meal each day (mean ± SD: 77, 0.78 ± 0.30 g/kg; 82, 0.83 ± 0.32 g/kg). On days in which the monkeys had to inhibit the longest for their banana pellets, they drank a similar dose of ethanol prior to the third meal (77, 1.0 ± 0.3 g/kg; 82, 1.0 ± 0.1 g/kg) compared to when the no-go time was brief (77, 0.8 ± 0.3 g/kg; 82, 0.8 ± 0.2 g/kg; $F(1, 2) = 4.4$, $p = 0.17$), the opposite of water intake, which was slightly but not significantly lower during sessions with long (77, 169 ± 58 ml; 82, 236 ± 51 ml) compared to brief (77, 247 ± 94 ml; 82, 302 ± 57 ml) waits, $F(1, 2) = 5.7$, $p = 0.14$. Response accuracy did not vary significantly across conditions. Thus, the data suggest that the cognitive challenges in this study did not influence ethanol consumption. Additional studies are needed to evaluate the role of psychogenic (cognitive or psychosocial) stress in the precipitation of binge drinking in heavier drinking subjects.

0734

BETWEEN SESSION AND WITHIN SESSION DELAY DISCOUNTING IN LONG EVANS AND ALCOHOL-PREFERRING P RATS

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Long Evans (LE) and alcohol-preferring P rats are two commonly used strains in alcohol drinking studies. In a paradigm that separates seeking and drinking, LE and P rats showed different patterns of behavior with P rats showing both excessive seeking and drinking of ethanol (Czachowski & Samson 1999; 2002). The present investigation sought to determine if these patterns are mirrored in measures of impulsivity, using both between and within session delay discounting paradigms. Both paradigms used delays of 0, 2, 4, 8 and 16 seconds, and 2% sucrose solution as the reward. The between sessions approach was conducted under nondeprived conditions (three daily sessions at each delay) and used an adjusting amount procedure where rats chose between a delayed fixed-magnitude or an immediate varying-magnitude reward, titrated to yield indifference points. Nonlinear regression of the hyperbolic function was then used to obtain k (a single measure of curve steepness). The within sessions paradigm was conducted using water-restriction and five daily blocks (one at each delay) of 12 trials. Delayed reward choices and the increase in immediate reward choices vs baseline were measured. The between session paradigm yielded no significant difference in k values between the two strains ($p=.66$). LE completed significantly fewer trials ($p<.001$) in the between session paradigm but not the within session ($p=.37$). In the within session paradigm a main effect of delay ($p<.001$) strain ($p<.001$) and an interaction between delay and strain ($p<.01$) were observed for delayed reward choice. Post hoc testing revealed the two strains to be different at every delay. The increase in immediate reward choice from baseline showed main effects of delay ($p<.001$) and strain ($p< .01$) as well as an interaction between delay and strain ($p<.01$). Post hoc testing showed the P rats to have greater increases in immediate reward choice at the 4, 8 and 16 second delays. The absence of a strain effect in the between sessions paradigm suggests no difference in impulsivity, however this paradigm was run without water restriction, and the LE had low performance rates. In the within session paradigm, P rats discounted delayed rewards at a higher rate than LE. These preliminary results are consistent with findings comparing high and low drinking rats and mice, and extend these findings to high and moderate drinking rats, suggesting that impulsivity may precede and predict excessive ethanol seeking and drinking.

0735

ETHANOL AND METHAMPHETAMINE'S EFFECT ON RATS' PERFORMANCE IN TWO TASKS THAT DISSOCIATE DELAY AND MAGNITUDE

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Ethanol use can lead to many potentially deleterious actions, such as drunk driving, increased aggression, and unprotected sex. One avenue by which ethanol may lead to these actions is by increasing impulsivity, as has been demonstrated in both animals and humans. Ethanol increases delay discounting (and thus increases impulsivity), but it is unknown whether this is due to an alteration in sensitivity to delays or in sensitivity to the magnitude of the reinforcers used in the task. Thus, we examined the effects of ethanol on rats' performance in tasks designed to measure delay sensitivity and magnitude sensitivity independently. We found that baseline measures of delay sensitivity and magnitude sensitivity were in line with previous research. We also verified that the task could measure acute effects by manipulating task parameters, which resulted in altered choice behavior within one session. Finally, we examined the effects of methamphetamine, which, unlike ethanol, *decreased* delay discounting in previous studies. Neither ethanol nor methamphetamine had any effect on either magnitude sensitivity or delay sensitivity in these tasks, suggesting that these tasks may measure a different underlying process than other delay discounting tasks. However, both ethanol and methamphetamine dose-dependently increased reaction times in the tasks. Interestingly, animals that were more sensitive to delay (but not magnitude) were less affected by ethanol's effects on reaction time. Despite this, sensitivity to delay did not predict ethanol's effects on general locomotor activity. Therefore, rats with greater sensitivity to delay may be resistant to the suppressant effects of ethanol on reinforced behavior.

0736

DISCRIMINATION OF ETHANOL AND NICOTINE MIXTURES: PARADOXICAL MECHANISMS OF OVERSHADOWING AND SYNERGY

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Training subjects to discriminate ethanol and nicotine as a compound interoceptive cue offers the advantage of studying a situational context in which individuals experience a history of conditioning with both drugs. This approach departs from the traditional one of training one drug to acquisition criteria, and then testing generalization, facilitation, or antagonism by the other drug. Earlier work from our laboratory suggested that a moderate ethanol dose (1.5 g/kg) overshadowed the discriminative stimulus (S^D) effects of nicotine, irrespective of nicotine dose magnitude (0.4–1.2 mg/kg) within the training drug mixture. The current work further explored interactions between ethanol and nicotine at the level of S^D effects by using a dose ratio strategy whereby incremental increases in ethanol dose (0.5, 1.0 and 2.0 g/kg = E) were trained in combination with a fixed nicotine dose (0.8 mg/kg base = 0.8N). Four groups of male C57BL/6 mice (n = 10/group) were trained to discriminate 0.8N, 0.5E+0.8N, 1.0E+0.8N, or 2.0E+0.8N from saline in standard 2-lever conditioning chambers. The 1.0E+0.8N group met acquisition criteria in significantly fewer training sessions than the 0.8N group (46±3 versus 70±7 sessions). Nicotine fully substituted (≥ 80% drug appropriate responding) in the 0.8N and 0.5E+0.8N groups at test doses of 0.8 and 1.2 mg/kg, respectively, but only partially substituted in the 1.0E+0.8N and 2.0E+0.8N groups. Conversely, ethanol exhibited no substitution in the 0.8N group, partial substitution in the 0.5E+0.8N group, and full substitution in the 1.0E+0.8N and 2.0E+0.8N groups. Pretreatment blockade with mecamylamine revealed that the direct activation of nicotinic acetylcholine (nACh) receptors was essential for producing the S^D effects in the 0.8N group, played a minor role in the 0.5E+0.8N group, and was unnecessary for the 1.0E+0.8N and 2.0E+0.8N groups. Assessment of ethanol generalization gradients in combination with 0.8 mg/kg nicotine resulted in significant leftward shifts in the ethanol dose-response curves when compared to ethanol only tests. Therefore, although the S^D effects of nicotine are overshadowed by discriminable doses of ethanol, nicotine does augment the potency of the ethanol cue. Identification of the receptor mechanisms underlying these interactive effects will aid in the development of pharmacological interventions for ethanol and nicotine co-abuse. Supported by NIH grant AA16849 (to MMF).

0737

FUNCTIONALLY DISCONNECTING THE BASOLATERAL AMYGDALA AND NUCLEUS ACCUMBENS CORE: EFFECTS ON CONTEXT-INDUCED RENWAL OF ALCOHOL SEEKING IN RATS

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Using pharmacological and optogenetics techniques we tested the hypothesis that neuronal projections from the basolateral nucleus of the amygdala (BLA) to the nucleus accumbens core (NACc) mediate context-induced renewal of alcohol seeking. Male, Long-Evans rats accustomed to drinking ethanol (EtOH, 20% v/v) were trained to discriminate between two 10-sec auditory stimuli (white noise or clicker), a CS+ that was paired with EtOH (0.2 ml/CS+, 3.2 ml/session), and a CS- that was not. Stimulus presentations (16 each per daily 54-min session) were controlled by independent, variable-time 67-sec schedules. Training occurred in operant conditioning chambers with a specific configuration of visual, olfactory and tactile contextual stimuli. Entries made into the fluid port to consume EtOH were measured before, during and after each CS. After 18–20 training sessions rats received 8 daily extinction sessions in a different context where both cues were presented as before, but without EtOH. At 24-hrs after the final extinction session, responding to the CS+ and CS- without EtOH was tested in the prior training context. During training rats responded more to the CS+ than the CS-, whereas across extinction port-entries during the CS+ gradually decreased. At test, control rats showed a selective increase in CS+ responding upon placement into the prior training context, indicative of context-induced renewal of alcohol seeking. This effect was blocked by pre-test, bilateral inactivation of the BLA, using gamma-amino-butyric-acid receptor agonists (M/B; 0.1 mM muscimol and 1.0 mM baclofen; 0.03 μl/side). Renewal was also attenuated in rats that received a unilateral infusion of M/B into the BLA and a unilateral infusion of either M/B or the dopamine D1-like receptor antagonist SCH23390 (0.6 μg/side) into the contralateral NACc. Preliminary results using optogenetics indicate that selectively inhibiting the BLA-NACc projection by unilaterally activating halorhodopsin-expressing BLA terminals within the NACc also impairs renewal. These results highlight the capacity of an alcohol context to stimulate relapse to alcohol seeking, an effect that requires functional activity in the BLA. They also implicate the BLA and NACc in a neural circuit that is required for Pavlovian conditioned responding to alcohol predictive cues in an alcohol-associated context. Supported by R01 AA 014925.

0738

THE EFFECT OF THE DOPAMINE D2 ANTAGONIST, RACLOPRIDE, IN THE DORSOLATERAL STRIATUM ON HABITUAL ALCOHOL SEEKING

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Our previous work indicates that operant responding for ethanol following limited (2 weeks) training is goal-directed and reduced by devaluation, but after 8 weeks of daily operant training, control has shifted to a habit-based system no longer sensitive to reward devaluation. Further, goal-directed control can be recovered following inactivation of the dorsolateral striatum (DLS) indicating that this structure plays a critical role in controlling habit-based performance. This study investigated the effects of intra-DLS administration of the dopamine D2 receptor, raclopride, on habitual responding, defined as responding insensitive to ethanol reward devaluation, following 8 weeks of alcohol self-administration.

Rats were trained to lever-press to earn ethanol (10% v/v) according to a random ratio 3 (RR-3) schedule for 8 weeks. The sensitivity of the lever-press response to devaluation was assessed by prefeeding the rats either ethanol or sucrose (2% wt/vol) prior to an extinction test. 10 min prior to the extinction test session, rats received an intra-DLS injection of saline or raclopride (0.2, or 1 μg/0.3 μl/side) over 1 min.

Rats pre-fed ethanol failed to reduce responding on the ethanol lever compared to sucrose pre-feeding, demonstrating habitual responding. Pretreatment with raclopride (0.2 μg) in the DLS reduced the number of lever-presses in the rats with ethanol pre-feeding ($p<0.01$), but not those with sucrose pre-feeding, indicating renewed sensitivity to devaluation.

The results confirm that that extended self-administration of a 10% alcohol solution produces habit-based responding and demonstrate that intra-DLS raclopride reduces this behavior, suggesting that dopamine D2 receptors in the DLS contribute to the expression of habit-based performance. Supported by R01 AA018025.

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PRAIRIE VOLES AS A NOVEL MODEL FOR STUDYING ETHANOL REWARD

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The current study investigated prairie voles as a novel model for studying ethanol reward, which is closely associated with alcohol abuse and the development of alcohol addiction. Prairie voles have long been utilized to study pair-bonding and parental/alloparental behavior. Recently, it has come to light that they voluntarily drink unsweetened ethanol, have a preference for ethanol, and show a social influence on their drinking behavior (Anacker et al., 2011; Anacker et al., 2011). The current studies demonstrate that prairie voles are useful as a model of the rewarding properties of ethanol because they show place preference for ethanol and voluntarily drink high levels of unsweetened ethanol. Adult male prairie voles were given ethanol injections (2 g/kg, 20% ethanol in saline, I.P.) immediately before being placed on one of two distinct tactile floor types. Saline injections were paired with the other floor type. After 12 conditioning sessions (15-min duration), animals were given a test day during which they were presented with both floor types for 30-min. Animals spent significantly more time on the ethanol-paired floor type ($p<.05$), suggesting a preference for ethanol-paired stimuli. In a separate study, singly housed adult male prairie voles were given continuous access to one bottle of 10% ethanol and one bottle of tap water for 14 days in the home cage, according to two-bottle drinking protocol. Animals consumed an average of 14.35 g/kg/day. A follow-up study investigated ethanol consumption during a limited access procedure. Adult male prairie voles paired with a male sibling were given access to a 10% alcohol solution for a 4-hr drinking period every other day for 14 days. Drinking sessions began at 16:00 (lights off at 20:00). During the drinking periods, animals were separated from their sibling and each was housed in a new cage. At the conclusion of the drinking period, animals were repaired in their home cage. Animals were not fluid restricted. Animals consumed an average of 3.88 g/kg/session. Taken together, the data suggest that ethanol has reinforcing properties in prairie voles, and that prairie voles may be a valuable model for studying ethanol reward.

0740

DIFFERENCES IN SENSITIVITY TO ETOH-INDUCED CONDITIONED TASTE AVERSIONS EMERGE AFTER PRE- OR POST-PUBERTAL GONADECTOMY IN MALE AND FEMALE RATS

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Prior work in our lab has focused on whether pubertal rises in gonadal hormones, previously shown to contribute to the emergence of a number of sex-typical behaviors, also contribute to sex differences observed in ethanol (EtOH) intake and sensitivity. We found that gonadectomy (GX) either prior to (Early) or after (Late) puberty increased EtOH intake in males to levels typical of adult females—an effect attenuated by testosterone replacement (Vetter-O'Hagen & Spear, 2011; Vetter-O'Hagen et al, 2011). To assess whether alterations in the aversive effects of EtOH might contribute to the testosterone-related suppression in EtOH intake, the present study examined the impact of GX on conditioned taste aversion (CTA) to EtOH in male and female Sprague-Dawley rats. Animals were either GX, received sham surgery (SH), or non-manipulated (NM) on postnatal (P) day 23 (Early) or 67 (Late) and tested for CTA to EtOH in adulthood ($\sim$P74). Rats were given 1 hr access every-other-day to 10% sucrose followed immediately by an i.p. injection of 1 g/kg EtOH or saline for 1 baseline and 5 test sessions. Animals were water deprived 50% on the day proceeding each session and given post-session ad libitum access to water. Test data were analyzed to determine the first day significant aversions emerged in each EtOH group (i.e., sucrose intakes significantly less than their saline-injected counterparts). In males, baseline sucrose intake differed with surgery age (early> late) and hormonal status (GX > NM and SH). Early GX males acquired the CTA more rapidly (day 1) than Early NM (day 5) and SH (> day 5) males. An opposite pattern emerged in Late manipulated males, with aversions developing more quickly in NM and SH (day 1 and 3, respectively) than GX (day 4) males. Among females, baseline intake differed only across surgery age (early> late). In contrast to Early males, Early GX females acquired the CTA (day 3) more slowly than Early NM and SH females (day 1). No consistent alterations emerged across groups among Late females. Thus, the absence of gonadal hormones at puberty exerted opposite effects in males vs females on EtOH CTA measured in adulthood—results that were distinctly different than following adult GX, particularly in males. Collectively, these data suggest that previously reported elevations in EtOH intake induced by GX in males are not related simply to GX-induced alterations in the aversive effects of EtOH indexed via CTA. [Work supported by R01 AA017355].

0741

MODELING ALCOHOL WITHDRAWAL VIA STIMULATION OF KAPPA-OPIOID RECEPTORS ENHANCES PRODUCTION OF 22-KHZ ULTRASONIC VOCALIZATIONS

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Alcohol Use Disorders, comprised of alcohol abuse and alcohol dependence, are a severe problem in the United States. High levels of comorbidity exist between alcohol dependence and negative affective disorders such as anxiety and depression during withdrawal. Alcohol-dependent individuals "self-medicate" by consuming alcohol to reduce the negative affective symptoms of withdrawal, which promotes excessive alcohol consumption. Given that there are no FDA-approved treatments for comorbid alcohol dependence and negative affect, it is important to understand the neurobiological mechanisms of dependence and withdrawal. Dynorphin (DYN), the endogenous ligand for kappa-opioid receptors (KORs), is increased in motivational and affective areas of the rat brain by alcohol dependence and has been shown to regulate excessive alcohol self-administration during acute withdrawal in dependent rats. Measurement of 22-kHz ultrasonic vocalizations (USVs) is an ethologically valid strategy that can be used to assess negative affective-like states in rats. Indeed, during acute withdrawal, alcohol-dependent rats with escalated patterns of alcohol self-administration also display an increased number and duration of 22-kHz USVs when compared to non-dependent rats. The goal of this study was to mimic an alcohol withdrawal-like state in rats via intracerebroventricular (ICV) infusions of the KOR-agonist U50,488 and assess negative affective-like behavior by measuring induced 22-kHz USVs. Male Wistar rats received an ICV infusion of one of four doses of U50,488 (0.0, 0.25, 2.5 or 25 μg) 15-min prior to the measurement of induced 22-kHz USVs. Two weeks later, animals received an ICV infusion of the KOR-antagonist nor-binaltorphimine (nor-BNI) 24-hrs prior to the same dose of U50,488 that was previously received and subsequently were assessed for 22-kHz USV production. U50,488 dose-dependently increased 22-kHz USVs, an effect sensitive to nor-BNI challenge. These results demonstrate that activation of KORs is sufficient to induce 22-kHz USVs and support the concept that DYN / KOR systems play an important role in the pathogenesis of alcohol withdrawal-induced negative affective-like states. Collectively, these results add to the field's understanding of the neurobiological mechanisms underlying alcohol dependence and provide an alternative strategy for the characterization of negative affective-like states during withdrawal.

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EFFECTS OF ADOLESCENT ETHANOL PRETREATMENT ON COCAINE CONDITIONED PLACE PREFERENCE IN MALE AND FEMALE RATS

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Adolescence is a time period unique in respect to neurodevelopment and its enhanced vulnerability to long-term alterations secondary to substance abuse. Exposure to alcohol, during adolescence appears to increase the predisposition of drug dependency in adulthood. Epidemiological reports indicate a high prevalence of alcohol and cocaine co-use. Interaction effects between alcohol and cocaine exposure have been reported. In animal models, ethanol (EtOH) has been shown to influence the rewarding and aversive properties of cocaine. However, the influence of EtOH pre-exposure during adolescence on future cocaine use has not been addressed. Age of exposure and sex are major factors in the development and expression of drug addiction. However, there is limited research investigating the interactive role of drug history, age of drug onset and sex on future drug use. Therefore, the long-term effects of adolescent EtOH exposure on the affective properties of cocaine was assessed by utilizing the cocaine conditioned place preference (CPP) paradigm. Specifically, we sought to investigate possible age and sex differences in the expression of CPP during adulthood, following chronic EtOH pretreatment during adolescence. Male and female rats were administered 1.75 g/kg i.p. EtOH or saline for 14 consecutive days during adolescence (postnatal day (PND) 30-43) or adulthood (PND 60-73). Following EtOH pretreatment, all rats underwent 30-days abstinence. Initial place preferences for the experimental apparatus were measured on PND 74 or 104. Drug conditioning took place for a total of 8 days. Rats pretreated with either EtOH or saline were administered either cocaine (10mg/kg, i.p.) or saline to the least preferred compartment. Post-conditioning preference scores for the drug-paired compartment were assessed. A total of 16 groups were used for the current experiment to examine age and sex differences in the expression of CPP, subsequent to chronic EtOH pretreatment. Preliminary results demonstrate a significant EtOH pretreatment and cocaine drug conditioning interaction effect. In addition, a trend for sex and age-dependent effects were observed to influence the percent of time spent in the drug-paired compartment after conditioning. Findings suggest that sex, the age of drug onset and drug history play an interactive role contributing to a unique vulnerability in the development and expression of drug addiction.

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EFFECTS OF ADOLESCENT ALCOHOL INTAKE ON RISK PREFERENCE IN ADOLESCENCE AND ADULTHOOD

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Adolescence marks a period of engagement in risky behaviors, particularly the consumption of alcohol. While increases in alcohol consumption may be fueled by increases in risk-taking, it is possible that alcohol consumption itself drives increased risk preference in a feed-forward manner. Rats that consumed alcohol during adolescence do show a preference to choose risky outcomes in adulthood during an extended period of abstinence. However, it is not known, whether adolescent alcohol intake alters risk preference during adolescence. To assess this, rats were given overnight access to a gelatin solution containing polycose and alcohol (EtOH+) or control gelatin (EtOH-) during adolescence (postnatal day 30–45), followed by abstinence for the remainder of the study. During both adolescence and adulthood, rats performed a risk task in which they chose between a 'certain' operant response for small reward and a 'risky' response for either a large reward or reward omission. The payoff probability of the risky option was varied randomly, rather than progressively, from day-to-day to control for effects of alcohol on perseverative responding. By modeling behavior to the optimal pattern of choices based on Matching Law, we found biases in judgment in EtOH+ rats. Preliminary data indicated that in adolescence, EtOH+ rats did not show an increase in risk preference compared to EtOH- rats. However, in adulthood EtOH+ rats demonstrated an increase in risk preference compared to EtOH- rats, even when the probability of risky reward was low. In general and regardless of treatment group, adolescent rats did a relatively poor job of matching their behavior to the optimize outcome compared to adults. The data support the view that increases in alcohol consumption may not be caused by increases in risk-taking during adolescence, since such increases were not apparent in our data. The changes in neural circuitry underlying a shift towards risk-preference following adolescent alcohol intake may not alter behavior during adolescence, but instead become evident in adulthood. Ongoing studies are examining the patterns of neural activity that accompany decisions about risk in adults with and without adolescent alcohol experience.

0744

CHRONIC SLEEP RESTRICTION HAS A SUSTAINED IMPACT ON SENSITIVITY TO ALCOHOL AND ALCOHOL CONSUMPTION

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Clinical reports show a high comorbidity between sleep disorders and alcohol abuse. This interaction appears to be bidirectional, such that pre-existing sleep disorders often lead to increased alcohol consumption, while chronic alcohol use often results in severe sleep disruptions. Though there have been some rodent studies modeling the effects of chronic alcohol exposure on sleep architecture, experimental models examining the effects of sleep impairments on alcohol behavior are lacking. This study used C57Bl6J mice in a chronic (72hr) sleep restriction paradigm to examine sensitivity to the motor-impairing effects of alcohol and alcohol consumption following recovery from disrupted sleep. Chronic sleep restriction was induced using intermittent treadmill activity for 72 hrs (repeated cycles of 4 hrs on, 2 hrs off), and mice were tested for sensitivity to the motor-impairing effects of alcohol (2g/kg) using the rotarod test 24 hrs, 2 weeks and 4 weeks after recovery from sleep restriction. Compared to undisturbed controls, sleep restricted mice were significantly less impaired on the rotarod after alcohol administration, an effect which was sustained for up to 4 weeks after recovery from sleep restriction. Separate cohorts of mice were then used to test alcohol consumption following one week recovery from sleep restriction, using the 2 bottle choice test in either continuous access or intermittent access paradigms. In both paradigms, undisturbed mice vacillated between high and low consumption during each alcohol access period, whereas the sleep restricted mice showed a stable consumption pattern. These results suggest that chronic sleep restriction induces a sustained reduction in alcohol sensitivity, an effect which may promote steady levels of alcohol consumption.

0745

ORAL DOXYCYLINE ADMINISTRATION REDUCES ALCOHOL CONSUMPTION AND INCREASES BEHAVIORAL SENSITIVITY TO ALCOHOL

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Doxycycline, a tetracycline derivative, is commonly employed in transgenic mouse models to control inducible transgene expression regulated by cell-specific inclusion of the tetracycline transactivator (tTA) and operator (tetO), and the transgene of interest. The ability to control transgene expression in an inducible and cell-specific manner has lead to a greater understanding of pathways involved in normal and pathological behaviors, though the potential non-specific impact of administration of doxycycline, a common antibiotic, on behavior and physiology has been largely overlooked. Of particular interest is the potential effect of doxycycline on alcohol behaviors, especially in light of recent findings showing altered alcohol consumption following administration of pro- or anti-inflammatory cytokines, such as LPS or minocycline, respectively. In this study, the effect of oral administration of doxycycline was examined in three mouse genotypes: wild-type, tTA-expressing and tetO-expressing C57Bl6/J male mice. Mice were administered a doxycycline (40g/kg) diet or regular chow for at least two weeks prior to testing alcohol consumption (drinking-in-the-dark), sensitivity to the hypnotic (loss of righting reflex) and motor-impairing (rotarod) effects of alcohol, as well as blood alcohol levels. Doxycycline administration significantly reduced consumption of 20% alcohol during 2 and 4 hr DID sessions. Interestingly, blood alcohol levels were also higher in mice on doxycycline, despite having consumed less alcohol. Doxycycline also increased sensitivity to the motor-impairing and hypnotic effects of 2.0 g/kg or 3.5 g/kg alcohol, respectively. Mice on doxcycline showed a moderate increase in blood alcohol levels under both of these conditions. These results extend on previous studies showing that neuroinflammatory agents alter alcohol consumption by showing that they also impact alcohol sensitivity and blood alcohol metabolism. Furthermore, the route of alcohol administration (i.e. oral or systemic) appears to differentially affect blood alcohol metabolism. Thus, the impact of doxycycline on alcohol behaviors should be considered when selecting an appropritate model for alcohol studies.

0746

ALCOHOL AND CIGARETTE SMOKE HAVE NEGATIVE EFFECT ON ALVEOLAR MACROPHAGES

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Aims: Alveolar macrophages (AMs) are the first ''barrier'' against respiratory pathogens in the lung. In addition to phagocytic properties, AMs also secrete a variety of pro-and anti-inflammatory cytokines. As most patients with alcohol use disorder (AUD) are smokers, we tried to characterize the influences of chronic alcohol consumption and smoke on AMs.
Methods: After approval from our ethics committee and informed consent 46 patients undergoing panendoscopic surgery were included in this pilot study: (A) 16 non-AUD and no smoker; (B) 15 non-AUD and smoker; (C) 4 AUD and no smoker; (D) 11 AUD and smoker. The stratification by alcohol abuse was carried out according to DSM IV criteria and alcohol-related questionnaires (AUDIT, CAGE) and smokers via Fagerstörm questionnaire. Exclusion criteria: age < 18 years, lung disease, liver failure, heart disease, current immunosuppressive therapy, state after transplantation and preoperative existing infections. After narcosis induction a standardized bronchoalveolar lavage was performed. HLA-DR (Ag/cell) and TLR2/4 as well as subsequently the concentrations of pro-and anti-inflammatory cytokines (pg/Mio cells) in the supernatant were specified via flow cytometry.
Results: We saw an inflammation in AUD patients with higher cytokine levels in A+B vs. C+D: IL-10 16.7 (0.0/39.1) / 72.3 (14.7/223.0) [p=0.025]; IL-1ß 33.9 (10.8/68.9) / 96.0 (29.2/123.3) [p=0.039] and a tendency of lower levels of HLA-DR and TLR: HLA-DR 501,765 (290,269/769,485) / 469,462 (270,334/643,280) [p=0.91]; TLR2 41,007.0 (17,081/78,716) / 30,687.0 (14,011/91,855) [p=0.77]; TLR4 69,649 (32,029/104,240) / 63,364 (35,880/108,352) [p=0.75]. In A vs. B significant lower HLA-DR 631,604 (315,347/829,408) / 403,455 (188,669/617,590) [p=0.027] and higher TLR2 19,275 (14,356/64,068) / 73,738 (41,007/81,714) [p=0.019]; TLR4 59,359 (28,786/92,315) / 89,967 (69,649/111,655) [p=0.03] expressions. The capacity to react adequately to LPS was reduced in AB vs. CD: IL-10 after 4h LPS: 33.9 (10.8/68.9) / 96.0 (29.2/123.3) [p=0.039]; TNF-α after 4h LPS: 6,141 (3,076/9,973) / 2,034 (160.2/6,588) [p=0.050] and IL-8 after 24h LPS: 112,769 (38,882/345,782) / 44,805 (7,909/178,510) [p=0.050]. Data: median (IQR) [Mann-Whitney U test].
Conclusions: AUD leads to an activation of AMs with functional impairment. Concomitant smoking amplifies these changes. As this was a small pilot study we are planning to verify these findings in a bigger trial.

0747

SPHINGOSINE-1-PHOSPHATE RECEPTOR-1 (S1PR1) ACTIVATION AMELIORATES ETHANOL-INDUCED ENDOTHELIAL BARRIER DYSFUNCTION.

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Ethanol at concentrations in the blood achieved after moderate to severe drinking can increase microvascular permeability. We tested the hypothesis that ethanol-induced endothelial hyperpermeability is caused by inactivation of Rac1 and disruption of normal VE-cadherin localization, and whether S1PR1 activation can restore the endothelial barrier integrity during ethanol treatment. Transendothelial electrical resistance (TER) of human umbilical vein endothelial cell (HUVEC) monolayers served as an index of barrier function before and after ethanol treatment (5–100 mM). VE-cadherin localization was determined by immunofluorescence labeling in fixed cells, or longitudinally in live cells expressing GFP-VE-cadherin. Rac1-GTP levels were determined by ELISA in HUVEC treated with 100 mM ethanol for 1, 5, 10, 30, 60, 90, and 120 minutes. The results show that ethanol decreases TER in a time- and concentration dependent manner, concomitant with disruption of VE-cadherin continuity and formation of small junctional gaps. Ethanol also significantly decreases Rac1-GTP for up to 60 min. (53% ± 5.8, 55% ± 5.1, 60% ± 5.3, 77% ± 8.9, and 73% ± 4.8 vs. control, respectively; $p<0.01$). Addition of the S1PR1 agonist SEW2871 (2 uM) at 5–10 min. after ethanol significantly shortens the recovery time to baseline TER (84 ± 12 min for control vs. 24 ± 1.5 min for SEW2871 5 min-post Ethanol and 24 ± 3.1 min for SEW2871 10 min-post Ethanol, $p<0.01$). However, SEW2871 does not increase Rac1-GTP. Our findings suggest that ethanol increases endothelial permeability by inactivating Rac1 and disrupting VE-cadherin binding between endothelial cells. S1PR1 activation can significantly attenuate the time course of ethanol-induced endothelial barrier dysfunction, however the mechanism remains elusive. Supported by NIH R21AA020049, T32AA007577, R01HL098215, and the ABMRF/Foundation for Alcohol Research.

0748

PI3K/AKT SIGNALING MEDIATES THE POSITIVE CARDIAC INOTROPIC EFFECT OF LOW ALCOHOL

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Studies have shown that low alcohol is associated with beneficial cardiovascular effects, while high alcohol is proven to be harmful. Previously we have shown that the survival pathway, PI3K, is essential for cardiac inotropy. Therefore, we hypothesized that ethanol may mediate its inotropic effects partially via PI3K pathway. Contractility and $[Ca^{2+}]_i$ measurements were performed on adult rat myocytes exposed to low (LA: 5 mM) and high (HA: 100 mM) doses of ethanol (2hr) in the presence or absence of PI3K inhibitor (LY 294002; 1 uM) or PI3K agonist, IGF-1 (10 uM). LA increased cellular and sarcomeric contraction associated with increase in the velocity of contraction. Relaxation and calcium sequestration was also improved by LA. Inhibition of PI3K negated the contractile effects of LA, but enhanced the relaxation ones. HA decreased the strength of contraction and increased speed of relaxation and calcium sequestration. IGF-1 reduced the negative contractile effects of HA. On the molecular level, HA increased Akt mRNA expression, however, no changes in protein levels were observed. Pressure-Volume loop data on the whole heart indicated a similar positive role for PI3K/Akt signaling pathway with LA as on single cardiac myocytes. Our results suggest that the regulation of PI3K/Akt activity is crucial for the positive LA- as well as the negative HA-induced inotropic effects. Furthermore, the translation of PI3K downstream target, Akt, is decreased with HA, which partly explains the detrimental inotropic effect of alcohol on the heart. Funded by NIH/NIAAA and NIH/NIGMS.

0749

ALCOHOL ATTENUATES AIRWAY CONSTRICTION IN PRECISION CUT MOUSE LUNG SLICES

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Alcohol can act as a bronchodilator and has historically been used to treat asthma. While these findings suggest that alcohol can act on airway smooth muscle, few studies have tested how alcohol affects airway smooth muscle (ASM) cells, the main effector cell of airway constriction. The precision cut lung slice system (PCLS) is an extremely useful model that can be used to determine airway function *ex vivo*, because lung architecture remains intact. Previously, we reported that alcohol exposure decreases airway hyperresponsiveness (AHR) in both naïve and allergic mice. We have also established that EtOH attenuates airway smooth muscle contraction in isolated primary rat airway smooth muscle cells by affecting the nitric oxide/PKG pathway. Based on these studies, we hypothesize that ethanol exposure attenuates methacholine (MCh)-induced airway constriction in PCLS. PCLS from C57BL/6 mice were prepared and used approximately 18 hours after being cut. A slice that contained a perpendicular cross section of an airway that contained beating cilia was inserted into a perfusion chamber and exposed to increasing doses of MCh in order to induce airway constriction and dose-responsiveness. Immediately after dose-responsiveness was established, the airway was contracted and exposed to 100 mM EtOH. Ethanol exposure resulted in a significant ($P < 0.05$) attenuation of contraction in the airways. In pre-ethanol airways, we observed an approximate 21.3% decrease in airway diameter compared to an 3.25% decrease in airway diameter subsequent to ethanol treatment at a 10 μM methacholine concentration signifying that ethanol attenuates ASM contraction. These data demonstrate that alcohol greatly attenuates ASM contraction and, for the first time, establishes that alcohol exposure blunts airway constriction in PCLS of naïve mice. Furthermore, our PCLS findings support that this model system is a comparable and suitable alternative to *in vivo* lung function data. Funded by PJO K99AA019744, JHS 5R37AA008769

0750

FETAL ALCOHOL EXPOSURE INCREASES TUMOR COLONIZATION IN THE LUNG: ROLE OF HYPOTHALAMIC BETA-ENDORPHIN

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The idea that exposure to adverse environmental conditions and lifestyle choices during pregnancy can result in fetal programming that underlies disease susceptibility in adulthood is now widely accepted. One area that has not been well studied is the impact of maternal alcohol abuse on the offspring's susceptibility to cancer. We have recently shown that fetal alcohol exposure altered mammary gland morphology with a characteristic of the hyperproliferative state prior to puberty. When fetal alcohol exposed rats were treated with a carcinogen, they showed a higher incidence of mammary tumors and progressed more frequently to a malignant phenotype. We hypothesized that higher cancer incidence in fetal alcohol exposed offspring might be a result of an abnormality in the physiological process(s) that prevents cancer development. It has been suggested that the effect of stress on the immune system may in turn affect the growth of some tumors. We have previously shown that a set of hormone secreting nerve cells in the hypothalamus, called beta-endorphin (BEP) neurons, plays a role in regulating stress response and immune function. Hence, we tested whether fetal alcohol exposure increases the incidence of tumor colonization of a breast adenocarcinoma cell line, and whether transplantation of BEP neurons affects tumor colonization in these fetal alcohol exposed rats. Pregnant female Sprague Dawley rats were fed with rat chow (Ad Lib), alcohol containing diet (Alcohol-fed), or an isocaloric liquid diet (Pair-fed). Their female offspring were transplanted with either BEP neurons or cortical cells as control. They were then inoculated with MADB106 cells in the jugular vein. Animals were sacrificed 4 weeks later and tumor granules in the lungs were counted. After tumor inoculation, fetal alcohol exposed rat had more tumor colonization in the lung comparing to ad lib and pair-fed animals. BEP transplantation reduced the stress hormone level of fetal alcohol exposed rats, and significantly prevented the appearance of tumor granules in the lung of control animals as well as fetal alcohol exposed animals. These data can be interpreted as preliminary evidence that a loss of BEP control of cancer cell clearance may be a cause for the increased cancer susceptibility in fetal alcohol animals. Furthermore, the data identify the potential use of BEP cell therapy for breast cancer prevention. (Supported by R01 AA11591 and R37 AA08757)

0751

LONG-TERM ALCOHOL DISRUPTS ZO-1 LOCALIZATION IN THE AIRWAYS OF DO11.10 MICE

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Tight junctions form a belt-like structure between adjacent cells whose degree of permeability changes according to external stimuli, physiological and pathological conditions. We have previously shown that alcohol increases tight junction permeability and disrupts tight junction proteins (ZO-1 and claudin-1) in cultured airway epithelial cells. However, little *in vivo* data exist concerning alcohol's effect on tight junctions, specifically ZO-1, in the epithelium of conducting airways. In other *in vivo* lung injury models alcohol feeding only causes increased permeability when combined with a concurrent injury such as infection or lung barotrauma. These studies focused only on alveolar-capillary lung injury, no careful examination of leak across the epithelium of the conducting airways has yet been completed. Furthermore, little is know how long-term alcohol and airway inflammation affect airway epithelial tight junctions. We hypothesize that long-term alcohol exposure reduces ZO-1 localization at the cell membrane and tight junction disruption results in increased airway permeability. To test these hypotheses BALB/c mice containing a T cell receptor transgene (DO11.10), making them more susceptible to ovalbumin (OVA) antigen, were fed 15% alcohol *ad libitum* for 6 weeks and given a single nasal instillation of OVA to trigger airway inflammation. Four hours post instillation mice were euthanized and bronchial alveolar lavage (BAL), tracheal and lung tissues were examined. Immunofluorescence studies of tracheal epithelium and bronchus revealed that ZO-1 localization was decreased at the cell membrane of conducting airways of alcohol-drinking mice compared to water-drinking mice regardless of OVA treatment. Increased BAL cell counts in OVA-exposed mice show that a single OVA installation caused an inflammatory airway response. However, we were surprised that OVA had no effect on ZO-1 localization in alcohol-fed mice. These results suggest alcohol alone disrupts normal ZO-1 distribution in the conducting airways and a more robust allergic mouse model may be needed to observe the effects of OVA on ZO-1 localization. Unlike what has been observed in other mouse airway injury models with alcohol feeding, our data suggests that in DO11.10 mice airway inflammation has no effect on the localization of ZO-1. Funding: 1F32AA019859

0752

ACUTE ALCOHOL INTOXICATION REDUCES LYMPHATIC MYOGENIC CONSTRICTION BY INHIBITING THE CA^{2+}-SENSITIZING RHOA-ROCK PATHWAY

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The RhoA-ROCK pathway is involved in [Ca^{2+}]-independent regulation of MLC20 phosphorylation through its inhibition of MLCP and, thus, the regulation of smooth muscle contraction. We previously showed that alcohol modulates the intrinsic contractile cycle of mesenteric lymphatics that provides the driving force for lymph flow; particularly that alcohol reduces myogenic constriction of these lymphatics in response to step increases in luminal pressure. We hypothesized that a change in either calcium signaling or sensitivity mediates the reduced myogenic responsiveness caused by alcohol. Acute alcohol intoxication was produced by intragastric administration of 30% alcohol through a surgically implanted catheter to conscious, unrestrained rats. Isovolumic administration of water (vehicle) served as control. Mesenteric lymphatics were isolated, cannulated and either loaded with Fura-2 AM or prepared for diameter measurements. Calcium and diameter measurements were performed at a basal intraluminal pressure of 2 cm H_2O and during pressure steps to 4, 6, 8, 10 and 12 cm H_2O for calcium and to 6 and 10 cm H_2O for diameter. RhoA-GTP levels were determined by an ELISA kit. Constitutively active (ca)-ROCK protein was introduced into the cells of lymphatics using TransIT-LT1 reagent. The results show that step increases in luminal pressure cause a gradual rise in [Ca^{2+}] in lymphatics from both the control and alcohol groups. However, RhoA-GTP was significantly reduced in lymphatics from the alcohol group, compared to control. Transfection of the ca-ROCK protein into isolated lymphatic vessels enhanced the myogenic response and tone in the alcohol treated group. We conclude that the alcohol-induced reduction in myogenic constriction in mesenteric lymphatics is due to inhibition of RhoA/ROCK-mediated [Ca^{2+}] sensitivity. Supported by NIH R21AA020049 and T32AA007577, and the ABMRF/Foundation for Alcohol Research.

0753

PROTEOMIC ANALYSIS OF ALCOHOLIC CARDIOMYOPATHY IN HUMAN HEART TISSUE

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Alcoholic cardiomyopathy (ACM) is caused by chronic alcohol abuse and leads in a dose-dependent manner to cardiac dysfunction in approximately one-third of alcoholics. ACM patients present with a depressed left ventricular (LV) ejection fraction and altered hemodynamic parameters consistent with dilated cardiomyopathy. Although several genes, proteins and signaling pathways related to cardiac structure, Ca^{2+} homeostasis and metabolism have been implicated in ACM pathogenesis, the mechanisms underlying the disease are not well understood. We obtained transplantation-quality LV heart tissue from alcoholics and control patients, who had been maintained on life support systems. Samples were lysed and total protein was fractionated into eight fractions by 1D SDS-PAGE. Peptide digests in fractions were analyzed with label-free liquid chromatography (LC) coupled to tandem mass spectroscopy (MS), using a FT-ICR mass spectrometer. Data were processed for quantitation and statistical analysis using Elucidator. We identified 117 differentially expressed proteins and visualized them on IPA pathway maps and DAVID canonical pathways to understand their biological relevance. Analysis revealed significant changes in 31 proteins in three pathways: the oxidative phosphorylation chain, cardiac contractile proteins and the citrate cycle. In the electron transport chain, alcohol mediates changes predominantly in proteins of mitochondrial complexes I and III in alcoholics without ACM, which progresses to include proteins of complex IV and V in alcoholics with clinical symptoms of ACM. These findings were validated by Selected Reaction Monitoring (SRM)-LC-MS/MS using standard peptides for six targeted proteins and derivatives labeled at the C-terminal end with heavy lysine ($^{13}C_6$, $^{15}N_2$). Targets were further validated with immunoblotting and enzymatic activity analysis to confirm the magnitude and the direction of the changes. The molecular signatures derived from the protein expression profiles in human heart tissue should be useful for studying the pathogenesis of ACM.

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0754

PIOGLITAZONE ATTENUATES ALCOHOL-INDUCED ALVEOLAR MACROPHAGE DYSFUNCTION VIA UP-REGULATION OF NOX4-RELATED MICRORNAS

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Objective: Alcohol abuse increases the risk of Acute Respiratory Distress Syndrome (ARDS) and respiratory infections through enhanced alveolar macrophage (AM) oxidative stress, leading to dysfunction. Since Nox4 is a primary source of oxidative stress in AMs and PPARg activation attenuates Nox4, we hypothesized that treatment with pioglitazone (PIO), a PPARg ligand, would attenuate alcohol-induced oxidative stress and rescue AM function by up-regulating Nox4-associated microRNAs (miRs)
Methods: AMs were obtained from the bronchoalveolar lavage (BAL) fluid of C57BL/6J mice fed alcohol (20% w/v) in the drinking water for 12 wks ± PIO (10 mg/kg/day by oral gavage during week 12). In parallel, MH-S cells, a mouse AM cell line, were treated with 0.08% ethanol for 3d ± 10 μM PIO on day 3. Nox4 mRNA and protein expression were measured by qRT-PCR and western blot. Reactive oxygen species were measured with DCFH-DA and Amplex Red assays. miRs bind to the 3'UTR of their target genes to post-transcriptionally down-regulate their translation. Levels of miRs (miR-92a/b and -363) which bind to the 3'UTR of Nox4 were assessed by qRT-PCR. AM phagocytosis was evaluated by *S. aureus* internalization.
Results: *In vivo* and *in vitro* studies with ethanol: 1) increased Nox4 expression, 2) enhanced oxidative stress, 3) reduced miR-92a/b and -363 levels, and 4) impaired phagocytic function. Treatment with PIO reversed these ethanol-induced derangements.
Conclusions: Chronic alcohol consumption induced AM oxidative stress and dysfunction, and these derangements were attenuated by PIO treatment. Our results suggest that treatment with PIO could provide a novel therapeutic approach to ameliorate alcohol-induced AM dysfunction following chronic alcohol ingestion by up-regulating Nox4-associated miRs.
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0755

BINGE ALCOHOL EXPOSURE CAUSES CANONICAL WNT PATHWAY DEREGULATION DURING EARLY FRACTURE HEALING

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Introduction: Binge alcohol exposure is a risk factor for fracture-related complications and is associated with 25–40% of all orthopaedic trauma cases. Tight regulation of β-catenin levels through activated GSK-3β, the main negative regulator of the pathway, is essential in the formation of new bone and cartilage during fracture healing. Stabilization of β-catenin promotes transcription of Wnt target genes required for osteoblast and chondrocyte differentiation immediately following injury. Beginning at day 6 post-fracture, we have previously shown that binge alcohol treatment decreases bone and cartilage formation at the fracture site, deregulates β-catenin protein levels, and disrupts Wnt transcriptional activity. This study aims to determine whether binge alcohol deregulates the expression of key Wnt target genes and the regulation of GSK-3β in the fracture callus during the early stages of healing.
Methods: C57BL/6 mice were exposed to i.p. alcohol (2g/kg) or saline for 3 consecutive days. One hour after the third injection, mice received a stabilized tibial fracture and were sacrificed 1, 2, or 3 days post-injury. Isolated fracture calluses were assessed for canonical Wnt protein levels and target gene expression.
Results: Blood alcohol levels averaged 200 mg/dl at the time of injury. RT-PCR analysis revealed that alcohol-treated mice displayed significantly decreased expression of Wnt target genes important for osteoblast and chondrocyte lineage commitment and differentiation, such as Runx2, Sox9, Wnt10b, and β-catenin. Alcohol did not change the expression of the endogenous Wnt inhibitors SOST, Dkk1, and Sfrp4 until day 3 post-fracture, where a decrease was observed. At the protein level, alcohol increased the amount of activated GSK-3β compared to saline controls at days 1 and 3 post-fracture. The deregulation of GSK-3β activation was associated with deregulation of stabilized β-catenin protein levels at the fracture site.
Discussion: Strict Wnt regulation during the early stages of fracture repair is essential in driving the differentiation of mesenchymal stem cells into osteoblasts and chondrocytes, which are required to form the fracture callus and initiate bone repair. These data show that alcohol exposure disrupts the tight regulation of Wnt/β-catenin signaling during early stages of healing, and may lead to long-term healing deficits by impairing the normal formation of the fracture callus.

0756

THE ROLE OF FOXO TRANSCRIPTION FACTORS IN ACUTE AND REPEATED BINGE MODELS OF ALCOHOL-INDUCED DEFICIENT BONE FRACTURE REPAIR

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Introduction: Alcohol abuse is a risk factor for impaired fracture healing. Binge drinking is the predominant alcohol abuse pattern associated with traumatic orthopaedic injury. During fracture repair, mesenchymal stem cells (MSC) are vital to normal healing because MSC differentiate into osteoblasts and chondrocytes required for callus formation. The differentiation of MSCs is a highly regulated process involving the canonical Wnt signaling pathway, which activates the transcription factor β-catenin. Oxidative stress is a major contributor to a plethora of pathogenesis related to alcohol abuse and bone health. Oxidative stress also activates the family of FoxO transcription factors, which also utilize β-catenin as a cofactor. We hypothesize that binge alcohol administration will inhibit fracture healing in mice by inducing systemic oxidative stress, activating FoxO-mediated oxidative stress signaling and concomitant antagonism of Wnt signaling.
Methods: 7–8 week old male C57BL/6 mice received intraperitoneal injections of ethanol (2g/kg) or saline for three consecutive days per week for two weeks. One hour after the last injection, the left tibia was stabilized with an intramedullar pin and surgically fractured. Animals in the acute binge group ceased further injections, while animals in the repeated binge group continued with daily ethanol injections until sacrifice. MSC were also exposed to ethanol in culture. Callus tissue and cultured cells were subjected to RT-PCR and western blot analyses.
Results: Both repeated and acute binge alcohol administration models led to deficient fracture repair as measured by a decreased callus volume, strength, and perturbed callus tissue composition. FoxO signaling was activated by alcohol exposure, and corresponded with significant deregulation of Wnt signaling within the fracture callus. Repeated binge alcohol administration led to greater inhibition of fracture repair, FoxO activation, and Wnt signaling perturbation in the callus as compared to the acute binge exposure group. Alcohol exposure dose-dependently increased FoxO-mediated oxidative stress signaling in cultured MSC.
Conclusions: These results illuminate a possible involvement of oxidative stress signaling as a mechanism underlying alcohol-induced deficiencies in fracture healing. The data suggests that alcohol-induced oxidative stress may play a key role in the detrimental effects of alcohol on skeletal health.

0757

DIFFERENTIAL EFFECTS OF ALCOHOL EXPOSURE AND SIV PROTEINS ON MESENCHYMAL STEM CELL ADIPO- AND OSTEOGENESIS

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Chronic alcohol consumption is associated with altered bone metabolism, decreased bone mineral density, increased risk of fractures, and a 3–5-fold higher prevalence of osteoporosis. Human immunodeficiency virus (HIV) infection is also associated with marked alterations in bone metabolism resulting in a high prevalence of osteopenia and osteoporosis. The incidence of alcohol abuse in HIV-infected patients has been estimated to be as high as 41%, leading to a greater risk for dysregulated bone metabolism. Among the underlying mechanisms proposed are disrupted anabolic hormone action, excess inflammation, and use of protease inhibitors. However, the direct viral protein-mediated effects of alcohol on osteoblasts, the cells responsible for the normal production of remodeled bone, or their precursors, mesenchymal stem cells (MSCs), are not known. The aim of this study was to investigate the impact of alcohol and viral proteins on differentiation potential of MSCs isolated from humeri of rhesus macaques. MSCs isolated from chronic alcohol-fed (3 months of 13–14g/kg BW/week; 30%w/v in water) or isocaloric sucrose control were cultured in 0, 100, and 500 ng/ml simian immunodeficiency virus (SIV) lysate concentrations with and without ethanol (50mM). Under adipogenic or osteogenic differentiation media, MSCs differentiate to osteoblasts and adipocytes through tightly regulated mechanisms. Our results show a trend for SIV protein-mediated enhanced MSC adipogenic differentiation without significantly affecting osteogenesis in cells isolated from alcohol-fed macaques. In contrast, SIV proteins appear to decrease adipogenesis while enhancing osteogenesis in MSCs exposed to alcohol *in vitro*. These results demonstrate direct SIV protein-mediated dysregulation of MSC differentiation, which we predict would result in enhanced bone marrow adipogenesis in alcohol-fed SIV-infected macaques. Thus, we propose that viral protein-mediated MSC disruption of differentiation balance may be an additional mechanism underlying the pathophysiology of bone metabolism in alcohol abusing HIV-infected patients. The MSC differential responses to SIV protein exposure specific to chronic *in vivo* vs. acute *in vitro* alcohol exposure warrant further study. (Supported by NIH grants AA09803, AA007577, and AA020312)

0758

IMPAIRED BROWN ADIPOSE TISSUE HOMEOSTASIS IN ALCOHOL CONSUMING MICE: A LINK WITH ALTERED RETINOID SIGNALLING?

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Alcohol abuse, and the disease and injury associated with it, have a profound effect on global health. While the primary organ affected by chronic alcohol consumption is the liver, another significant morbid consequence of alcohol consumption is its effect on the body's ability to regulate its temperature (thermoregulation), particularly in relation to hypothermia. It has recently become apparent that brown adipose tissue (BAT) has a hitherto underappreciated physiological effect on body heat generation in humans (thermogenesis), leading to a renewed research focus on this tissue. Our data from mice chronically consuming alcohol, as a component of the Lieber-DeCarli liquid diet, reveals a decrease in intra-scapular BAT (iBAT) mass, with a corresponding dysregulation in body temperature maintenance. It is already known that retinoids (vitamin A and its metabolites) are important mediators of brown adipose differentiation and function. Interestingly, we have observed an increase in the retinoid content of iBAT in alcohol consuming mice, which is correlated with a change in the expression of genes regulated by retinoic acid. Continuing research is focused on establishing a definitive link between alcohol's effect on retinoid signalling and brown adipose tissue function. In summary, chronic alcohol consumption in mice is associated with a decrease in iBAT mass and an inability to maintain body temperature; we are investigating whether this change is associated with alcohol's effect on retinoid signalling (Supported by NIAAA Grant RC2 AA019413 and R21 AA020561).

0759

MENSTRUAL CYCLES DURING ETHANOL SELF-ADMINISTRATION IN FEMALE RHESUS MONKEYS (MACACA MULATTA)

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Alcoholism in women and chronic ethanol self-administration in animals has been reported to disrupt reproductive function, although with wide species and individual differences. The current longitudinal study assessed menstrual cycle quality during ethanol self-administration using 3.3–4 year-old female Indian rhesus monkeys (*Macaca mulatta*, n = 13). Most rhesus monkeys have begun ovulating by 3.5 years of age (Zehr et al. 2005 Biol Reprod 72). Menstrual data were obtained before (9 months) and during (9 months) 22 h/d self-administration of ethanol (4% w/v) and water (n = 6) or isocaloric maltose-dextrose and water (n = 3), or during consumption of a laboratory diet for 18 months (n = 4). Under the laboratory diet 33.5 ± 10.1% of cycles were of normal duration (25–31 days; Quadri and Spies 1976 Biol Reprod 14) and ovulatory (defined as peak progesterone ≥ 4 ng/ml; peak progesterone, 10.9 ± 0.8 ng/ml). Prior to the introduction of maltose-dextrose or ethanol (4 months), normal ovulatory cycles occurred in 1/1 maltose-dextrose and 1/3 ethanol subjects for which plasma progesterone was measured at this early stage of the experiment when the monkeys were being trained for awake venipuncture, with peak serum progesterone 6.1 ng/ml and 5.5 ± 1.3 ng/ml, respectively. During the 5 months of introduction of maltose-dextrose or ethanol induction, respectively, 39 ± 6% (peak progesterone, 8.7 ± 1.1 ng/ml) and 56 ± 13% (10.1 ± 1.7 ng/ml) of cycles were normal and ovulatory. All monkeys that had 22 h/d access to ethanol and water were heavy drinkers (> 3.5 g/kg/d). For three (of 6) monkeys, a majority (77–100%) of menstrual cycles were of irregular duration and/or anovulatory. For the other three monkeys, a majority (57–88%) of menstrual cycles were of normal duration and ovulatory (peak progesterone 9.8 ± 1.0 ng/ml), despite drinking > 4.0 g/kg ethanol per day on average (equivalent of 16 drinks). The data highlight individual differences in sensitivity to reproductive dysfunction due to ethanol. The monkeys with resistance to ethanol-induced disruption of menstrual cycles had the greatest peak progesterone and percentage of normal ovulatory cycles prior to ethanol access. Thus, heavy ethanol drinking during peri-pubescence, prior to the onset of regular ovulatory cycles, could impair reproductive capacity and circulating progesterone, with implications for neuroactive steroid interactions with ethanol.

0760

ALTERED PFC EXPRESSION OF GLIAL MARKERS IN MICE WITH A HISTORY OF BINGE ALCOHOL DRINKING

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Much of the preclinical research on the molecular adaptations resulting from alcohol exposure has been centered on neuronal populations. Glial cell types may also mediate the effects of alcohol given their roles in regulating nerve impulse conduction, glutamate and GABA neurotransmission, maintaining the extracellular milleu, and their expression of many neurotransmitter receptors. The present immunoblotting study was intended to examine a variety of glial cell subtype-specific proteins involved in the functional integrity of the forebrain, including the dorsal and ventral prefrontal cortex (dPFC and vPFC respectively). C57BL/6J mice underwent 30 days of 20% alcohol drinking under DID procedures. On day 1 of withdrawal, tissue was extracted for immunoblotting for a variety of markers of astrocytes, oligodendrocytes and microglia. Alcohol experience resulted in an increase of Connexin 30 (Cx30) within the dPFC and increases in glutamine synthetase (GS), myelin oligodendrocyte glycoprotein (MOG), and a trend towards significance for proteolipid protein (PLP) within the vPFC. The increased astrocytic markers, GS and Cx30, are consistent with earlier data obtained from rodents undergoing protracted alcohol withdrawal from a more prolonged alcohol drinking regimen and may reflect the activation of astrocytes regulating excessive glutamatergic neurotransmission during ethanol withdrawal. While we anticipated a decrease in myelin-related proteins following alcohol drinking, given the reductions in white matter volume of chronic human alcoholics, myelin structure and composition changes with neuronal activity. Thus, increases in MOG and PLP may reflect the hyperexcitability during early ethanol withdrawal.

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ETHANOL INDUCES PARALLEL CHANGES IN HIPPOCAMPAL HISTONE H3 PHOSPHORYLATION AND C-FOS PROTEIN EXPRESSION

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Post-translational histone modifications represent an important epigenetic mechanism for the control of gene expression. Recent evidence shows that histone H3 phosphorylation (pHis-H3) regulates ethanol-mediated changes in gene expression in the liver; however, ethanol's effects on pHis-H3 in the brain have yet to be examined. Two paradigms were used to investigate ethanol's effects on pHis-H3 in the hippocampus, measured by quantitative immunohistochemistry. In the first, adult male Sprague-Dawley rats were gavaged with 0, 1, 2.5, or 5 g/kg ethanol and were euthanized 2 hours later. In the second, rats were made ethanol-dependent using the Majchrowicz model (25% w/v ethanol diet every 8 hours for 4 days). Ethanol-dependent rats were euthanized 2 or 16 hours following the last dose so that pHis-H3 could be assessed during intoxication and at peak withdrawal. BECs ranged from 68±5.9 mg/dL for 1g/kg to 267±16 mg/dL for 5g/kg in the acute study, while peak BECs in ethanol-dependent rats reached 418±16 mg/dL. Acute ethanol exposure dose-dependently altered hippocampal pHis-H3 ($p<0.01$). Specifically, 1g/kg ethanol increased the number of pHis-H3+ cells in all neuronal layers. In contrast, 2.5 and 5g/kg ethanol inhibited pHis-H3, an effect that was confined to the granule cell layer (GCL). pHis-H3 was also altered in ethanol-dependent rats ($p<0.01$). At peak intoxication, GCL pHis-H3 was reduced by 66%; however, pHis-H3 was increased in all hippocampal neuronal layers during peak withdrawal. These studies demonstrate that pHis-H3 is highly sensitive to alcohol, but the genes affected and the functional implications of this epigenetic change are unknown. Because pHis-H3 has been shown to regulate the transcription of c-fos, an immediate early gene expressed by activated neurons, we hypothesized that c-fos protein expression would parallel ethanol-induced changes in pHis-H3. Indeed, acute ethanol exposure dose-dependently altered c-fos with 1g/kg increasing and 5g/kg attenuating GCL c-fos expression. In addition, hippocampal c-fos was decreased in ethanol-dependent rats during intoxication, but was significantly increased at peak ethanol withdrawal. Ethanol's parallel effects on pHis-H3 and c-fos suggest that pHis-H3 regulates ethanol-mediated changes in c-fos expression. The regulation of hippocampal c-fos expression by pHis-H3 has important implications for ethanol-induced changes in neuronal plasticity. Funded by NIAAA R01AA016959.

0762

EPIGENETIC REGULATION OF BRAIN-ENRICHED MICRORNA MIR-124 EXPRESSION UNDER ETHANOL DEPENDENCE AND RELAPSE

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Relapse has been recognized as a major problem of ethanol dependence. However, the pathogenesis of both dependence and relapse has never been established. Recently, it has been reported that brain-enriched microRNA miR-124 play a critical role in the dependence of abused drugs, such as cocaine. Moreover, we found that acute ethanol administration caused the long-lasting increase in the expression of miR-124 in mouse brain. In the present study, we investigated the expression of miR-124 in mouse ethanol dependence and relapse model. Mice were treated with liquid diet containing ethanol for 10 days. Using the escalating ethanol dosage schedule, the mice were fed the ethanol diet as follows: 1st day: 1 w/v%; 2nd and 3rd day: 3 w/v%; 4th and 5th day: 4 w/v% and from the 6th to 10th day: 5 w/v% ethanol diet, respectively. The pair-fed control mice were given the same volume of ethanol-free liquid diet with glucose substituted in isocaloric quantities for ethanol. The mice chronically treated with ethanol revealed severe withdrawal signs. At the 11th day, the mice were killed by decapitation and the limbic forebrain (containing nucleus accumbens), lower midbrain (containing ventral tegmental area) were dissected. Northern blotting analysis for detection of microRNAs in the brain was performed. The expression of miR-124 was significantly increased in limbic forebrain and lower midbrain following chronic treatment of ethanol. These findings suggest that changes in the expression of miR-124 may occur in mesolimbic dopaminergic system, contributing to the development of ethanol dependence. Chronic ethanol consumption significantly increased the levels of acetylated histone H3 in both brain regions. We established a mouse ethanol relapse model using combination with liquid ethanol diet and conditioned place preference. The expression of miR-124 was significantly decreased and acetylated histone H3 was significantly increased in limbic forebrain and lower midbrain in ethanol relapse state. We previously found that the intracerebroventricular administration of histone deacetylase inhibitor significantly increased expression of miR-124. These findings suggest that histone acetylation regulate the expression of miR-124 expression under ethanol dependence and relapse.

0763

ALCOHOL CAUSES INHIBITION OF HISTONE DEACETYLASE (HDAC) 3, 4, AND 10 IN THE AIRWAY EPITHELIUM

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Alcohol impairs the airway epithelium's innate immunity, of which toll-like receptors (TLR) are important components. TLR2 senses components of the gram- positive cell wall and initiates an inflammatory signaling cascade. After brief alcohol exposure, TLR2 expression increases. With prolonged exposure, TLR2 expression is decreased. Little is known about the mechanism of this decrease. Histone deacetylases (HDACs) are enzymes that remove acetyl groups from histones. This changes the conformation of DNA wound around the histone and can modify transcription. We hypothesized that prolonged alcohol exposure may modulate HDAC activity and lead to decreased TLR2 expression.

To determine whether HDAC inhibition plays a role in TLR2 expression, Normal human bronchial epithelial (NHBE) cells were treated for 24 hours with the HDAC inhibitor, Trichostatin A (TSA). TLR2 expression was measured using qRT-PCR. The TSA-treated cells had reduced TLR2 expression compared to cells treated only with media. This supports that HDAC inhibition may lead to decreased TLR2 expression.

To determine whether alcohol modulates any members of the HDAC family, we exposed NHBE cells to ethanol for 4, 24 and 48 hours ($n=5$), and performed qRT-PCR for HDAC 1-10. There was a decrease in HDAC3 ($p< .0001$), 4 ($p<.01$) and 10 ($p<.02$) after alcohol exposure, suggesting that alcohol has a very specific effect on these HDACs, versus a global effect.

To determine whether alcohol's decrease in HDAC 3, 4 and 10 has an effect on overall HDAC activity, NHBE were exposed to 100 mM ethanol for 6, 24 and 48 hours. HDAC activity was measured and there was a significant decrease at 24 hours ($n=4$, $p=.03$).

This work demonstrates that alcohol decreases HDAC 3, 4 and 10 expression in the airway epithelium. These decreases potentially lead to the decrease in TLR2 expression after prolonged alcohol exposure. In most cases, HDAC inhibition leads to increased transcription. Our data suggests that TLR2 is unique in its decrease in expression after HDAC inhibition. It is possible that the conformational changes induced by HDAC inhibition decreases the physical association between transcription factors and enhancers of the gene. It is also possible that alcohol exposure is changing the actetylation of NFκB subunits, which can also lead to decreases in NFκB-mediated transcription. Further research will focus on how HDAC 3, 4, and 10 inhibition leads to decreased TLR2 expression. (Supported by NIH K08AA019503.)

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ANALYSIS OF VIRAL GENOTYPIC DIVERSITY IN THE ETHANOL-TREATED SIV-INFECTED MACAQUE MODEL

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Chronic alcohol abuse has been associated with more rapid HIV disease progression. In the ethanol-treated, SIV-macaque model, higher plasma viral loads and a shortened median time to death are observed when compared to sucrose-treated controls. In this study, we sought to evaluate the genotypic diversity of the virus expressed in alcohol-treated and control animals over time, to determine if increased viral levels were associated with the selective amplification of specific viral genotypes. The hypervariable region of the SIV envelope gene (V1-V2) was amplified by RT-PCR from sequential plasma samples obtained from a cohort of macaques receiving chronic ethanol dosing via gastric catheter ($n=12$) or isocaloric sucrose ($n=12$). Using a heteroduplex tracking assay, we determined V1-V2 diversity by analyzing the complexity of the banding pattern observed after annealing of PCR products to a radiolabeled probe and electrophoresis on a non-denaturing gel. This highly diverse region of the SIV genome provides a sensitive target for monitoring genotypic diversity and selection. Percent divergence of the viral population over time was quantified using ImageQuant software. Although alcohol-treated animals displayed higher plasma viral levels, V1-V2 diversity levels were similar to sucrose-treated controls during the early stages of infection through set-point. During the chronic phase of infection (4–6 months post inoculation), slightly lower levels of diversity were observed in the alcohol-treated group as compared to controls, indicating that fewer viral variants are expressed as disease progresses; an observation consistent with the selective expression of genotypes. While the envelope V1-V2 region allows us to enumerate genotypes, it may not capture critical changes in other regions. Selective mutations in the regulatory regions of the virus, which control rates of viral expression, can affect viral expression in the chronic alcohol environment. Future studies will focus on the diversity of the promoter region in the viral LTR, as well as the analysis of viral genotypes contained in specific cell types and tissue reservoirs.

0765

DISSECTING ENDOPLASMIC RETICULUM STRESS RESPONSE IN ALCOHOLIC PANCREATITIS

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Chronic pancreatitis (CP) is a major health problem among alcohol abusers. The mechanism of CP is not well understood primarily due to the lack of animal model(s). In a dose-dependent study, earlier, we reported pancreatic injury and endoplasmic reticulum (ER) stress in hepatic alcohol dehydrogenase (ADH) deficient (ADH^-) deer mice vs. ADH normal (ADH^+) deer mice fed 3.5% ethanol for 2 months *via* Lieber-DeCarli liquid diet. Regulators of ER stress response or unfolded protein response (UPR) have key role in adaptation and prevention of ethanol-induced ER stress. Since alcoholic pancreatitis is a chronic disease, we assessed regulators of UPR in the pancreas of ADH^- deer mice fed 3.5% ethanol daily for 6 months *via* liquid diet. ER stress was assessed by measuring the glucose-regulated protein 78 (GRP78, a marker of ER stress) and UPR signaling system by Western blot analysis using respective antibodies in post nuclear fraction of pancreatic homogenates. We found a small increase in GRP 78 in animals fed ethanol as compared to pair-fed controls. However, the levels for inositol-requiring enzyme (IRE)-1α and X-box binding protein (XBP)-1 and phosphorylated protein kinase RNA activated (PKA) ER Kinase (PERK) and CCAAT/enhancer binding protein (C/EBP) homologous protein (CHOP) were significantly increased in ethanol-fed animals vs. pair-fed controls. Our data on UPR signaling cascade indicates involvement of IRE-1α /XBP-1 and PERK/CHOP branches in correctional measures of ethanol-induced ER stress in the pancreas of deer mice. Although UPR response is an adoptive and correctional mechanism against ER stress, prolonged ER stress can result in inflammatory response. Therefore, a detailed analysis of downstream UPR signaling events along with evaluation of inflammatory responses in our chronic ethanol feeding model could enable us understand the mechanism of alcoholic pancreatitis and develop its prevention. This work was supported by NIAAA grant, AA019812.

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PROTEIN KINASE A (PKA) AND NEURONAL TRYPTOPHAN HYDROXYLASE (TPH2) IN THE DORSAL RAPHE NUCLEUS OF ALCOHOLICS: EFFECTS OF EARLY LIFE ADVERSITY

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Early life adversity (ELA) is associated with increased alcohol abuse risk in adulthood. Chronic alcohol abuse depletes brain serotonin (5-HT), which is synthesized by the stress-sensitive rate-limiting enzyme tryptophan hydroxylase (TPH2) in the dorsal (DRN) and median (MRN) raphe nuclei. We have reported a paradoxical increase in TPH2 in the DRN of alcoholics, potentially compensatory to low 5-HT. Since PKA phosphorylates TPH2 to enhance catalytic activity, we sought to determine whether phosphorylated TPH2 (pTPH2) and PKA are altered in alcoholics, and if so, how it is affected in alcoholics that have reported ELA.
I*n situ* hybridization and immunoautoradiography were performed to assay postmortem TPH2 mRNA and protein in the DRN of 16 pairs of age and sex matched non-psychiatric controls (C) and alcoholics (Alc). In a subset of 9 pairs, western blots were done to measure PKA and p-TPH2 protein. Lifetime alcoholism, medical, and psychiatric history were obtained from next-of-kin. DSM IV diagnosis and ELA were determined by psychological autopsy and included parental separation or loss, childhood abuse and neglect.
There was 20% more TPH2 and 10% more pTPH2 protein in the DRN of alcoholics compared to controls (TPH2: F=8.72, p=0.001; pTPH2: t=–2.57, p=0.02). TPH2 mRNA was also elevated in alcoholics compared to controls (F=3.96, p=0.024). Alcoholics without ELA had 17% more pTPH2 than alcoholics with ELA (Alc*ELA interaction, F=6.62, p=0.02). Alcoholics with no ELA had 36% more PKA than controls (p=0.03) and 41% more PKA than alcoholics with ELA. In alcoholics, but not controls, pTPH2 was positively correlated with PKA (r=0.95, p=0.02). While there was no difference in DRN TPH2 protein optical density with respect to adversity, alcoholics without ELA had larger DRN area of TPH2 protein distribution compared to controls and alcoholics with ELA which had markedly reduced area of TPH2 protein distribution (C: 5.8±4.5 mm^2, Alc without ELS: 8.7±6.3mm^2 *vs.* Alc with ELA 3.7±2.4mm^2, F=4.3, p=0.04).
The findings indicate more PKA and pTPH2 protein in alcoholics. In contrast however, alcoholics with early life adversity have less PKA, less pTPH2 and reduced area of TPH2 expression suggesting that ELA permanently alters the expression and regulation of the stress-sensitive enzyme TPH2.

0767

PLATELET-DERIVED GROWTH FACTOR-BB ACTIVATES CELL CYCLE BY SUPPRESSING MIR-373* EXPRESSION IN HUMAN ACTIVATED HEPATIC STELLATE CELLS

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After liver injury hepatic Stellate cells (HSC) undergo a phenotypic change referred to as transdifferentiation or activation that plays a key role in the development of liver fibrosis. Even though multifarious cellular changes occur with HSC activation, the expression of PDGF-BB and its receptor play an important role in this activation process at the HSC migration and proliferation level. Recent data suggest that microRNAs (miRNA) are involved in the regulatory mechanisms of fibrosis; moreover they mediate diverse processes including cell proliferation. However, their participation in HSC proliferation modulated by PDGF-BB is unknown. In an attempt to address this crucial question, we evaluated the effects of PDGF-BB on the miRNA expression profile associated with HSC proliferation in HSC in culture. We have demonstrated that PDGF-BB induced cell proliferation and Cyclin D1 expression based on MTT and Western blot analyses, respectively. MiRNAs microarray analysis revealed that PDGF-BB altered the expression of 53 miRNAs, of which miR-373* in particular was strongly down-regulated by PDGF-BB. We confirmed this down-regulation by qPCR. Using miRANDA Software, a miRNA target genes predictor, we found that proteins that control cell cycle namely Cdk1 and CdK2, are targeted by miR-373*. Furthermore, protein and mRNA expressions of Cdk1 and CdK2 were significantly up-regulated. These results suggest that miRNAs regulate the activation of HSC and indicate that PDGF-BB requires the participation of miRNAs to exert its effect in activated HSC (This work was supported by NIH R01 AA010541-17 S1''Role of Acetaldehyde on PDGF-BB induced HSC Migration and Proliferation'').

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PROTEASOMAL DEGRADATION OF SKI IS AN IMPORTANT EVENT IN ACETALDEHYDE-MEDIATED UP-REGULATION OF THE HUMAN α2 (I) COLLAGEN GENE IN HEPATIC STELLATE CELLS

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Ethanol-induced liver cirrhosis is a leading cause of death. Ethanol induces liver fibrosis by a multi-factorial process, involving several liver cell types, including hepatic Stellate cells (HSC), the main producers of type I collagen in the liver. Previous work from our laboratory has shown that acetaldehyde, the first metabolite of ethanol, up-regulates the expression of the human α2 (I) collagen (COL1A2) gene via a de novo protein synthesis-independent and PI3K-dependent mechanism, and that the early acetaldehyde-mediated effects involve phosphorylation and nuclear translocation of Smad 3 and Smad 4 containing complexes which bind to the COL1A2 promoter. In order to demonstrate the obligatory requirement of proteasomal degradation of SK1 for the action of acetaldehyde in the fibrogenic process, we have determined the effects of acetaldehyde on the expression of COL1A2 gene in human hepatic Stellate cells. Human HSC were co-transfected with the -378 COL1A2LUC reporter construct and a Smad 4 vector followed by treatment with acetaldehyde. COL1A2, fibronectin and TGF-β1 were analyzed using Northern Blot Hybridizations and Run-on Transcription Assays. Ski, Smad2, Smad 3 or Smad 4 from nuclear extraction were analyzed using Western Blot technique and a Co-precipitation of Smad 4 with Ski was performed. In this communication, we show that Smads 3 and 4 are limiting factors in COL1A2 gene up-regulation induced by acetaldehyde and that this ethanol metabolite enhances Smad 3 and 4 at the mRNA and protein levels. We further show that Ski, a member of the Ski/SNO family of Oncogene, is co-localized in the nucleus with Smad 4 and that acetaldehyde induces their co-translocation to the cytosolic compartment where Ski is degraded by proteasome. We also demonstrate that inhibiting proteasomal degradation of Ski by lactacystin blunts acetaldehyde-dependent COL1A2 up-regulation but has no effect on the expression of fibronectin. Overall, these data suggest that acetaldehyde stimulates COL1A2 up regulation by enhancing the expression and activation of gene transactivators, such as Smads 3 and 4, while also inhibiting the expression of transcriptional repressors, such as Smad 7 and Ski. We speculate that drugs that prevent proteasomal degradation of repressors targeting the COL1A2 gene could have potent anti-fibrogenic properties (This work was supported by NIH 5R01AA009231 Alcohol-induced liver fibrosis: an in vitro model)

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ETHANOL OXIDATION REGULATES EARLY GROWTH RESPONSE-1 (EGR-1) GENE TRANSCRIPTION IN RECOMBINANT HEPG2 CELLS

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Background: Previously, we reported that ethanol-induced triglyceride accumulation occurred partially through elevation of the transcription factor, early growth response-1 (Egr-1) in HepG2-derived VL-17A cells that express alcohol dehydrogenase (ADH) and cytochrome P450 2E1 (CYP2E1). Ethanol oxidation enhanced Egr-1 protein content, which was preceded by elevation of its mRNA. Ethanol exposure also caused stabilization of the Egr-1 protein, which participates in ethanol-induced triglyceride accumulation (ACER, 35: 51A, Abst 162, 2011). Here, we sought to determine whether enhanced Egr-1 synthesis occurred by ethanol-induced activation of the Egr-1 gene promoter.
Methods: Ethanol metabolizing VL-17A cells were co-transfected with an Egr-1 promoter construct and with pRL-TK vector, an internal control for transfection efficiency. Transfected cells were subsequently incubated for 24 hr with or without 50mM ethanol in the presence or absence of 4-methylpyrazole, an ethanol oxidation inhibitor. Firefly and rennila luciferase activity in cell lysates were measured using Dual Luciferase Reporter Assay System (Promega).
Results: Ethanol treatment for 24 hr induced Egr-1 promoter activity by 1.6-fold over untreated control cells. The increased Egr-1 promoter activity caused by ethanol exposure was completely blocked by the inclusion of 4-methylpyrazole. 4-methylpyrazole alone had no effect on Egr-1 promoter activity.
Conclusion: Our results indicate that ethanol metabolism increased Egr-1 RNA and protein by increasing Egr-1 gene promoter activity. We propose that the primary ethanol metabolite, acetaldehyde likely binds to Egr-1 promoter region to initiate Egr-1 mRNA transcription.

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ROLE OF POL III GENE DEREGULATION IN ALCOHOL-ASSOCIATED BREAST CANCER*

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Transcription of RNA polymerase (Pol) III-dependent genes, such as 5S rRNA and tRNAs, are elevated in both transformed and tumor cells. Brf1, a subunit of TFIIIB complex, specifically regulates RNA Pol III gene transcription. Changes in Pol III gene transcription and Brf1 expression are tightly link to cell transformation and tumor formation. Alcohol consumption is more pronounced in ER+ (estrogen receptor positive) breast cancer cases than in ER- cases. However, the molecular mechanism remains to be determined. Alcohol-induced deregulation of Pol III gene transcription may be fundamental to the development of breast cancer. By using different normal and cancer breast cell lines, we have found that alcohol increases Pol III gene transcription in both normal nd cancer breast cell lines. The induction in breast cancer cells is significantly higher (5~6 fold) than in normal and is ER dependent. E2 (17β-estradiol) causes a small alteration of these genes, whereas ethanol works with E2 to dramatically increase Pol III gene transcription. Our results further indicate that ethanol markedly stimulates phosphorylation of JNK1, but not JNK2 in MCF-7 cells. The cellular levels of Brf1 protein and mRNA are increased in ethanol-treated MCF-7 cells. Inhibition of JNK1 by JNK inhibitor and JNK1 siRNA decrease activity of ER-response-element reporter, ERα and Brf1 expression, and Pol III gene transcription. Reduction of ERα by its siRNA decreases Brf1 expression and Pol III gene transcription. Our analysis has demonstrated that both ethanol and E2 individually increase the rate of MCF-7 cell proliferation while ethanol plus E2 together produces an additional increase in this rate. Additionally, we have observed that control cells and ethanol-treated MCF10A cells do not undergo colony formation, E2 alone induces colony formation. Ethanol in combination with E2 produces larger and more numerous colonies than E2 alone. Repression of ERα or Brf1 by their siRNAs decreases alcohol-induced cell transformation. Our results support the idea that alcohol activates JNK1 to enhance ERα expression, which in turn enhances Brf1 expression and Pol III gene transcription to bring about greater phenotypic changes. Together, our studies indicate that ethanol-induced deregulation of Pol III genes may play a critical role in alcohol-associated ER+ breast cancer.*The project is supported by NIH AA017288 to S.Z. **Corresponding author: zhong@usc.edu. Tel: 626-628-7693 or 323-442-1141.

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DETERMINING THE ROLE OF ETHANOL IN THE INITIATION OF ORAL SQUAMOUS CELL CARCINOMA USING A 4-NITROQUINOLINE 1-OXIDE MURINE CARCINOGENESIS MODEL

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Background: Oral squamous cell carcinoma (OSCC) remains one of the deadliest diagnosed cancers with 40,000 new reported cases and 13, 000 estimated deaths a year in the U.S. The majority of deaths associated with OSCC are typically due to chronic tobacco and alcohol use. Epidemiological studies have confirmed that the relative risk (RR) of OSCC in never smokers and never drinkers are 7 and 3, respectively. However, the RR of OSCC rises to 34.1 in persons who are chronic alcohol and tobacco abusers. Although both chronic alcohol and tobacco consumption in humans have been identified as major risk factors in initiating OSCC, there is limited knowledge concerning how these etiologic factors contribute to molecular alterations involved in the initiation of OSCC.
Method: To mimic the synergistic activity of chronic tobacco and alcohol abuse, we have combined the 4-Nitroquinoline-1-oxide (4NQO), a soluble carcinogenic surrogate for tobacco exposure, murine model with the Meadows-Cook ethanol model. In this study, we generated five experimental groups in which mice were treated with 100 ug/mL 4NQO or propylene glycol (vehicle control) in their drinking water for eight weeks followed with 20% (w:v) ethanol (after a 7 day acclimation period) or normal water treatment for eight weeks. The experimental groups were divided as follows: 1) no treatment; 2) ethanol only; 3) 4NQO only; 4) 4NQO and ethanol; and 5) 4NQO and ethanol with administration of ethanol during the last week of 4NQO treatment. Cellular and molecular alterations in the tongues and esophagi of the experimental groups were analyzed by histology, immunohistochemistry, and Western blotting.
Results: Analysis of the mice treated as described is in progress. However, the various treatments groups of 4NQO and 4NQO with ethanol show increased Ki-67 levels, a marker of cellular proliferation. We are measuring markers of cellular proliferation (Epidermal Growth Factor Receptor); angiogenesis (Vascular Endothelial Growth Factor Receptor); metastasis (E-cadherin); and tumorigenesis.
Conclusion: This study demonstrates the use of an appropriate animal model in observing the induction of OSCC using the 4NQO murine model. Further work will be conducted to identify the potential role of ethanol in the initiation of OSCC by observing potential changes in the expression of oncogenes, tumor suppressors, and stem cell markers in the oral cavity.

7. FETAL ALCOHOL SYNDROME / DEVELOPMENT

0772

PRENATAL ALCOHOL EXPOSURE IS RELATED TO ALCOHOL ODOR RESPONSES IN OLDER TEENS

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Purpose: Building on the Miller & Spear (2006) model of developmental and trans-generational risk for alcohol abuse and alcoholism, we assessed associatively learned responses to prenatal alcohol exposure (PAE) as a teratogenic neurobehavioral outcome in older teens/young adults. Based on preclinical research (e.g., Molina et al, 1995; Chotro et al, 2007) and research on mothers and children (e.g., Faas et al, 2000; Mennella & Beauchamp, 1998), we hypothesized that PAE leads to positive associations with alcohol which enhance later recognition and perceived intensity or pleasantness of alcohol's sensory characteristics (odor) by older teens.
Methods: At 19 yrs, 75 participants were identified from our longitudinal prospectively identified cohort. Odor recognition ability was assessed using the University of Pennsylvania Smell Identification Test (Doty, 2008). Responses to alcohol odors were examined via self-report of perceived "pleasantness" and intensity, and correct identification of various alcohol and non-alcohol odors. PAE was assessed retrospectively at a 14-yr teen visit when mothers were again queried about their drinking during the same pregnancy. Relation between PAE and teen responses to alcohol odors were examined using multiple regression controlling for other prenatal exposures and multiple maternal/caregiver variables: custody status, age at conception, marital status, education, IQ, psychopathology; environment: SES, home quality, number of children in home; and teen factors: gender and age at testing. Variables were entered into the regression in this order: covariates and other prenatal exposures followed by PAE.
Results: Even after controlling for multiple potential predictors of teen alcohol use, retrospective PAE significantly predicted teen ratings of alcohol odor pleasantness (β=.39, p<.01). Of the other odors, only tap water pleasantness was related significantly to PAE (β=.32, p<.05). PAE was not related to odor recognition or rated intensity.
Conclusions: Controlled analysis from our prospective longitudinal cohort demonstrated that PAE is related to teen responses to alcohol odors, and not to other odors. This finding supports our hypothesis that positive associations to the chemosensory properties of alcohol are learned prenatally. Future analyses will examine how teen odor responses may be related to alcohol preference, alcohol-seeking, and high-risk alcohol-related behaviors in teens.

0773

AN FMRI STUDY OF BRAIN NETWORK INTERACTIONS IN SYNDROMAL AND NON-SYNDROMAL CHILDREN WITH FASD

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Cognitive impairment in fetal alcohol spectrum disorder (FASD) is most severe in children who meet diagnostic criteria for full or partial fetal alcohol syndrome (FAS/PFAS), but significant deficits are also seen in non-syndromal heavily-exposed (HE) children. Using fMRI, we recently found differences in working memory-related cortico-striatal-cerebellar *activation* between syndromal and non-syndromal alcohol-exposed children (Diwadkar et al., 2012). But effects on regional brain *interactions* have not previously been investigated in FASD. In this study, we used psycho-physiological interaction (Friston et al., 1997), a seed-based method for assessing modulatory interactions between brain regions. We hypothesized that prenatal alcohol exposure would affect the degree to which the dorsal anterior cingulate cortex (dACC), an important cognitive control region, modulates activity in fronto-striatal-cerebellar regions known to mediate working memory. A verbal 1-back task was administered to 47 children (17 with FAS/PFAS, 13 HE, and 17 controls; age 8.9–10.6 yr). In the 1-back condition, the child presses the left key if the letter appearing on the screen is the same as the previous letter; the right key, if it is not. In 0-back, s/he presses the left key to the letter *D*; otherwise, the right. Time series from the dACC ($p<.05$, effects of interest) were convolved with the psychological contrast of interest (1-back > 0-back) to investigate modulatory effects of the dACC. Inter-group differences were evaluated in a second level analysis of variance. When compared with controls, the FAS/PFAS group showed significantly greater modulation by the dACC of several brain regions known to mediate working memory, including dorsal prefrontal cortex, inferior frontal gyrus, superior parietal cortex, basal ganglia, and cerebellum. Similar, albeit somewhat weaker, effects were seen in the HE group. These data suggest that fetal alcohol exposure disrupts the efficiency of cortico-striatal-cerebellar function, so that greater modulation by a key executive control region is required to perform a simple 1-back task. This increased executive control may constitute a compensatory mechanism for functional deficits in the regions that mediate working memory. This study provides the first demonstration of extensive effects on brain network interactions in children with FASD.

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0774

EFFECTS OF FETAL ALCOHOL EXPOSURE ON ACQUISITION RATES IN VISUOSPATIAL AND VERBAL LEARNING

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Verbal and visuospatial learning and memory have been extensively studied in individuals with fetal alcohol spectrum disorders (FASD). Previous studies have shown deficits in learning in both domains. The purpose of this study was to investigate the dynamics of verbal and visuospatial learning in children with FASD from Cape Town, South Africa. The sample was comprised of 59 Cape Coloured (mixed ancestry) children who are participating in the 9-year follow-up of a longitudinal FASD study, comprised of children with fetal alcohol syndrome (FAS), partial FAS (PFAS), heavy exposed (HE) nonsyndromal children, and controls. Children were administered a visuospatial associative learning test and the California Verbal Learning Test-Children's Version (CVLT-C), a test of episodic learning. Learning rates were estimated by fitting negatively accelerated response functions ($y=1-e^{-kx}$) to each child's performance across trials on each learning task. Significant differences in learning rate were found on the CVLT-C [$F(2, 51) = 5.03$; $p < .01$] with those in the FAS/PFAS and HE groups showing slower learning rates than controls (both ps $< .05$). A marginally significant difference in learning rate was found on the visuospatial associative learning task [$F(2, 49) = 3.01$; $p = .059$] with those in the FAS/PFAS group having slower learning rates than the HE group ($p < .05$). Significant differences in peak performance (capacity) were found on the CVLT-C [$F(2, 51) = 5.83$; $p < .01$] with those in the FAS/PFAS and HE groups showing less learning capacity than controls (both ps $< .05$). No exposure group differences in capacity were found on the visuospatial associative learning task [$F(2,49) = 0.15$; n.s.]. These data indicate that prenatal alcohol exposure affects learning rates similarly in both tasks, but only episodic learning capacity is vulnerable, while associative learning is spared. The finding of deficits in learning rates in both tasks suggests a non-specific impairment in information processing and integration related to prenatal alcohol exposure. The finding that capacity was affected on the episodic recall task suggests that fetal alcohol exposure may affect the interaction of hippocampal and frontal regions, which is necessary for episodic recall. No capacity deficits were found on the associative learning task, which is primarily dependent on hippocampal activity alone.

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0775

SENSORIMOTOR TRAINING TO AFFECT BALANCE, ENGAGEMENT, AND LEARNING IN CHILDREN WITH AND WITHOUT FETAL ALCOHOL SPECTRUM DISORDERS

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Purpose: We describe the immediate training effects of a virtual reality (VR) computer-based intervention that manipulates sensory input during standing balance, the Sensorimotor Training to Affect Balance, Engagement, and Learning (STABEL) system, in children with fetal alcohol spectrum disorders (FASD) and children with typical development (TD). We expected that children's use of sensory information for balance would change after practice with the STABEL.
Methods: Ten children with FASD and 10 with TD without alcohol exposure, ages 8–16 years, participated. All children were tested pre and post intervention with the Multi-Modal Balance Entrainment and Response (MuMBER) system, which measured the children's ability to weight sensory input during standing balance by determining the amplitude and timing with which children match their body sway frequency to small frequency visual, tactile, and support surface oscillations. A Qualysis motion analysis system captured body sway movements. The STABEL entailed three 10-minute sessions of practice where children moved their bodies to drive a virtual plane through obstacles. Visual and support surface input was systematically varied via VR goggles and compliant support surfaces to 'force' use of vestibular sensory information during standing. Pre/post outcome measurements on the MuMBER were velocity, postural sway area and gain for visual, tactile and support surface oscillations. Mixed repeated measures ANOVAs were used to compare differences between MuMBER variables pre/post intervention and between groups.
Results: Generally, children with FASD showed significantly larger and faster postural sway and higher gain to support surface (vestibular) stimuli than children with TD both in pre and post MuMBER testing ($p< 0.001$). After the STABEL training, both groups showed significantly increased velocity of postural sway ($p< 0.001$), but only children with TD demonstrated significantly higher gain to support surface stimuli ($p< 0.001$).
Conclusion: Children with FASD and children with TD generally showed similar patterns of change during MuMBER testing after the STABEL. However, children with TD showed a larger response to the support surface stimuli, which may imply that they varied their use of vestibular input for postural control after STABEL practice. Children with FASD may need more STABEL practice to change use of sensory information for balance. Future research using longer STABEL practice appears warranted.

0776

AROUSAL REGULATION AND STRESS REACTIVITY IN INFANTS WITH MODERATE TO HEAVY PRENATAL ALCOHOL EXPOSURE

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Purpose: The overarching goal of this pilot study was to describe sleep, temperament and arousal regulation among 6–15 month old infants with moderate to heavy prenatal alcohol exposure (PAE) compared to a low risk control group. Findings on infant affective and regulatory responses to a social stressor are presented.
Methods: Parent-infant dyads completed the Still Face Paradigm (SFP; Tronick et al., 1978), a standardized method for studying infant affect and stress reactivity. Infant affective responses were digitally recorded and coded using the Infant and Caregiver Engagement Phases system (ICEP; Weinberg &Tronick, 1999) during each SFP phase 1) normal play interaction; 2) still-face episode, a social stressor where the caregiver does not interact with the infant; and 3) reunion episode. Salivary cortisol as an index of physiological reactivity was sampled at baseline, 15 and 30 minutes after the SFP. Parents completed standardized questionnaires on infant regulatory behaviors and temperament.
Results: Nine infants with PAE (10.7 ± 3.1 months, 77% female) and nine controls (10.7 ± 2.9 months, 44% female) participated. All were in their biological mother's care. PAE was documented with the FBAS. Infants with PAE showed a higher proportion of negative affect (44%) averaged across all SFP phases compared to controls (29%). Controls showed more positive engagement (19%) and social monitoring (19%) behaviors compared to those with PAE (13% and 9%, respectively). Infants with PAE had higher cortisol levels at all 3 time points with significantly higher baseline levels [.26 mg/dl (.12 SD)] than controls [.11 mg/dl (.03 SD; $p < .05$]. No significant group differences were seen on parent reported regulatory behaviors (Infant Toddler Symptom Questionnaire; DeGangi, 1995) or temperament (Infant Behavior Questionnaire-R; Gartstein & Rothbart, 2003).
Conclusion: As hypothesized, infants with PAE showed more negative affect and fewer caregiver focused behaviors during a social stressor. However, for neither group did salivary cortisol levels follow the expected increase 15 minutes post stressor or decline at 30 minutes. Findings suggest the SFP may not have provoked physiological stress reactions for either group. However, higher baseline cortisol levels for infants with PAE combined with increased rates of negative affect are consistent with previous reports of behavioral and L-HPA axis dysregulation in infants and animal models, warranting further investigation.

0777

THE IMPACT OF PRENATAL ALCOHOL EXPOSURE ON NEUROPHYSIOLOGICAL ENCODING AND MEMORY IN UKRANIAN INFANTS 12-18 MONTHS POSTPARTUM

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To assess neurodevelopmental outcome associated with prenatal alcohol exposure (PAE), cardiac orienting responses (ORs) were assessed during habituation/dishabituation information processing paradigms with 12–18 mo old infants.
Methods: The subset of participants who were assigned to *no intervention* from an on-going randomized clinical trial study, carried out in Rivne, Ukraine, on the impact of micronutrient supplements were used. Auditory and visual stimuli were presented in 10 habituation and 5 dishabituation trials. The responses to the habituation stimuli reflect encoding and responses to the dishabituation stimulus reflect the additional use of memory skills. Heart rate (HR) was aggregated by sec. Baseline HR was collected for 30 sec prior to stimulus onset and then 9 sec post-stimulus from which difference values were computed over the first 3 trials of each condition.
Results: Using a repeated measures analysis of covariance, the between subjects factor was PAE (yes or no) and the within subjects factors were stimulus (auditory or visual), condition (habituation or dishabituation), trial (1–3), and second (1–9). Covariates were child's age and baseline HR. A significant PAE by sec interaction effect was found (F (8,232) = 2.21, p < .027). HR decelerations were significantly less among those with a positive history of PAE as compared to those without PAE on sec 1–5 and 9 but did not differ on sec 6–8. This effect was modified by the nature of the stimulus (Stimulus * PAE* Second Interaction: F (8,232)= 2.09, p <.037) with PAE having greater deficits in their response to the visual stimuli than the auditory and by the learning condition (Condition*Stimulus*PAE*Second Interaction: F (8, 232)=3.82, p < .000) with the effect being stronger in the habituation rather than the dishabituation trials. Conclusion. PAE adversely impacts neurophysiological encoding and memory of environmental events. The rate of deceleration, as indicated by the differences in HR changes over time, was adversely affected by a history of PAE despite the groups not differing during the peak trough interval, where maximum HR decelerations typically occur. This pattern of responses reflects a delay in encoding the environmental events and occurred regardless of the nature of the stimulus and the learning condition (habituation or dishabituation) but ORs were more negatively impacted by PAE when using the visual stimuli and during habituation.

0778

FETAL ALCOHOL SPECTRUM DISORDERS AND THEORY OF MIND: AN EXPLORATORY STUDY OF SOUTH AFRICAN CHILDREN

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'Theory of mind' (ToM) refers to the ability to understand and make inferences about other people's intentions, feelings, and beliefs. Although children with fetal alcohol spectrum disorders (FASD) are known to have deficits in social-cognitive function, little is known about ToM in FASD. ToM ability including affect recognition was assessed using a developmentally sensitive ToM battery including: First- and Second-order False Belief, Strange Stories, Faux-Pas, Reading the Mind in the Eyes, and the NEPSY-II Affect Recognition subtest. General intelligence on the WISC-IV and executive function were also assessed as potential mediating variables. This battery was administered to 63 Cape Coloured children at 9–11 years, who are participating in a longitudinal study on FASD in Cape Town, South Africa. The current study is an initial exploration comparing children with fetal alcohol syndrome (FAS), partial FAS (PFAS), and nonsyndromal heavily exposed (HE) children to typically developing children born to abstaining or light drinkers from the same community. Due to a lack of South African norms and a potential cultural or language influence on ToM development, performance of the typically developing participants was used as the norm against which the children with FASD were compared. No group differences were seen on First- and Second-order False Belief and NEPSY-II's Affect Recognition tasks. Findings on the Faux-Pas task just missed significance. However, significant group differences were present on the Strange Stories test, with the most impressive differences on Reading the Mind in the Eyes test, $F(3,59) = 10.98$, $p<.001$. *Post hoc* tests indicated that FAS and PFAS groups performed worse than HE and controls, ps<.01. Moreover, the effect on the Eyes test persisted after control for WISC-IV IQ and numerous tests of executive function, $F(3,338) = 3.52$, $p<.05$, indicating a specific deficit that does not merely reflect poorer cognitive or executive function. In general, children with FAS and PFAS performed similarly to each other on all tasks and more poorly than HE and Control groups, and Controls did not perform significantly better than the HE group on any task. These findings suggest that deficits in higher order ToM function may play a significant role in the social-cognitive behavioral impairment described in children with FAS and PFAS. Grants: NIAAA R01AA016781, U01AA014790, U24AA014815, two supplements to RO1AA09524; Joseph Young, Sr., Fund, State of MI.

0779

VISUOSPATIAL SKILLS MEDIATE THE EFFECT OF FACIAL AFFECT RECOGNITION ON THEORY OF MIND IN CHILDREN WITH PRENATAL ALCOHOL EXPOSURE

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Background: Children with heavy prenatal alcohol exposure (AE) have deficits in theory of mind (ToM); the ability to attribute mental states to others. Multiple abilities impact ToM performance including visuospatial processing (VP) and affect recognition (AR). Studies have also reported the influence of VP on AR, suggesting a relation between AR and ToM that is influenced by VP. The purpose of this study was to determine if a relation between AR and ToM existed in alcohol-exposed children, to assess if VP mediated this association, and understand potential differences between clinical groups.
Methods: Children (7–16 years old) completed the NEPSY-II. Subjects consisted of children with heavy prenatal alcohol exposure (AE, n=46), non-exposed children with ADHD (ADHD, n=24), and typically developing children (CON, n=40). The Baron and Kenny method of mediation measured the mediating effect of VP on the relation between AR and ToM within groups. Thus, linear regression was used to test if: AR predicted VP (path A), AR predicted ToM (path B), VP predicted ToM (path C), VP decreased or eliminated significance between AR and ToM when included as a mediator (path C').
Results: With age and sex as covariates, the omnibus mediation test revealed that paths A-C were significant and that VP served as a partial mediator between AR and ToM (path C'). Further, within-group analyses with covariates indicated that paths A-C were significant for the AE and CON groups. Moreover, VP served as a total mediator for the relation between AR and ToM (path C') solely in the AE group, with a partial mediating effect present for the CON group. Path B was not significant in the ADHD group, suggesting no VP mediating effect for ADHD children as the predictor and outcome variables were not associated.
Conclusions: The current study showed differences in the relations between AR, VP and ToM between groups. As with previous studies, AR and ToM were associated in all groups, but VP proved to have significant (and total) mediating effect only for the AE group suggesting a unique relation between these factors in alcohol-exposed children. In addition, these results were significant beyond the influence of age and sex, which have been shown to influence ToM. Thus, these results may reflect differential effects of development across the groups, which may help discriminate clinical profiles. Research supported by NIAAA grants R01 AA019605 and T32 AA013525.

0780

ATTENTION NETWORKS IN CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE: COGNITIVE EFFORT

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Background: The current study examined whether a measure of cognitive activity, based on pupillary response during a cognitive measure of attention, could be used to accurately identify children with histories of heavy prenatal alcohol exposure (AE) from non-exposed controls.
Methods: Subjects (8–12y, M=10.99) comprised two groups: children with AE (N=27) and typically developing controls (CON, N=26). Groups were matched on age, sex, handedness, race/ethnicity, and SES. Subjects were administered the attention network test, a computerized task that examines three independent but interrelated networks of attention: alerting, orienting, and executive control. During this testing, all subjects were eyetracked and a pupil-based measure of cognitive effort, the Index of Cognitive Activity (ICA), was obtained.
Results: ICA and reaction time (RT) data for the three network contrasts were calculated and data were analyzed using discriminant function analysis (DFA) and multivariate analysis of variance (MANOVA). DFA results revealed that the combination of 3 ICA scores and 3 RT scores could be used to accurately classify subjects ($p < .05$). Overall classification accuracy was 77% (78% AE, 77% CON). The results of the MANOVA revealed a significant effect of group, F (6,46) = 2.29, $p = .05$, supporting the DFA. In addition, as a preliminary investigation, a small group of subjects with ADHD were tested and compared to children with AE. These limited data suggest that the two clinical groups can be accurately classified ($p < .05$). Overall classification accuracy was 73% (78% AE, 68% ADHD).
Conclusion: Findings suggest that ICA differs in children with AE and controls and can be used to distinguish these groups. Thus, this measure may have clinical utility in the diagnosis of alcohol-affected individuals. Additional examination of ICA over time (rather than network) may provide additional information. Preliminary findings also indicate that additional studies comparing ICA data for subjects with AE and ADHD may help further distinguish these groups.
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0781

ATTENTION NETWORKS IN CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE: NEURAL ACTIVATION

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Background: Fetal alcohol spectrum disorders are characterized by attention deficits. The current study examined the nature and specificity of these deficits by comparing neural activation of children with histories of heavy prenatal alcohol exposure (AE) to non-exposed controls during a measure based on a strong theoretical model of attention functioning (e.g., Posner et al., 2006).
Method: Subjects (13–16y, M=15.10) comprised two groups: children with AE (N=24) and typically developing controls (CON, N=9). Groups were matched on age, sex, handedness, race/ethnicity, and SES. During fMRI, subjects were administered the attention network test, a computerized task that examines three independent but interrelated networks of attention: alerting, orienting, and executive control. Data were analyzed using independent sample t-tests.
Results: Groups did not differ on task accuracy; however, the CON had overall faster reaction times compared to the AE group ($p < .05$). Statistically significant group differences in BOLD response were observed in all three attention networks (cluster size > 1,000 microl; $p < .05$). In the alerting network, the CON group showed greater BOLD response than the AE group in the bilateral superior/middle and inferior temporal gyrus, middle occipital gyrus, left inferior parietal lobule, and left postcentral gyrus, whereas, the AE group showed greater BOLD response in regions of the medial frontal gyrus, right precentral gyrus, and right paracentral lobule. In the orienting network, the AE group had greater activation mainly in areas of the inferior and middle frontal gyri and the middle temporal gyrus. During the executive network condition the CON group had greater activation in parietal regions, while children in the AE group showed greater activation in the cuneus, posterior cingulate, superior and middle temporal gyrus, hippocampus, and cerebellum.
Conclusions: Results support prior findings suggesting that attention may be particularly sensitive to the teratogenic effects of AE and further indicate that distinct neural mechanisms underlie the attention network in children with AE compared to nonexposed typically developing peers. In the majority of the clusters, children in AE group showed greater activation, which may result from atypical neuroadaptive processes or brain alterations.
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0782

ATTENTION NETWORKS IN CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE: NEUROBEHAVIORAL PERFORMANCE

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Background: Fetal alcohol spectrum disorders are characterized by attention deficits. The current study examined the nature and specificity of these deficits by comparing performance of children with histories of heavy prenatal alcohol exposure (AE) to non-exposed controls using a measure based on a strong theoretical model of attention functioning (e.g., Posner et al., 2006).
Methods: Subjects (8–12y, M=10.99) comprised two groups: children with AE (N=27) and typically developing controls (CON, N=26). Groups were matched on age, sex, handedness, race/ethnicity, and SES. Subjects were administered the attention network test, a computerized task that examines three independent but interrelated networks of attention: alerting, orienting, and executive control. Data were analyzed using a 2 (group) x 3 (network) repeated measures ANOVA.
Results: Results indicate that children with AE were impaired on alerting and executive control aspects of attention. Omnibus tests revealed significant main effects of network ($F(2,102) = 12.89$, $p < .001$) and a network X group interaction ($F(2,102) = 3.89$, $p = .024$). The main effect of group was not significant ($F(1,51) = 0.28$, $p = .560$). Pairwise comparisons indicated that the AE group was significantly worse on alerting ($p = .035$) and marginally worse on executive control ($p = .052$) networks than the CON group. There were no group differences on orienting attention in this sample ($p = .821$). In addition, as a preliminary investigation, a small group of subjects with ADHD were tested and compared to children with AE. These limited data suggest that the two clinical groups can be differentiated on executive control of attention ($p = .050$) but were similar on the orienting and alerting networks.
Conclusion: Findings suggest that children with AE are impaired in distinct aspects of attention function. Specifically, children with AE show impairment in alerting and executive control attention networks. Evaluation of underlying mechanisms of attention allows for greater understanding of brain regions affected by AE and suggests that areas in the frontal and parietal cortical sites (alerting) and areas in the cingulate gyrus and some lateral prefrontal areas (executive control) might be especially affected in these children.
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0783

FACIAL MEMORY DEFICITS IN CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE ARE BETTER ACCOUNTED FOR BY OTHER FACTORS

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Background: Heavy prenatal alcohol exposure (AE) results in facial memory impairments. The present study examined whether deficits are (1) attributed to encoding or retrieval and (2) are accounted for by spatial abilities.
Methods: Subjects were children (5–16y, M=10.90) with AE ($n = 48$) and typically developing controls (CON, $n = 48$). Facial memory was tested using NEPSY-II Immediate and Delayed Memory for Faces (MF) and visuospatial processing (VP) was tested using NEPSY-II Design Copy (DC) and Geometric Puzzles (GP). Group differences on MF were examined using a 2 (Group) X 2 (MF Condition) repeated measures ANOVA. To evaluate the contribution of visuospatial abilities, 2 hierarchical regressions were analyzed with Group and VP subtest entered as step 1 predictors, and the Group x VP subtest interaction entered as a step 2 predictor.
Results: The AE group was significantly ($p<.05$) worse than CON on both MF conditions, but there was no significant Group X Condition interaction. Given no differences between memory conditions, only immediate MF was pursued. For DC, regression analyses revealed that step 1 (VP and Group) accounted for a significant ($p=.012$) amount of variance in MF performance. Specifically, DC significantly predicted MF across all groups ($p=.030$). However, step 2 (interactions) did not result in a significant increase in explained variance. For GP, regression analyses revealed that step 1 accounted for a marginally significant ($p=.061$) amount of variance in MF performance but neither group nor GP was a significant predictor of MF. Step 2 resulted in a marginally significant increase in explained variance ($\Delta R^2=.075$). Specifically, the Group X GP interaction was marginally significant ($p=.075$).
Conclusion: The results support previous findings of deficits on measures of facial memory in children with AE but suggested that these deficits require additional study. Specifically, the finding that there were no differences between immediate and delayed conditions indicates that deficits in facial memory may be due to encoding rather than retention deficits. Additionally, these results suggest that deficits are not specifically due to impairments in facial memory per se in children with AE, but are better accounted for by factors such as learning and visuospatial processing.
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0784

PRENATAL ALCOHOL EXPOSURE X ADHD: INTERACTIVE EFFECTS ON ADAPTIVE FUNCTIONING

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Background: Prenatal alcohol exposure (AE) and attention-deficit/hyperactivity disorder (ADHD) both have effects on adaptive behavior in children. Although several studies have compared children with AE or ADHD, no study has examined the interaction between these two factors on adaptive functioning. The current study examined this interaction by including children with and without AE and ADHD.
Methods: As part of a multisite study, primary caregivers of 318 children (8–16y, M=12.36) completed the Vineland Adaptive Behavior Scales-II (VABS-II). Four subject groups were included: with AE and ADHD (AE+, $n = 78$), with AE but without ADHD (AE-, $n = 37$), nonexposed with ADHD (ADHD, $n = 71$), and nonexposed without ADHD (CON, $n = 132$). VABS-II domain scores (Communication, Daily Living Skills, Socialization) were analyzed using three, 2 (AE) X 2 (ADHD diagnosis) between-subjects ANCOVAs, with Age included as a model covariate.
Results: There were significant main effects of AE ($p < .001$) and ADHD ($p < .001$) on Communication, Daily Living Skills, and Socialization domains. For all domain scores, children with AE had lower scores than those without AE and children with ADHD had lower domain scores than those without ADHD. Age was a significant covariate ($p < .01$) in all analyses. There was a significant AE X ADHD interaction [$F(1, 310) = 7.76$, $p = .006$] effect for Communication scores, but not Daily Living Skills or Socialization domains ($p > .40$). The AE+ group had lower Communication scores than the AE- ($p < .001$) and ADHD ($p < .001$) groups, which did not differ from each other. All three clinical groups had lower Communication scores than the CON group ($p < .001$).
Conclusion: Consistent with previous studies, both AE and ADHD elevate the risk of adaptive dysfunction. However, AE exacerbates the effect of ADHD on communication abilities in children, whereby children with both AE and ADHD have significantly poorer outcomes than those with either condition alone. These results further demonstrate the unique effects of AE on this functional domain and support the use of specialized clinical services in this population.
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0785

PRENATAL ALCOHOL EXPOSURE X ADHD: INTERACTIVE EFFECTS ON NEUROPSYCHOLOGICAL PERFORMANCE

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Background: The adverse effects of heavy prenatal alcohol exposure (AE) and attention-deficit/hyperactivity disorder (ADHD) on neuropsychological functioning have been well documented independently. The current study examined the interaction between these factors on cognitive ability in children.
Methods: As part of a multisite study, 344 children (8–16y, M = 12.28) completed the Wechsler Intelligence Scale for Children-IV (WISC-IV), and selected subtests of the Delis-Kaplan Executive Function System (D-KEFS) and the Cambridge Neuropsychological Test Automated Battery (CANTAB). Four groups were tested: children with AE and ADHD (AE+, n = 90), with AE but without ADHD (AE-, n = 38), nonexposed with ADHD (ADHD, n = 80), and nonexposed without ADHD (CON, n = 136). Neuropsychological performance was analyzed using a 2 (AE) x 2 (ADHD) MANOVA for each measure.
Results: The three MANOVAs indicated significant ($p < .05$) main and interactive effects on overall WISC-IV, D-KEFS, and CANTAB performance. Follow-up univariate tests revealed significant main effects of AE and ADHD on all analyzed variables except for AE on D-KEFS Tower Test, and ADHD on CANTAB Intra-Extra Dimensional Shift Stages Completed (IED). AE x ADHD interactions were significant for two WISC-IV index scores (Verbal Comprehension, Perceptual Reasoning), three D-KEFS subtests (Design Fluency, Verbal Fluency, Trail Making), and two CANTAB subtests [IED, Spatial Working Memory (SWM)]. For all measures, clinical groups were more impaired than controls. Both AE groups were more impaired than the ADHD group on Verbal Comprehension and Perceptual Reasoning, although all clinical groups were similarly impaired on Design Fluency, Trail Making, IED, and SWM.
Conclusion: Both ADHD and AE increase impairment across neuropsychological domains. AE resulted in greater verbal comprehension and perceptual reasoning deficits than ADHD; however, both AE and ADHD groups had impaired D-KEFS and CANTAB performance. These results support prior findings of neuropsychological deficits in children with AE and nonexposed children with ADHD. Clinically, these findings demonstrate task-dependent patterns of impairment across clinical groups and indicate discrete profiles of deficits resulting from AE and/or ADHD. These patterns may facilitate the creation of a more precise neuropsychological profile and assist in the identification of alcohol-exposed children.
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0786

PROSPECTIVE MEMORY IN FETAL ALCOHOL SPECTRUM DISORDERS (FASD)

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Memory deficits associated with FASD have been widely reported in studies of retrospective memory (Manji et al., 2009). While memory researchers have studied prospective memory (PM), or the ability to realize and act on delayed intentions, in clinical populations (Ellis, 1996) they have yet to explore PM in FASD. PM is believed to be reliant on intact episodic memory and executive function (EF), which are known to be impaired in FASD (Kliegel et al, 2008; Rasmussen, 2005). To test the role of EF in PM, focality of the PM cue and attentional demands of the task were varied. Event-based PM data were collected from 89 children (M age=11.9 yr): 29 with fetal alcohol syndrome (FAS) or partial FAS (PFAS), 32 heavy exposed nonsyndromal (HE), and 28 controls born to abstainers/light drinkers. Children completed two versions (Focal or Non-Focal) of the Dresden Cruiser (Voigt et al., 2011), a computerized car game that measures PM at two difficulty levels (easy or difficult). The focal version required participants to refuel a car when encountering a yellow car; the non-focal version to refuel when encountering a more distal yellow flower on the side of the road. There were significant between-group differences for both difficulty levels of the focal task, ps<.05. *Post-hoc* pairwise comparisons indicated that the FAS/PFAS group refuelled fewer times than the HE and control groups. There were also significant between-group differences for the easier level of the non-focal version of the task, p=.01, with the FAS/PFAS group refuelling fewer times than both HE and control groups; results for the harder level of the non-focal task fell short of conventional levels of significance, p=.07. A continuous measure of fetal alcohol exposure (M oz absolute alcohol (AA)/day) was significantly related to both levels of nonfocal PM (easy, r=-.30, p<.005; difficult, r=-.38, p<.001). Regression analyses indicate that the effect on the more difficult nonfocal PM condition persisted after control for three EF assessments (WISC-IV Working Memory IQ, Children's Color Trails Test 2, and Verbal Fluency) and WISC-IV IQ, β=-.27, p<.05. These findings support the hypothesis that fetal alcohol exposure impacts negatively on PM. Moreover, the effect on the more challenging nonfocal PM condition persisted after control for EF, suggesting a distinct PM impairment over and above any existing difficulties with EF. Grants: NIH R01AA09524, U01AA014790, R01AA016781; NRF/DAAD; UCT

0787

MODERATE FETAL ALCOHOL EXPOSURE IMPAIRS ENRICHMENT-MEDIATED NEUROGENESIS IN THE ADULT MOUSE HIPPOCAMPUS

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Gestational exposure to moderate levels of alcohol results in decreased hippocampal function in adulthood. Adult hippocampal neurogenesis represents a novel form of CNS plasticity associated with both cognitive and psychiatric function. We previously demonstrated that moderate alcohol exposure during gestation impairs the adult hippocampal neurogenic response to behavioral challenge with enriched environment in mice (Choi et al. 2005). To determine the maturational stage in the production of adult born neurons affected by fetal alcohol exposure (FAE), we utilized nestin-CreER^{T2}: YFP bitransgenic mice to fate map adult nestin+ neural stem cells within the hippocampus. Pregnant nestin-CreER^{T2}:YFP mice placed on a reverse light:dark cycle were provided 10% ethanol in 0.066% saccharine (FAE) or saccharine alone (control) for 4 hrs of the dark cycle daily throughout gestation (BACs ~80 mg/dl) (Brady et al. 2011). At weaning, tamoxifen was injected into all male mice for 5 consecutive days (180 mg/kg/day, i.p; only males were used for these experiments). FAE and saccharin control mice were segregated into standard housing (3 mice per 28.5 x 18 x 12 cm cage) or enriched housing conditions (6 mice in 36 x 36 x 30 cm cage with running wheel and toys changed weekly) and sacrificed 10 weeks later (n=8 mice per group). The following markers were used to classify adult born YFP+ cells as type-1 stem cells (GFAP+/S100β-), transit amplifying cells (PCNA+/DCX-), proliferating neuroblasts (PCNA+/DCX+), postmitotic immature neurons (PCNA-/DCX+), mature neurons (NeuN+) and astrocytes (GFAP+/S100β+). Phenotypic analysis was performed using confocal stereology methods. Statistical analysis revealed a significant housing x FAE interaction in postmitotic immature neurons ($F(1,28)=6.61$; p=.016) and mature neurons ($F(1,28)=4.93$; p=.035). These data demonstrate that moderate fetal alcohol exposure severely impairs enrichment-mediated increases in survival and maturation of adult born dentate granule neurons.
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0788

NICOTINE SYNERGIZES WITH ETHANOL TO REGULATE THE EXPRESSION AND FUNCTION OF ETHANOL-SENSITIVE MIRNAS AND NACHR SUBUNITS IN FETAL NEURAL STEM CELLS

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Alcohol and nicotine are often co-abused, and though this co-abuse often persists during pregnancy, little is known about the combined effects of these drugs of abuse on specific molecular mechanisms that control fetal development. Our research, focused on the second trimester-equivalent period of neurogenesis, previously found that ethanol promoted the proliferation and dysregulated maturation of fetal neural stem cells. Moreover, these effects were partly due to suppression of four specific microRNAs (miRNAs), miR9, miR21, miR153 and miR335 (Sathyan et al, J. Neuroscience, 2007). In this current series of experiments we therefore examined the extent to which nicotine altered the expression of ethanol-sensitive miRNAs in fetal neural stem cells. Gestational day 12.5 mouse fetal murine cerebral cortical-derived neurosphere cultures were exposed to ethanol, nicotine and mecamylamine, a noncompetitive nicotinic cholinergic receptor (nAChR) antagonist, individually or in combination, for five days, to mimic exposure during the in vivo period of neurogenesis and additionally neurosphere cultures were also treated for 24 hrs. Levels of miRNAs, miRNA-regulated transcripts and nAChR subunit mRNAs were assessed by qRT-PCR. In contrast, nicotine behaved as functional antagonist for all ethanol-sensitive miRNAs, and this effect was mediated by stem cell nicotinic acetylcholine receptors (nAChRs). Moreover, ethanol decreased expression of nAChR subunit mRNAs and, like mecamylamine, prevented the nicotine associated increase in α4 and β2 nAChR transcripts. Nicotine at 1 uM (a dose attainable by smokers) significantly prevented the ethanol-induced suppression when administered concurrently with ethanol. Higher pharmacological doses of nicotine were less effective antagonists of ethanol's effects, and at 100 uM of nicotine, no antagonism was observed, due presumably to the desensitization of nicotinic receptors. These data collectively show that, ethanol and nicotine exert mutually antagonistic, nAChR-mediated effects on teratogen-sensitive miRNAs in fetal NSCs. Supported by a grant from NIAAA, R01AA013440 to RCM.

0789

ALCOHOL ALTERS CELLULAR DNA METHYLATION PROGRAM IN GROWTH RETARDED CORTEX AND HIPPOCAMPUS

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Alcohol exposure leads to developmental deficits through multiple mechanisms. However how does alcohol affect the common growth retardation of developing nervous system remains elusive. Neural development is orchestrated under complex intrinsic program. We and others have recently demonstrated that DNA methylation, which regulates gene expression, precedes neural stem cell and neural tube differentiation. Alcohol which can restrict methyl donor is recently found to alter DNA methylation. Here, we further demonstrate that DNA methylation is a program which mediates neuronal migration and differentiation in cortex and hippocampus, and how alcohol affects the program. C57BL/B6J mice pregnant dams were treated from embryonic day 7 (E7) to E15 or E17 with 4% v/v alcohol liquid diet, isocaloric pair-fed or chow-fed. Whole embryos or brains were collected at E15, E17 or postnatal (P) day 7, and processed for 5-methylcytidine (5mC) and 5-hydroxylmethylcytidine (5hmC) immunostaining. Alcohol delayed the growth and maturity of developing cortex and hippocampus by approximately 1–2 day at E17. Alcohol significantly reduced brain weights, reduced cortical plate thickness, and delayed dentate gyrus formation. The 5mC mark was high in the subventricular zone and subplate cells, gradually lost upon finishing migration, and the 5mC+ cells became dispersed mosaically in the cortical plate at E17. However, this process was hindered by alcohol resulting in incomplete migration with delayed 5mC transition in cells clustered in the cortical plate of thinning cortex. The 5hmC, which played a role in maintaining stem cell property, expressed high in the proliferating ventricular zone in controls, and was reduced in alcohol groups. In the developing hippocampus, 5hmC-im increased as the migrating pyramidal cells reached the Ammon's horn. Alcohol decreased 5hmC+ cells in intermediate zone and in the stratum pyramidale. At P7, 5hmC was highly expressed in the subgranular cell layer in dentate gyrus, where 5mC expression was low. Alcohol delayed dentate gyrus development and significantly reduced 5hmC in subgranular layer. This study showed that DNA methylation program was highly regulated and correlated with neuronal migration and maturation in hippocampus and cortex. This process is subjected to environmental input by alcohol, possibly by altering epigenetic process mediating critical genes expression for neuronal differentiation. AA016698 & P50AA07611 to FCZ.

0790

PRENATAL ALCOHOL EXPOSURE ALTERS DNA METHYLATION PROGRAM DURING CRITICAL DEVELOPMENTAL PERIOD OF THE MAMMALIAN CEREBELLUM

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Prenatal exposure to alcohol has been linked to Fetal Alcohol Spectrum Disorder (FASD) which encompasses various developmental deficits, including cardinal brain retardation. Although many mechanisms (e. g. oxidative stress, apoptosis) have been studied, how alcohol leads to neurodevelopmental disorders remains elusive. We have recently proposed that alcohol, acting as a methyl donor suppressor, interferes with DNA methylation, which we have further demonstrated to play a permissive role during neural tube differentiation. This study aims to examine the role of the DNA methylation in cerebellar development and the influence of prenatal alcohol exposure. Using a mouse model of prenatal alcohol exposure (liquid, 4% v/v, administered across gestational period E7-17, pups reared by surrogate foster mothers) as well as isocaloric pair-fed and control animals, we performed immunohistochemical analyses of the DNA methylation marker 5-methylcytosine (5meC) and a recently identified derivative, 5-hydroxymethylcytosine (5hmC) across critical periods of postnatal cerebellar development (P7, P21, P28). We observed that the methylation of two major classes of cells, Purkinje and granule, are unique and transition through methylation and de-methylation states across development. Additionally, subpopulations of granule cells exhibit distinct DNA Methylation Programs, or DMPs, relative to their mitotic and migrational status (P7). Alcohol has been previously shown to delay migration of granule cells from the external layer to their internal layer position. The results of our alcohol treatment further show that granule cell DMP is concordantly hindered. Taken together our study concludes that the DMP of the cerebellum is timely and cell-specific and can be altered by moderate fetal alcohol exposure. Further, this study suggests a novel mechanism for the inhibited migration of granule cells of the cerebellum upon fetal alcohol exposure and provides support for the idea that alcohol can exploit epigenetic machinery to alter transcriptional regulation during neurodevelopment-a focus of our forthcoming work. AA016698 & P50AA07611 to FCZ

0791

EFFECT OF ETHANOL ON ABC CHOLESTEROL TRANSPORTERS AND CHOLESTEROL LEVELS IN THE DEVELOPING RAT BRAIN

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Ethanol is a teratogen that causes severe effects to the developing brain. The deleterious effects of ethanol on the developing brain may be due to the disruption of cholesterol homeostasis as cholesterol deficiencies cause brain anomalies associated with cognitive and behavioral abnormalities similar to the ones reported in Fetal Alcohol Spectrum Disorders. We have previously shown that ethanol causes a decrease in total cholesterol in astrocytes *in vitro*, through the up-regulation of the cholesterol transporters ATP-binding cassette A1 (ABCA1) and G1 (ABCG1), resulting in an increase of cholesterol efflux from these cells. In this study, we investigated the effects of prenatal alcohol exposure on ABCA1, ABCG1, and cholesterol levels in an *in vivo* animal model. We hypothesized that ethanol may upregulate ABC cholesterol transporters in the brain of rat fetuses exposed to ethanol during gestation, which may lead to brain cholesterol depletion. Pregnant rats were fed: i) an *ad libitum* liquid diet (control group); ii) an *ad libitum* liquid diet containing ethanol (36% of total caloric intake; ethanol group); iii) an isocaloric liquid diet in the amount consumed by paired pregnant rats in the ethanol group (pair-fed group) from gestational day (GD) 6 to 21. ABCA1 and ABCG1 protein levels and cholesterol levels were measured in the neocortex of male and female fetuses at GD 21. We found that the levels of ABCA1 and ABCG1 in the neocortex of ethanol-treated fetuses were up regulated when compared to pair-fed animals. The separate analysis of male and female fetuses revealed that upregulation in ABCA1 and ABCG1 levels was significant in female fetuses but not in males. To explore the consequences of increased cholesterol transporter expression, we measured levels of cholesterol in the neocortex of fetuses in the three treatment groups. We found that the levels of cholesterol were significantly reduced in the ethanol group compared to the levels of cholesterol in pair-fed animals. Also in this case separate analysis of the male and female fetuses revealed that cholesterol levels were significantly reduced only in female fetuses. Based on these results, we conclude that *in vivo* ethanol exposure during gestation decreases cholesterol content in the brain by upregulating the cholesterol transporters ABCA1 and ABCG1; these effects may be responsible, at least in part, for the neurodevelopmental deficits caused by ethanol (Supported in part by AA017180).

0792

EFFECTS OF ALCOHOL ON ASTROCYTE CHONDROITIN SULFATE PROTEOGLYCANS: IMPLICATIONS FOR FETAL ALCOHOL SPECTRUM DISORDERS

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Astrocytes play a major role in neuronal development. We have previously shown that astrocyte treatment with ethanol inhibits neuritogenesis in astrocyte-neuron co-cultures. Proteoglycans (PGs) can inhibit neuronal migration and development and are synthesized by astrocytes. PGs consist of a core protein attached to linear chains of glycosaminoglycans (GAGs) negatively charged by the presence of sulfate groups. Chondroitin sulfate PGs (CSPGs) are the most abundant inhibitory PGs in the brain; their inhibitory properties depend on both the core protein and the GAG chains. Arylsulfatase B (ASB) and galactose-6-sulfatase (GALNS) degrade GAGs by removing specific sulfate groups. We hypothesized that ethanol may increase the GAG content in astrocytes by inhibiting the activity of these two enzymes. Primary astrocyte cultures were treated with or without 75 mM ethanol for 24 h. We found that ethanol inhibited ASB activity from 102.4 (±3) nmol/mg protein/h (control) to 65.3 (±1.6) nmol/mg protein/h ($p < 0.001$ by unpaired *t*-test) and GALNS activity from 7.5 (±0.4) nmol/mg protein/h in (control) to 4.2 (±1.6) nmol/mg protein/h ($p < 0.001$). Ethanol also inhibited the activity of two other sulfatases (arylsulfatase A and steroid sulfatase), but did not affect alkaline phosphatase activity and increased lactate dehydrogenase activity, suggesting a specific inhibitory effect of alcohol on sulfatases. A decrease in ASB and GALNS activity is expected to increase GAG content. Indeed, we found that total GAG content was increased by ethanol from 11.7 (± 0.9) μg/mg protein (control) to 20.2 (± 1.7) μg/mg protein ($p< 0.001$); chondroitin-4-sulfate content (the specific target of ASB activity) was also increased from 7.0 (± 0.23) μg/mg protein (control) to 12.0 (± 0.6) μg/mg protein ($p< 0.001$). Ethanol also induced a small but significant increase in the transcription of the core-protein components of neurocan and brevican, two brain-specific PGs (1.3 ±0.05; $p<0.001$ and 1.8 ± 0.2; $p<0.01$ fold increase in neurocan transcription and 1.3 ±0.04; $p<0.001$ and 1.5 ± 0.2; $p<0.05$ fold increase in brevican transcription by 75 mM and 100 mM ethanol, respectively). In summary, ethanol inhibits the activity of ASB and GALNS, increases chondroitin sulfate content, and the expression of neurocan and brevican. These effects may represent a novel mechanism involved in the neurodevelopmental effects of ethanol. (Supported in part by AA-017180).

0793

OMEGA-3 FATTY ACID SUPPLEMENTATION RESCUES HIPPOCAMPAL LEARNING AND MEMORY DEFICITS ASSOCIATED WITH FETAL ALCOHOL SPECTRUM DISORDERS

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Alcohol consumption during pregnancy can significantly damage the developing brain. Because the exact nature of the damage can depend upon the amount consumed, and the time it is consumed during the pregnancy, the damage can manifest in wide array of disorders that are grouped under the term Fetal Alcohol Spectrum Disorder (FASD). One problem consistently observed in FASD is an impairment in learning and memory processes, particularly those that involve the functioning of the hippocampal formation. Experimentally we can study deficits caused by FASD by looking at long-term potentiation (LTP), a biological model of learning and memory that is easily observed in the hippocampal dentate gyrus. In this study we have observed deficits in LTP in anaesthetized adult males that have been exposed to alcohol prenatally. Biochemical analyses of the brains of these animals revealed that these deficits in LTP were also accompanied by reductions in neuronal antioxidants; in particular glutathione.
To try and ameliorate the deficits caused by prenatal alcohol exposure, we gave animals' access to a diet supplemented with omega-3 fatty acids. Omega-3 fatty acids are important for membrane fluidity and participate in many signaling cascades in the brain. They are also associated with preventing neurocognitive decline, decreasing inflammation, and reducing indications of depression. In the present study we show that Omega-3 fatty acid supplementation in FASD newborns completely rescues deficits in LTP and increases glutathione levels into adulthood. Furthermore, glutathione depletion itself can mimic the effects of FASD for LTP, indicating that a reduction in glutathione alone can significantly impair the functional capacity of synapses. These results indicate that omega-3 fatty acids may be an important addition to the diet of children suffering from FASD and may be able to "rescue" the deficits in learning and memory common with this disorder.

0794

EFFECTS OF MODERATE PRENATAL ETHANOL EXPOSURE ON KAINATE RECEPTOR FUNCTION IN THE CA3 HIPPOCAMPAL REGION

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The hippocampus is involved in learning and memory, which have been shown to be impaired in fetal alcohol syndrome. The CA3 hippocampal region is implicated in spatial memory. CA3 pyramidal neurons (PNs) receive excitatory input from the mossy fiber (MF) pathway, which is mediated in part by kainate receptors (KARs). Prenatal ethanol exposure decreases ^{3}H-vinylidene KA binding in the stratum lucidum of the CA3 (Farr et al., *Neurotoxicology and Teratology*. 10: 563–568, 1987) indicating reduced expression of KARs. Along with the MF pathway, CA3 PNs also receive excitatory input via the associational/commissural (A/C) pathway, formed by the axons of other CA3 pyramidal neurons. This pathway makes the CA3 PNs highly excitable and possibly plays a role in memory storage and retrieval. Presynaptic KARs have been identified at A/C connections and shown to decrease non-NMDA receptor-mediated field excitatory postsynaptic potentials (fEPSPs). We investigated the effects of prenatal ethanol exposure on the function of KARs located at the A/C synapses. Mouse dams were exposed to ethanol using a voluntary drinking paradigm, and consumed an average of 5.64 ± 0.35 g ethanol/kg/day throughout pregnancy (approximate BEC is 70 mg/dL). Horizontal sections were taken from offspring on postnatal days 20–23 and non-NMDA fEPSPs were evoked by stimulating the stratum lucidum in the presence of 50 μM picrotoxin and 50 μM DL-AP5. As expected, an mGluR2/3 agonist that blocks MF responses (2 μM DCG-IV) did not affect the A/C-mediated events. Average fEPSP amplitude at a stimulation intensity (1.0 mA) that produced a maximum response was 2.03 ± 0.44 mV for control and 1.5 ± 0.3 mV for ethanol groups (P = 0.395; n=4). Stimulation intensity was lowered to produce a 70% of the maximum fEPSP amplitude and 250 nM KA was bath applied. This produced a reduction in fEPSP amplitude of 68.1% ± 5.8 in controls, and 51.3% ± 4.9 in the prenatal ethanol group, P = 0.07 by unpaired t-test; n = 4). These preliminary findings suggest that moderate prenatal ethanol exposure does not significantly affect the function of KARs in the A/C pathway.
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0795

EFFECT OF VARIED LEVELS OF VOLUNTARY ETHANOL CONSUMPTION DURING PREGNANCY ON DENTATE GYRUS LONG TERM POTENTIATION IN ADULT MALE RAT OFFSPRING

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Introduction: We previously reported that a mean daily voluntary consumption of 2.82 g ethanol / kg, which produces a mean maternal peak serum ethanol of 84 mg/dL, significantly diminishes dentate gyrus long-term potentiation (LTP). In the present study, we examined the prenatal ethanol dose-dependent nature of the LTP deficit and sought to identify an ethanol consumption threshold and maternal serum ethanol concentration for producing ethanol-induced LTP deficits.
Methods: Long-Evans rat dams voluntarily consumed either a 0% or 5% EtOH in 0.066% saccharin water for four hours each day throughout gestation. The seventeen ethanol-drinking rat dams used in this study consumed a mean of 2.36 g/kg EtOH/day (range: 1.5–3.2 g/kg/day). LTP was measured in adult male offspring (3–5 months old) from the seventeen ethanol dams and fifteen control dams using the methods reported previously (J. Pharmacol. Exp. Ther. 334: 191, 2010). For this study, the degree of synaptic potentiation above pre-tetanus baseline at 60 minutes post-tetanus was used as the measure of LTP magnitude.
Results: As reported previously, LTP was significantly reduced in the dentate gyrus of prenatal ethanol-exposed offspring compared to saccharin controls. In addition, a mean ethanol consumption-dependent relationship existed with the magnitude of the LTP deficit. A nonlinear regression analysis revealed a significant correlation between ethanol consumption during pregnancy and the degree of LTP impairment ($p < 0.01$). Moreover, this regression line crossed the saccharin control LTP mean minus its standard deviation at 2.5 g/kg/day. This level of ethanol consumption is estimated to result in a peak maternal serum ethanol concentration of approximately 70 mg/dL (~15 mM EtOH).
Conclusions: These results suggest that the threshold for LTP deficits in adult rat offspring is a maternal serum ethanol concentration of 70 mg/dL. We predict that similar serum ethanol concentrations will diminish hippocampal-sensitive learning and memory in this rodent model of FASD. Supported by AA17068 and AA019884.

0796

FETAL ETHANOL EXPOSURE ELEVATES AGONIST-STIMULATED G_i/G_O PROTEIN-MEDIATED RECEPTOR-EFFECTOR COUPLING IN MULTIPLE BRAIN REGIONS OF ADULT RAT OFFSPRING

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Purpose: We have observed that prenatal ethanol exposure elevates histamine H_3 receptor-effector coupling to G_i/G_o proteins in dentate gyrus. In the present study, we examined the effect of prenatal ethanol exposure on histamine H_3 receptor-effector coupling in other brain regions. In addition, we examined whether the effects of other neurotransmitter or neuromodulatory agonists whose actions are mediated via G_i/G_o proteins were similarly affected by prenatal ethanol exposure. Methods. Long-Evans rat dams voluntarily consumed an average of 2.72 g/kg/ day of a 5% ethanol solution four hours each day throughout gestation. This level of consumption produces a mean peak serum ethanol concentration of 84 mg/dL. Saggital sections collected from the brains of adult offspring were incubated with 100 pM [^{35}S]-GTP γ S in the absence and presence of seven different selective receptor agonists: 1) Methimepip (H_3), 2) 8-OH-DPAT ($5HT_{1A}$), 3) DAMGO (m-opioid) 4) Neuropeptide Y (NPY), 5) WIN 55,212 ($CB_{1/2}$), 6) cyclopentyladenosine (A_1), and 7) Methylthio-ADP (P_{2Y}). Basal and agonist-stimulated [^{35}S]-GTP γ S binding was measured in thirteen different brain regions. Results. Agonist-stimulated [^{35}S]-GTP γ S binding by the histamine, cannabinoid, adenosine and purinergic receptor agonists was significantly increased in dentate gyrus of prenatal ethanol-exposed offspring compared to controls. NPY- and mu-opioid-stimulated [^{35}S]-GTP γ S binding was significantly increased in the hippocampal CA_3 region of prenatal ethanol-exposed rats. Several other increases in agonist-stimulated [^{35}S]-GTP γ S binding were noted in frontal and parietal cortices, cerebellum and nucleus accumbens. Conclusions. These results suggest that the effects of prenatal ethanol exposure on receptor-effector coupling to Gi/Go proteins occurs in multiple brain regions and is not limited to the H_3 receptor-effector system. The mechanism by which prenatal ethanol exposure increases receptor-effector coupling is not known, but may relate to long-lasting alterations in cellular signaling systems regulating the ability of metabotropic receptors to couple to G-proteins. Further, these results underscore a growing impression that prenatal exposure may alter an ethanol-exposed offspring's responsiveness to a variety of neuroactive substances, including illicit substances as well as medications used in the treatment of children with FASD.
Supported by NIAAA grants AA17068 and AA19884.

0797

NEONATAL ALCOHOL EXPOSURE IN MICE ALTERS DENDRITIC MORPHOLOGY IN THE CAUDATE PUTAMEN INDEPENDENTLY OF ADENYLYL CYCLASE 1/8 FUNCTION

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Exposure of the developing fetus to alcohol can have multiple deleterious effects, including behavioral abnormalities, learning disorders, attention deficit disorders, mental retardation, and executive functioning abnormalities, collectively defined as fetal alcohol spectrum disorder. During early brain development there is a period of tremendous synapse formation, termed synaptogenesis, which is an important time for dendritic growth and remodeling as afferent networks are formed. During this time, neurons are especially sensitive to the damaging effects of ethanol. Ethanol acts to potentiate $GABA_A$ receptor activity and to antagonize NMDA receptor mediated calcium entry. This antagonism results in impairments of intracellular signaling pathways, such as those involving the calcium/calmodulin-stimulated adenylyl cyclases (ACs) 1 and 8. Recent evidence demonstrates that neonatal mice lacking both AC1 and AC8 (DKO) have increased vulnerability to ethanol-induced neurotoxicity in the striatum compared to WT controls. However, the long term effects on neuronal development are still unclear. Therefore, wild type (WT) and DKO mice were treated with a single dose of 2.5 g/kg ethanol or saline at P5-7. At P30, mice were sacrificed and brains processed for dendritic analysis using the Golgi-Cox method. Medium spiny neurons (MSNs) from the caudate putamen were analyzed for dendritic complexity (using the Sholl analysis), number of branches, branch points, terminal branches, total dendritic length, average length/dendrite, and soma size. In WT mice, neonatal ethanol decreased all measures of dendritic morphology in surviving neurons. Genetic deletion of AC1/8 decreased specific measures of dendritic morphology (including dendritic complexity (Sholl), number of tertiary and quaternary branches, branch points, terminal branches, total dendritic length, and average length/dendrite) and soma size of MSNs compared to WT controls in the absence of ethanol. Ethanol further decreased the total dendritic length, branch points, and terminal branches in DKO mice compared to DKO controls . These data indicate that a single exposure to ethanol during the synaptogenesis period is sufficient to cause long-term deficiencies in the dendritic morphology and soma size of MSNs in the caudate putamen and that this outcome is not dependent on the functional status of AC1 and AC8.

0798

STRESS-INDUCED PLASTICITY OF THE DOPAMINE SYSTEM IS ALTERED FOLLOWING PRENATAL ALCOHOL EXPOSURE

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There is considerable overlap between the brain's stress systems and the mesocorticolimbic dopamine reinforcement/motivational pathways, with stress interacting with the neurobiological pathways implicated in drug reward, and conversely, drug use activating stress systems. Past research suggests alterations in stress responsivity can provide a pathway for increased neurobiological vulnerability to substance use problems. Importantly, an increased prevalence of substance use problems is observed among individuals with FASD, and both stress systems and dopamine systems are and known to be altered by prenatal alcohol exposure (PAE). The present study investigated alterations in stress-dopamine interactions following PAE by examining the effects of stress on levels of dopamine receptors in key brain regions central to mediating both stress responsivity and reinforcement/motivation in female and male rats. Pregnant Sprague-Dawley females were assigned to 1 of 3 prenatal treatments on day 1 of pregnancy: 1) Alcohol (prenatal alcohol exposure, PAE) - liquid diet containing 36% ethanol-derived calories; 2) Pair-fed (PF) - isocaloric liquid diet with maltose-dextrin substituted for ethanol, g/kg body wt/day of gestation; and 3) Control (C) – pelleted version of the control liquid diet *ad libitum*. In adulthood, male and female offspring were assigned to either non-stress (undisturbed throughout) or stress (10 days of chronic variable stress, 2/day) conditions. Preliminary results suggest that downregulation of dopamine receptors occurs following chronic variable stress in the nucleus accumbens and striatum in C males and females, but not in PAE rats. These novel results suggest that PAE may inhibit stress-induced plasticity of the dopamine system, and may influence vulnerability to the neurobiological effects of subsequent stressors and/or substance use. Additionally, the current results add to our understanding of the bi-directional interaction between stress and reinforcement/motivation systems, and highlight important and unique alterations that may contribute to the increased prevalence of substance use problems observed in individuals with an FASD. (Supported by the Canadian Foundation for Fetal Alcohol Research to LG and JW, NIH/NIAAA R37 AA007789 to JW, and IMPART to KU).

0799

EFFECTS OF VOLUNTARY EXERCISE ON CELL MORPHOLOGY IN THE MEDIAL PREFRONTAL CORTEX OF RATS EXPOSED TO ALCOHOL DURING THE THIRD TRIMESTER EQUIVALENT

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Developmental alcohol exposure in humans can result in a wide range of deficits collectively referred to as Fetal Alcohol Spectrum Disorders. FASD-related impairments in executive functioning such as goal-directed behavior, attention, and temporal planning suggest damage to the PFC. Moderate to high levels of alcohol exposure during the prenatal or early postnatal period produces decreased overall frontal brain size in humans (Rasmussen, 2005) and reductions in medial PFC (mPFC) pyramidal neuron dendritic morphology in rodents. Previous research from our lab demonstrated that neonatal alcohol exposure decreased basilar dendritic complexity but did not affect spine density in Layer II/III mPFC pyramidal neurons. These data could suggest a decrease of inhibitory inputs from the mediodorsal nucleus of the thalamus conveyed by interneurons, which could account for hyperactivity as a result of early exposure to alcohol. The current study evaluates the effect of neonatal alcohol exposure on mPFC Layer III basilar dendritic morphology in adolescent male rats (postnatal day (PD)42) and investigates the role of voluntary exercise as a possible therapeutic intervention for the alcohol-induced deficits. This study employed an animal model of binge-drinking during the third trimester of pregnancy. Rats were either intubated with alcohol (alcohol exposed, AE; 5.25g/kg/day); sham intubated (SI), or remained with the mother (suckle control, SC) on PD4-9. Half of the animals were placed in cages with free access to running wheels (WR) on PD30-24, while the other half served as inactive control (social housing, SH). Rats were anesthetized and perfused on PD42 and brains were processed for Golgi-Cox staining. Preliminary results indicate a decrease in total dendritic length of Layer III mPFC basilar dendrites in AE/SH animals compared to control animals. In addition, across all postnatal groups, the total length of basilar dendrites is significantly increased in animals exposed to WR compared to relative SH controls. Basilar dendrite complexity (length, bifurcations, branching characteristics) and spine density analysis for Layer III neurons in the mPFC is underway. Together the data suggest voluntary exercise may help ameliorate neonatal alcohol-induced mPFC deficits. Supported by U of DE internal funds.

0800

VOLUNTARY WHEEL RUNNING INCREASES FOSB/ΔFOSB EXPRESSION IN THE DENTATE GYRUS OF RATS EXPOSED TO ALCOHOL DURING THIRD TRIMESTER EQUIVALENT

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Developmental alcohol exposure can permanently alter brain structure and function, contributing to the behavioral and cognitive deficits seen in children with Fetal Alcohol Spectrum Disorders. Previous work demonstrated that neonatal alcohol exposure in rats impairs the survival of new neurons in the hippocampal dentate gyrus (DG) while not affecting cell proliferation. Exposure to wheel running (WR) augments cell survival in control but not alcohol-exposed (AE) rats. The current study investigates possible mechanisms underlying the decreased cell survival seen in AE animals, including hippocampal activity patterns that may affect normal cellular maturation processes. Male AE pups received 5.25 g/kg/day of alcohol on postnatal days (PD)4-9 in a binge-like manner. Two control groups were used: sham-intubated (SI) and suckle control (SC) pups. On PD30, rats were divided into either WR (24 hr voluntary access, 3/cage) or social housing (SH; 3/cage). In Experiment 1, animals received 200 mg/kg BrdU (i.p) on PD42 and were sacrificed 2 hrs later. In Experiment 2, all rats were placed in SH on PD42 after BrdU injection and sacrificed 30 days later (PD72). Cell proliferation in the DG (BrdU+ labeling on PD42) was not affected by AE. WR increased cell proliferation in all groups. WR did not enhance cell survival in AE rats at PD72 but did increase survival in controls, suggesting that AE rats are not gaining lasting benefits from WR as seen in controls. The immature neuronal marker doublecortin (DCX) was used to assess changes to the cell maturation process. AE animals do not differ from controls in number of DCX+ cells within the DG on PD42, demonstrating that neonatal AE does not have a long-term effect on the generation of immature neurons. These data suggest that impaired cell survival in AE animals is a result of alterations to later stages of the cell maturation process. Cellular activity of mature neurons within the DG was evaluated using the marker for the inducible transcription factors FosB/ΔFosB. Quantitative image analysis of immunostaining for FosB/ΔFosB revealed that WR increases FosB/ΔFosB+ cells within the DG in both AE and controls at PD42, suggesting that WR induces cellular activation in AE rats in a manner similar to controls. Overall, these data suggest that the mechanisms underlying the compromised cell survival in the DG following neonatal alcohol exposure are subtle and require further investigation. Supported by NIH AA09838.

0801

WITHDRAWN

0802

EFFECT OF GLUTAMINE SUPPLEMENTATION ON FETAL GROWTH AFTER THIRD TRIMESTER EQUIVALENT CHRONIC ALCOHOL EXPOSURE: OVINE MODEL

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Glutamine (GLN) has been shown todiminish whole body proteolysis, increase protein synthesis and is used clinically as a nutrient supplement in low birth weight infants. We previously reported that 3rd trimester equivalent acute ethanol exposure reduces the availability of fetal GLN and related amino acids (AAs). We hypothesized that glutamine supplementation concurrent with alcohol infusionsmay serve a protective role and mitigate the negative developmental effects on fetal growth resulting from third trimester equivalent prenatal alcohol exposure.Pregnant sheep were assigned to 4 groups: pair-fed saline control, ethanol, ethanol+GLN or saline+GLN. Ethanol or saline infusions were given intravenously (IV) over 1 hour from gestation day (GD) 99 to 121, 3 consecutive days per week to mimic a weekend binge drinking pattern.The 1stfour doses of ethanol were 1.75, 2, 2.25 and 2.25 g/kg respectively and thereafter were 2.5 g/kg. 100 mg/kg of GLNdose was administered IV as a 4.5%w/v aqueous bolus three times a day. Surgery was performed on GD 116 to place catheters in the maternal and fetal vasculature. On GD 121, treatment was started at 0 minute and blood samples were collected at 0, 5, 15, and 60 minutes. Plasma AAs were analyzed using HPLC.In the ethanol group, at the end of 60 minute, plasma concentration of fetal GLN wasdecreased by 26% more than that of the saline group (p=0.115). To analyze the role of prenatal ethanol exposure and GLN supplementation on fetal body growth, a3rd trimester equivalent chronic ethanol treatment from GD 109 to 132 was utilized, dividing ewes into the same 4 groups as above. Animals were sacrificed on GD132 and fetal body growth parameters were measured. Prenatal ethanol exposure reduced fetal thoracic girth, head width, height and body length compared to the saline control group (p= 0.093, 0.003, <0.001 and 0.008 respectively). GLN supplementation showed a protective effect; thoracic girth, head width and height was improved in the ethanol+GLN group compared to the ethanol group (p= 0.094, 0.007 and 0.024 respectively). We conclude that GLN supplementation has the potential to ameliorate fetal growth retardation caused by prenatal ethanol exposure.
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0803

PHARMACOKINETIC STUDY OF GLUTAMINE SUPPLEMENTATION IN MATERNAL AND FETAL COMPARTMENT AFTER ACUTE ALCOHOL EXPOSURE IN SHEEP

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The effect of an acute alcohol exposure on the transplacental exchange of glutamine (GLN) after maternal administration was studied using a sheep model. Pregnant ewes were assigned to 5 groups: saline control, GLN control, alcohol, alcohol+GLN at 30 mg/kg dose and alcohol+GLN at 100 mg/kg dose. Catheters were surgically placed into the maternal and fetal circulation on gestational day (GD) 116. On GD 121, alcohol (1.75 mg/kg) or saline infusions were given intravenously (IV) over one hour, with GLN administered as an IV bolus at the start of the experiment. Blood samples were collected at multiple time points and plasma GLN concentrations were analyzed by high performance liquid chromatography. Pharmacokinetic analyses using standard non-compartmental models were performed using the PK package of R software (Jaki and Wolfsegger, 2010). Statistical analyses were performed using a mixed effects model (PROC MIXED of SAS 9.2) following a log transformation of the plasma concentrations to assess the impact of time and treatment effect on plasma GLN concentrations. Maternal and fetal area under the curve (AUC) and peak concentration (C_{max}) were computed for all groups. In the maternal compartment, a spontaneous decrease in GLN bioavailability after the start of the alcohol infusion was observed (AUC^{saline}= 254.39 ± 21.81, AUC^{alc}= 235.03 ± 26.65); GLN bioavailability continued to decrease during the alcohol infusion and increased after the alcohol infusion ended. The 100 mg/kg dose prevented the depreciation in GLN bioavailability seen in the alcohol group (AUC^{alc}= 235.03 ± 26.65, C_{max}^{alc}= 0.39; $AUC^{alc/G100}$= 390.74 ± 34.89, $C_{max}^{alc/G100}$= 4.22). In the fetal compartment, GLN bioavailability exhibited a sinusoidal pattern in the saline group. A similar sinusoidal pattern was observed in the alcohol group, but at much lower GLN bioavailability (AUC^{saline}= 486.31 ± 58.18, AUC^{alc}= 461.63 ± 74.81). Maternal GLN administration in the alcohol groups enhanced GLN bioavailability in the fetal compartment (AUC^{alc}= 461.63 ± 74.81, $AUC^{alc/G30}$= 568.26 ± 50.96, $AUC^{alc/G100}$= 574.13 ± 57.63). A gradually increasing pattern of GLN bioavailability was observed in the fetal compartment after maternal GLN administration. We conclude that acute prenatal alcohol exposure reduces the bioavailability of GLN, and GLN supplementation enhances the GLN bioavailability in the maternal and fetal compartments.
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0804

EFFECTS OF CHOLINE SUPPLEMENTATION ON THE VULNERABILITY OF OVINE LAMB CEREBELLAR PURKINJE CELLS IN RESPONSE TO 1ST TRIMESTER BINGE ALCOHOL EXPOSURE

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Human MRI and autopsy studies reveal abnormal cerebellar development in children exposed to alcohol prenatally, irrespective of the period of exposure. Despite such known adverse effects, women continue to drink while pregnant, making it necessary to identify methods to reduce the teratogenic effects of alcohol. One known adverse effect of drinking while pregnant is the deprivation of the essential nutrient choline (Zeisel 2006). It has been previously reported that pre- and perinatal choline supplementation in animal models mitigates alcohol's effects on spatial learning and has improved neuronal plasticity (Li et al 2004, Medina 2011). In the sheep model, where all three trimester-equivalents of human brain development occur in utero, the cerebellum is vulnerable to prenatal alcohol exposure during all trimesters. We hypothesized that in the sheep model, choline supplementation would have an ameliorative effect on Purkinje cell loss in response to alcohol exposure. This study consisted of 3 groups: 1st trimester-equivalent alcohol/choline (A/C), 1st trimester-equivalent alcohol/placebo (A/P), and normal control (NC). Alcohol (1.75 g/kg) infusions mimicked a human binge pattern; 3 consecutive days of infusions per week. Infusions were given on gestational day (GD) 4-42. Cerebella were harvested on post-natal day 150 and processed for stereological cell counting. Purkinje cell number for the A/P and A/C groups were not significantly different (12.61±0.1, 13.1±0.1 x 10^7 mean ± SEM, N = 7,6 respectively), but both of these groups were significantly reduced compared to the NC group (16.4±0.1 x 10^7 mean ± SEM, N = 5). These data demonstrate alcohol-induced Purkinje cell loss in both alcohol exposed groups. We conclude that fetal cerebellar Purkinje cells are sensitive to alcohol exposure at any time during gestation and that women who engage in drinking are at a high risk of giving birth to children with cerebellar damage, even if drinking ceases after the first trimester. Though choline has potential as an intervention strategy to mitigate the neurodevelopmental defects from prenatal alcohol exposure, it does not prevent Purkinje cell loss at this dose and pattern of alcohol in the sheep.
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0805

PRELIMINARY ANALYSIS OF THE IMPACT OF MICRONUTRIENT SUPPLEMENTS ON NEUROPHYSIOLOGICAL ENCODING AND MEMORY IN UKRANIAN INFANTS 12-18 MONTHS POSTPARTUM

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The role that micronutrients play in ameloriating the negative impact of prenatal alcohol exposure (PAE) was explored in a randomized clinical trial conducted in Rivne, Ukraine. To assess neurodevelopmental outcome, cardiac orienting responses (ORs) during an information processing paradigm were obtained from 12–18 mo old infants.
Methods: Women who differed in prenatal alcohol use were recruited during pregnancy and randomized to group: None, Multivitamin/Minerals (M/M), and Multivitamin/Minerals plus Choline (M/M + Choline). The habituation stimuli were presented for 10 trials and the dishabituation stimulus were presented for 5 trials. The responses to the habituation stimuli reflect encoding and responses to the dishabituation stimulus reflect the additional use of memory skills. Heart rate (HR) was collected at a rate of 1000 samples per sec and then aggregated by sec. Baseline HR was collected for 30 sec prior to stimulus onset and then 9 sec post-stimulus onset from which difference values were computed for analysis for the first 3 trials of each condition.
Results: A repeated measures analysis of covariance was used. The between subjects factors were PAE (yes or no) and intervention group (None, M/M, or M/M+Choline). The within subjects factors included stimulus (auditory or visual), condition (habituation or dishabituation), trial (1–3), and second (1–9). Covariates were child's age and baseline HR. Between subjects effects included a significant intervention effect ($F(2,54)=4.693$, $p < .013$) and a trend for an interaction effect between intervention and history of PAE ($F(2, 54)=3.03$, $p < .057$). Post hoc comparisons indicated that those in the M/M+ Choline group had greater ($p < .001$) HR deceleration ($HR\Delta=6.8$) as compared to the None group ($HR\Delta=1.6$). A trend ($p < .087$) was found for the M/M ($HR\Delta=3.1$) being lower than the M/M+ Choline group but this group did not differ from the None group. Relative to the interaction, among those without PAE, those in the M/M+ Choline performed better than those in both other groups. Among those with PAE, both intervention groups performed better than the no intervention group but did not differ from each other.
Conclusion: Preliminary analysis suggested that choline supplementation during pregnancy may provide beneficial impact to offspring's encoding and memory functioning regardless of PAE and multivitamin supplementation alone may provide a beneficial impact to infants with PAE.

0806

CHOICES: AN INTERVENTION TO REDUCE THE RISK OF ALCOHOL-EXPOSED PREGNANCY (AEP) CAN BE IMPLEMENTED IN DIVERSE SETTINGS

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Purpose: As alcohol is the most preventable cause of intellectual disability in the USA, dissemination of effective interventions to prevent AEP is critical. CHOICES, a motivational interviewing (MI) based intervention with women at risk of an AEP, was proven efficacious in randomized, controlled trials in a variety of settings. CDC has sponsored demonstration projects to determine if and how this research can be translated into practice in populations with high rates of alcohol use and pregnancy. CHOICES was part of the completed FAS-PACE Stepped Care project in Colorado, and is the basis of STD-CHOICES, currently underway in Denver and Baltimore STD clinics.
Methods: The CHOICES intervention comprises 2 face to face counseling sessions and 1 booster call after each session, with follow-up obtained 3 and 6 months after session 1. Eligible participants are reproductive age, heterosexually active women drinking at high-risk levels (4 or more drinks on 1 occasion or 8 or more drinks weekly), and not using effective contraception. Using MI techniques, including a decisional balance exercise and importance/readiness/confidence rulers, the Interventionist helps the woman set goals for alcohol and/or contraceptive use that would lower AEP risk. Reduced risk for AEP is defined as reducing drinking below high-risk levels, using effective contraception, or both. FAS-PACE used Public Health nurses, social workers, and substance abuse counselors (CAC) who went to a variety of settings including food banks, probation offices, WIC offices, domestic violence shelters, and colleges in four counties. STD-CHOICES in Baltimore uses a social worker in the Druid Clinic. Denver uses a CAC and Medical Assistants, in the Denver Metro Health Clinic. The social worker and a patient navigator screen in Baltimore, clinicians screen in Denver. MI experts trained all Interventionists.
Results: FAS-PACE obtained follow-up on 85/244 women, with 86% at reduced risk of AEP at both 3 and 6 months. For the STD-CHOICES sites, follow-ups and % at reduced risk at 3 and 6 months are: Baltimore 59/113, 64% and 74%; Denver 40/81, 81% and 83%.
Conclusions: Preliminary results from these CDC demonstration projects indicate the CHOICES intervention can be implemented successfully using different models of venue, screening and personnel delivering the intervention, suggesting that agencies working with women to reduce risk of AEP will be able to choose a model to fit their resources.

0807

EPIDEMIOLOGY OF FETAL ALCOHOL SYNDROME IN SOUTH KOREA: AN ACTIVE CASE ASCERTAINMENT STUDY

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In general, females in Asian countries consume less alcohol than those from Western countries although alcohol consumption among females in Korea have been increasing. Fetal alcohol syndrome (FAS) is a serious consequence of drinking during pregnancy and little information is available on the rates of FAS in Asian countries. This study estimated the prevalence of FAS in South Korea using an active case ascertainment approach in two different settings, general schools (N=12) and institutions for children with intellectual disability (N=8). Within the general schools 7,785 children were screened on height and weight and those falling under the 10th percentile were selected for subsequent physical examination (n=224), including a dysmorphology assessment. Intellectual function and attention capabilities were examined by utilizing a standardized neurocognitive test, WISC-III(Wechsler Inteligence Scale for Children, 3th ed.)and computerized continuous performance test. Parental interviews were conducted to obtain information about maternal drinking history. In the institutional settings, physical exams, including the dysmorphology assessment were performed on all children. In the general schools the prevalence of FAS was 0.28%, whereas in the institutions for intellectual disability the prevalence was 14.9%. These rates are not dissimilar to those reported in western countries. These data extend extremely limited studies on the prevalence of FAS in S. Korea and demonstrate the need for increased screening and diagnoses of FAS in various community and clinical settings.
Notification:Research performed in conjunction with the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD) and supported by NIAAA grants U24 AA014811 and Korea Centers for Disease Control and Prevention.

0808

AN EPIDEMIOLOGY OF DIAGNOSING THE FULL SPECTRUM OF FASD

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Active case ascertainment methods were used in this fourth wave of research in the Western Cape Province of South Africa to examine the full spectrum of fetal alcohol spectrum disorders (FASD). By refining our methodology since 1997, we were able to examine carefully for children at the lower end of the spectrum, those with alcohol related neurodevelopmental deficits (ARND). Additionally, we included analyses of alcohol exposure during the index pregnancy of randomly-selected normal controls. Therefore, this study provides further insight into the operationalization of the 1996 Institue of Medicine criteria for diagnosing FASD. All children for whom consent was given were first screened on their height, weight, and head circumference (N = 747), and those who were at or below the 25th centile for height and weight, or head circumference, and the randomly-selected controls were advanced to full dysmorphology examinations (n = 356). The sample of children was evenly split on gender (49.8% male, 50.2% female), and the mean age was 81.4 months (6.8 years). Children with a preliminary diagnosis of any FASD diagnosis and controls were administered a 2-hour battery of cognitive and behavioral tests. Biological mothers were interviewed concerning use of alcohol during the index pregnancy. Case conferences including all three domains of the study: dysmorphology, neurobehavior, and maternal risk factors determined the final diagnosis. Sixty-eight children (19.1%) received a final diagnosis of FAS, 14.9% a diagnosis of Partial FAS (PFAS), 35 children (9.8%) received a diagnosis of ARND, 13.2% were exposed normal controls, and 43.0% were found to be unexposed controls. The data indicate that the prevalence of the full spectrum of FASD may be greater than currently accepted estimates. Presented will be an epidemiologic summary of the children's FASD traits, relative differences between groups as they exist by sex, birth order, socioeconomic status, cognitive and developmental characteristics, and key traits of their mothers and family histories. This research was funded in part by the NIAAA awards AA09440, AA11685, and AA015134 and The National Center on Minority Health and Health Disparities.

0809

HIGH RISK PREGNANT WOMEN AND CASE MANAGEMENT: EFFICACY OF PREVENTION IN A COMMUNITY WITH THE HIGHEST FETAL ALCOHOL SYNDROME PREVALENCE IN THE WORLD

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South Africa has the highest recorded prevalence of Fetal Alcohol Spectrum Disorders (FASD) in the world. Caused by maternal drinking, FAS is preventable and characterized by unique facial features, growth retardation, and developmental delays. Case management (CM) can help women access resources needed to reduce drinking or increase abstention from alcohol during pregnancy. In this study, CM is designed to determine whether the rate of FASD can be reduced over time, focusing on indicated prevention to provide support to women who are known to drink heavily during pregnancy. CM was implemented by trained project officers using Motivational Interviewing (MI) and Community Reinforcement Approach (CRA) techniques to encourage positive changes in drinking habits. MI is a person-centred therapy that elicits and strengthens motivation for change. CRA is an evidence-based behavioral approach for treating substance abuse problems to assist clients in maintaining a sober lifestyle. Data for the initial participants (n = 30; 97% Coloured, 3% Black) indicated risk factors commonly associated with maternal drinking and FASD, including young age at time of pregnancy (= 24.3 years), low education (= < 8^{th} grade), low religiousity (> 33% report never attending church), and unemployment (>75% do not work for money). The majority (69%) of the sample report that half or more of their current friends drink alcohol. Ninety percent believed they were pregnant at the time of intake. Nearly half (48%) report their lives to be very or extremely stressful, and at intake, nearly half (42% a very high percentage in this South African population) believed they currently had a drinking problem. Mean AUDIT scores show significant improvement from baseline to 6 month follow-up (20.3 down to 9.7). Measures for total drinks consumed on weekends, total drinks over the past seven days, and total number of drinking days in the past week, were also reduced. Results show the efficacy of CM, while also showing the difficulty of making enduring change in an environment where weekend drinking for recreation and sociability remains popular. CM for prevention is useful to help women abstain or reduce their alcohol intake during pregnancy. Data gathering and analysis continues. This research was funded in part by NIAAA (RO1 AA09440 and RO1 AA11685) and The National Center on Minority Health and Health Disparities (NCMHD).

0810

THE HAWAI'I FETAL ALCOHOL SPECTRUM DISORDERS TASK FORCE – CHALLENGES AND PROGRESS IN BUILDING A COMPREHENSIVE STATEWIDE SYSTEM

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Purpose: The Hawai'i Fetal Alcohol Spectrum Disorders (FASD) Task Force was initiated less than a decade ago as a primary entity to help plan, guide, facilitate, and oversee statewide initiatives in the education and awareness, screening, identification, prevention, interventions, and services related to fetal alcohol spectrum disorders. An historical assessment of the Task Force activities was conducted to map the challenges and progress made in the goal of building a comprehensive statewide system for FASD.
Method: Archived documents from the Task Force and the Hawai'i Department of Health were examined, (e.g., PRAMS and Birth Defects Reports), and informal face-to-face or phone interviews were conducted (e.g., State FASD Coordinator, other agency collaborators). These sources provided quantitative and qualitative information about the Task Force's planned or prioritized, and implemented activities, as well as the major outcomes, challenges, and successes.
Results: Though an iterative process, the Task Force has conducted needs assessments, strategic planning, and prioritized inter-agency and multi-sectoral collaborative activities, reflecting incremental gains in expanding initiatives in prevention, screening, public awareness, and education and training over time. The creation of a State FASD Coordinator position within the past several years was significant in catalyzing increased and sustained support for FASD initiatives and extending collaborative networks with national experts/teams, community-based organizations, and other local agencies to leverage resources in a time of economic strain. Needs assessments by the state and other community data indicate that prenatal alcohol use is significant, and that health, educational, and social services seek education and training opportunities to address the issues of FASDs in practice. Recent efforts have looked to develop or enhance foundations in a systematic and collaborative approach for currently challenging areas such as data and surveillance, research, and education and training to help improve screening, identification and prevention systems.
Conclusion: A strategic and informed approach to building a statewide comprehensive system can become an iterative and resource-dependent process. Key leadership, stakeholder commitment and support, and prioritization by the state is essential in order to continue to make progress and drive policy directions to reduce and prevent FASDs in Hawai'i.

0811

ALCOHOL, TOBACCO, AND DRUG USE AS REASONS FOR PREGNANCY TERMINATION

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Background: Concern about effects of alcohol and drug use during pregnancy is intertwined with debates about abortion. Early papers about Fetal Alcohol Syndrome called for chronic alcoholic women to consider abortion. Recently, there has been concern that promoting alcohol abstinence during pregnancy leads women to terminate otherwise wanted pregnancies. Legal scholars argue that prosecutions of pregnant women using drugs punish women for not having abortions. However, there is little published research to address these concerns. The purpose of this study is to describe how women report alcohol, tobacco, and/or drug use (ATOD) as reasons for deciding to have abortions and assess differences between women reporting and not reporting ATOD as reasons.
Methods: This mixed methods study uses baseline data from the UCSF Turnaway Study, a five-year prospective study designed to assess the effect of receiving or being denied an abortion on women's physical and mental health and socioeconomic well-being. The Turnaway Study dataset includes a sample of 956 women who sought an abortion at one of 30 U.S. clinics between 2008 and 2010. Qualitative data were analyzed through thematic coding. Quantitative data were analyzed using t-tests, Mann-Whitney tests, Chi-square tests, Fisher exact tests, and logistic regression.
Results: 4.8% of women reported ATOD as a reason, about evenly divided between alcohol and drug use, with some overlap. Women described concerns that their ATOD had affected their baby's health and that their or their partner's ATOD would influence their ability to parent. More than half reporting ATOD as a reason had binge drank and/or had an eye-opener or blackout in the month before discovering pregnancy. Half had used drugs in the month before discovering pregnancy, with 74% of these using drugs more than once/week. Although two-thirds smoked tobacco, no woman reported tobacco only as a reason. Only one woman reporting ATOD as a reason had planned her pregnancy.
Conclusions: Women reporting ATOD as a reason for abortion do not appear to be terminating otherwise wanted pregnancies. While they reported drinking, smoking, and using drugs at levels that could increase chances of having adverse pregnancy outcomes, evidence-based information to help women characterize and understand levels of risk associated with these patterns of alcohol and drug use is needed.

0812

PROMISING THERAPY OF NEURAL STEM CELL TRANSPLANTATION FOR FASD MODEL - A NEW STRATEGY FOR NEURAL NETWORK RESCONSTRUCTION AND BEHAVIOR RECOVERY

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Recent clinical neuroimaging studies have revealed a possible relationship between morphological brain changes and the manifestation of psychiatric disorders such as depression, schizophrenia, and alcoholism. Although its biological mechanism is still unclear, the emerging evidence suggests that the alteration of neurogenesis is the key factor for the morphological brain changes of these psychiatric disorders. In our previous work, we analyzed the mechanism of neural network disruption by ethanol using cultured cells, and found a suppressive effect of ethanol on neural stem cell (NSC) differentiation. We also demonstrated that antidepressants, mood stabilizers and atypical antipsychotics stimulate NSC differentiation in cells inhibited by ethanol, indicating that their contribution to neural network repair was impaired.
In the present work, we demonstrate the usefulness of intravenous transplantation of NSCs to fetal alcohol spectrum disorder (FASD) model rats for the purpose of reconstructing the impaired neural network and investigating the possibility of regenerative therapy for patients with neurobehavioral deficits of FASD. We have shown the potential migration of transplanted NSCs into the brain by visualizing a fluorescent cell marker and radioisotope, as well as the possible recovery of behavioral abnormalities observed in FASD model rats such as anxiety-like behaviors, memory/cognitive function, and social interaction. We further assessed the characteristics of transplanted cells and found more migrated cells in the cingulated cortex, amygdale and thalamus than in other areas in the model rat brain. In the Amygdala,Cingulate Cortex and hippocampus areas, the FASD model rats numbers of parvalbumin positive cells was reduced and the NSC transplantation partially recovered these disturbances. In the amygdala and cingulate cortex, intravenous NSC transplantation appears to partially regenerate expression of PSD95 in FASD model rats.
These results indicate that intravenous NSC transplantation has the potential to become a therapeutic intervention for FASD patients.

0813

PROSPECTIVE ASCERTAINMENT OF INFANTS IN TWO COMMUNITIES IN THE WESTERN CAPE; IDENTIFYING PREDICTORS OF FETAL ALCOHOL SPECTRUM DISORDERS IN INFANCY

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Fetal alcohol spectrum disorders (FASD) are caused by the deleterious effects of maternal alcohol consumption during pregnancy. FASD's are the most common environmentally induced form of mental retardation in the world, potentially affecting 1% of all children born in the United States. Fetal alcohol syndrome (FAS) is the most clinically recognizable form of FASD and is characterized by a pattern of minor facial anomalies, prenatal and postnatal growth retardation, and functional or structural central nervous system (CNS) abnormalities. However, the effects of alcohol on the developing fetus represent a continuum, with full-blown FAS merely the ''tip of the iceberg.'' The highest documented prevalence of FAS in the world has been documented to be 80 per 1,000 in the mixed race population of the Western Cape Province in South Africa. The consequences of FASD are life long, and the behavioral and learning difficulties are often greater than the degree of neurocognitive impairment. Thus, early diagnosis and referral for early intervention services is imperative. However, while application of diagnostic guidelines for FASD in older children and adolescents can be difficult, diagnosis in the infant is rarely attempted because of the lack of documented specificity of the phenotype in the newborn. Yet, identification and referral within the first few months of life may represent the most crucial time in the affected child's lifespan for initiation of early intervention services. Between October 2008 and May 2011 NIAAA-funded researchers investigated predictors of FASD and developmental outcome in early infancy in a cohort of 965 alcohol-exposed and unexposed infants prospectively ascertained during pregnancy. We utilized three methodologies to approach this issue: growth and standardized dysmorphology assessment of subjects and controls at birth, 6 weeks, 9 months and 18 month intervals, respectively; standardized developmental assessments (using age appropriate assessment tools) at the same intervals; and digital photography at each interval.

0814

IMPLEMENTING AND EVALUATING THE INSTITUTE OF MEDICINE (IOM) MODEL FOR PREVENTION OF FETAL ALCOHOL SPECTRUM DISORDERS (FASD)

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The rate of fetal alcohol syndrome (FAS) and Partial FAS (PFAS) in this South Africa community has been quite constant and extremely high for the 15 years that NIAAA-funded researchers have studied it locally (7–9%). And the prevalence of FASD overall has most recently been found to approach 20%. Prevention was therefore necessary to improve public health, and evaluating the efficacy of FASD prevention presented both a unique challenge and a unique opportunity. In 2007, a trial of the Institute of Medicine (IOM) -recommended model of comprehensive prevention was funded in an attempt to reduce the high prevalence of FASD in this community. The IOM model utilizes multiple levels of approach: universal, selected, and indicated. It seems to be particularly well-suited for this community where the modal binge drinking pattern linked to high rates of FASD is normative and entrenched among a significant proportion of the female and male population. Therefore, prevention had to address changes in norms, institutions, and social conditions, as well as screening for, identifying, and providing case management and other services to high risk, female drinkers. Multiple measures of process and outcome evaluation are being utilized to assess the efficacy of each level of the prevention. This poster will provide an overview of the IOM prevention model and multiple evaluation measures of specific applications of the model to reflect on overall prevention efficacy and the success, or lack thereof, at each of the three levels. FASD prevention is proving to be most efficacious at the secondary and tertiary levels, but the three levels are complimentary.

0815

COMPARISON OF DRINKING PRACTICES, KNOWLEDGE, AND ATTITUDES OF ADULTS RESIDING IN COMMUNITIES TAKING PART IN THE FAS PREVENTION STUDY IN SOUTH AFRICA

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Between October 2008 and June 2010 community surveys were conducted in two wine growing regions of the Western Cape Province comprising the intervention and comparison communities of the NIAAA-funded South African Fetal Alcohol Syndrome Prevention Study. The purpose of the study was to assess drinking behavior, to guide interventions and to serve as a baseline for later assessing the impact of various interventions at population level. A cross-sectional survey was undertaken of adults randomly selected from urban and peri-urban areas and from neighboring farms. The questionnaire was adapted from prior community surveys used in the USA and South Africa. Interviewers took respondents through the questionnaires in either English or Afrikaans. Interviews were conducted with 384 respondents in the intervention community and 207 respondents in the comparison communities. Across sites between 61% and 67% of respondents were male and the average age for males and females ranged between 36 and 38 years. Two-thirds of respondents were ''Coloured'' (of mixed racial descent). Over 80% of respondents resided in urban areas, except for males in the comparison communities, where 61% were from farms. Unemployment rates ranged from 10% for males in the comparison communities to 30% for females in the intervention community. Over half (55%) of the males in the comparison communities were farm workers. Forty-six percent of the females and 75% of the males in the comparison communities reported drinking in the past year, with over a third of female drinkers (38% in the comparison communities and 34% in the intervention community) and between a half and three-quarters of male drinkers (51% in the intervention community and 75% in the comparison communities) exhibiting symptoms of hazardous or harmful drinking. Three-quarters or more of respondents did not think that alcohol should be made more available in the province, and over two-thirds indicated that it was equally harmful for a woman to drink during any of the trimesters of pregnancy. Unfortunately the survey indicated that more than 30% of women had never had a health worker speak to them about the effects of drinking during pregnancy, and over 10% of females interviewed had never heard of FAS or fetal alcohol syndrome. The findings reinforce the need for interventions to address harmful use of alcohol in both communities and also to address gaps in knowledge regarding the effects of drinking during pregnancy.

0816

SELECTIVE PREVENTION OF FASD: SCREENING WOMEN IN ANTENATAL CLINICS FOR REFERRAL TO CASE MANAGEMENT

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A key component of this NIAAA-funded study to prevent fetal alcohol spectrum disorders (FASD) in the Western Cape Province of South Africa is to contact women on their first visit to the antenatal clinics for an assessment of drinking levels during their current pregnancy and therefore, the risk for producing a child with an FASD. Antenatal clinics are usually held over four days of each week in different locations in our prevention and comparison communities. Since late 2008 through June 2011, 2,550 women have been contacted and enrolled. Seventy-nine percent of the women were ''Coloured'' (a proper South African term meaning of mixed racial ancestry), 18% were Black, and 3% were White. Generally, these women were extremely positive and open to the brief intervention about the risks of drinking during their pregnancy. In fact, the women who attend these clinics are used to long periods of waiting, and very little time is actually spent with health care workers. The fact that our staff spent time with these women made the women feel special, and the individual attention given to everyone contributed to the success of these efforts. Two instruments are used to assess the use or abuse of alcohol, the Alcohol Use Questionnaire (AUDIT), and the Self-Administered Questionnaire (SAQ). After completing the assessment tools, any risky drinking behavior was discussed with the women in a non-judgmental manner, and every woman was motivated by receiving factual, prevention information and informed that stopping drinking at any time during the pregnancy would benefit their baby. In the prevention community, if a woman was consuming alcohol in a risky manner, our staff member invited the women to become involved in the case management component of our study. Women in the comparison communities are referred to Provincial health officials or non-governmental organizations. Data analysis continues. This research was funded in part by the NIAAA (RO1 AA09440, RO1 AA11685, and RO1 AA015134) and The National Center on Minority Health and Health Disparities (NCMHD).

8. DETERMINANTS OF ALCOHOL CONSUMPTION IN HUMANS

0817

AVOIDANT COPING MEDIATES THE RELATIONSHIP BETWEEN POST-TRAUMATIC STRESS SYMPTOMS AND NEGATIVE ALCOHOL-RELATED CONSEQUENCES

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Rates of co-occurring Post Traumatic Stress Disorder (PTSD) and alcohol misuse in returning war Veterans are high and impairment due to the first may be compounded by the negative consequences of alcohol misuse. However, the mechanisms that perpetuate the co-occurrence of PTSD and alcohol-related consequences have yet to be completely elucidated. Previous research has suggested that experiential avoidance impacts the relationship between PTSD and alcohol misuse. The current study's aim was to examine whether the use of avoidant coping strategies, including denial, venting, behavioral disengagement, and self-blame, mediate the relationship between PTSD and negative alcohol-related consequences. Participants (N =136; 84.6% male; 34.3% racial/ethnic minority) were Operation Enduring Freedom/Operation Iraqi Freedom Veterans enrolled in Project SERVE (I01RX000304; PI: Morissette) at the Veterans Affairs VISN 17 Center of Excellence for Research on Returning War Veterans. Participants completed a battery of measures including the PTSD Checklist – Military Version (M = 47.3, SD = 11.9, Range = 17–85), Brief COPE, and the Rutgers Alcohol Problems Index (M = 6.0, SD = 11.9, Range = 0–50). A second-order factor analysis was performed on the Brief COPE that indicated a two-factor structure of active and avoidant coping, which was used in mediation analysis. Results indicated that endorsing symptoms of PTSD was predictive of reported alcohol-related consequences (β= .14, p < .01) as well as active coping (β = -.07, p < .01) and avoidant coping (β = .06 p < .001). Furthermore, avoidant coping (β = 1.51, p < .01) but not active coping (β = -.21, ns) was predictive of reported negative alcohol-related consequences. Mediation analysis indicated that avoidant coping acted as a full mediator of the relationship between PTSD symptoms and alcohol-related consequences reported in Veterans (β = .05, ns). Gender did not have any significant effects on the data analyses, however, age was included as a covariate. Taken together, findings indicate that Veterans with PTSD symptoms who refuse to acknowledge stress, vent, disengage behaviorally, or blame themselves may be more likely to experience alcohol-related consequences than those who use active coping strategies. Results suggest that treatments which aid Veterans with PTSD in the reduction of avoidant coping strategies may decrease negative alcohol-related experiences and therefore improve their overall functioning.

0818

THE RELATIONSHIP BETWEEN POSTTRAUMATIC EMOTIONAL NUMBING AND ALCOHOL USE AMONG RECENT COMBAT VETERANS

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Veterans of Operations Enduring Freedom and Iraqi Freedom (OEF/OIF) face high rates of comorbid posttraumatic stress (PTSD) and alcohol use disorders (AUD). Research among Veterans of previous wars has found support for the self-medication hypothesis as an explanation for comorbid PTSD and AUD. The present study sought to expand upon these findings by examining specific PTSD symptom clusters as they relate to alcohol use among OEF/OIF combat Veterans. A recent study (Jakupcak et al., 2010) found that self-reported emotional numbing symptoms were uniquely associated with alcohol misuse among OEF/OIF Veterans. Accordingly, we hypothesized that PTSD symptom severity, and emotional numbing in particular, would uniquely predict subsequent alcohol use. This adds to existing research by using a longitudinal design to assess symptoms via clinical interviews.
Participants were 64 OEF/OIF Veterans with PTSD symptoms and hazardous alcohol use (AUDIT score ≥ 8). Measures administered at baseline included the Clinician-Administered PTSD Scale and the Timeline Follow-Back (TLFB). Participants then completed 28 days of PTSD symptom and drinking ecological momentary assessment (EMA). The TLFB was also administered again one month post-baseline. Multiple regression analyses tested which predictors were uniquely related to the number of drinks consumed during the 30 days pre- and post-baseline. Controlling for relevant demographic or military variables, post-baseline alcohol use was not significantly related to emotional numbing symptom severity or any other PTSD symptom cluster. However, pre-baseline alcohol use was uniquely related to emotional numbing severity (ß = .295, p = .05). While there was a significant relationship between emotional numbing and alcohol use prior to the baseline interview, a similar relationship between post-baseline alcohol use and PTSD severity was not found. This may be due to the self-monitoring nature of the post-baseline assessment period (i.e., measurement reactivity). While self-medication of emotional numbing symptoms may have been occurring prior to baseline, the baseline interview and EMA, in particular, may have increased participant awareness of their use of alcohol to cope with their PTSD symptoms, effectively disrupting the cycle of self-medication.

0819

RISK MECHANISMS AMONG TRAUMA EXPOSURE, PTSD SYMPTOMS, AND ALCOHOL AND DRUG PROBLEMS

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Although it is well-known that posttraumatic stress disorder (PTSD) and substance use disorders (SUDs) commonly co-occur, the mechanisms that link PTSD to SUDs remain poorly understood. The proposed study utilized longitudinal data from a high-risk community sample (*n*= 377; 54% males; 73% non-Hispanic Caucasians) to test a series of hypotheses that link PTSD symptoms with alcohol and drug problems. Specifically, this study examined whether pre-trauma substance use problems increase risk for trauma exposure (the high-risk hypothesis) or PTSD symptoms (the susceptibility hypothesis), whether PTSD symptoms increase risk for later alcohol/drug problems (the self-medication hypothesis), and whether the association between PTSD symptoms and alcohol/drug problems is due to shared familial risk factors (the shared vulnerability hypothesis).
This study contained pre-trauma measures of substance use problems and family risk factors. A composite pre-trauma family adversity variable was formed from measures of family conflict, stress in the family environment, parental alcoholism, and other parent psychopathology in order to reflect a combination of factors that are likely to increase risk for both PTSD and substance use problems. A series of logistic and negative binomial regressions were performed in a path analysis framework. Results showed that pre-trauma substance use problems did not significantly increase risk for trauma exposure or PTSD symptoms. However, PTSD symptoms during early adulthood predicted significantly higher levels of both alcohol and drug problems during adulthood (*p*'s < .05). The effect was significant over and above the influences of trauma exposure, pre-trauma substance use problems, pre-trauma family adversity, gender, and ethnicity. Moreover, the influence of pre-trauma family adversity on risk for future drug problems was fully mediated by PTSD symptoms for males and partially mediated by PTSD symptoms for females.
These results add to a growing body of literature in support of the self-medication hypothesis, such that PTSD symptoms may causally influence risk for future alcohol or drug problems. Results did not support the high-risk, susceptibility, or shared vulnerability hypotheses. By utilizing prospective data and controlling for baseline levels of substance use problems, this study increases our understanding of the PTSD-SUD link

0820

PROBLEM DRINKING AND DRUG ABUSE IN WOMEN SEXUAL ASSAULT SURVIVORS: ROLE OF TRAUMA HISTORY, COPING, AND PTSD

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Women sexual assault survivors report more problem drinking and substance abuse compared to other women. Among survivors, those with histories of trauma may be at increased risk of such negative outcomes compared to those without other traumas (Ullman, Filipas, Townsend, & Starzynski, 2005). We examined the links between trauma history, substance-related coping, PTSD, and problem drinking and substance abuse in women survivors of sexual assault from a diverse community sample (N= 1,900). Participants were women sexual assault survivors; 85% of these women had experienced a completed or attempted rape. They were primarily African American (45.3%) or White (34.6%) and ranged in age from 18 to 78 (*M* = 36.57%). Participants have completed Wave 1 of a longitudinal survey. Results from this study will be reported in this presentation. Trauma history was assessed with measures of: child abuse, including sexual abuse (Sexual Experiences Survey, Testa et al., 2004), physical abuse, and other traumatic life events, using the Revised Stressful Life Events Questionnaire (SLESQ-R, Green et al., 2006). We assessed (a) drinking (and other substance use) to cope, using a 2-item subscale of the Brief COPE (Carver et al., 1989) and a 5-item drinking to cope measure from Cooper et al. (1995), (b) tension-reduction expectancies, using a 5-item subscale of the Alcohol Effects Questionnaire (Rohsenow, 1983), (c) problem drinking, using the 25-item Michigan Alcoholism Screening Test (Selzer, 1971) and 5 items designed to detect problem drinking in women specifically (Richman, 2000), and (d) drug abuse, using a modified version of the Drug Abuse Screening Test (DAST-10, McCabe et al., 2006). PTSD symptoms were assessed with Foa's Posttraumatic Stress Diagnostic Scale (PDS, Foa, 1994). Structural equation modeling analyses will be conducted to examine whether the associations of two types of childhood trauma (i.e., sexual abuse, physical abuse) with PTSD symptoms and alcohol/drug problems are mediated by other adult traumatic events and victims' use of alcohol and substances to cope, controlling for the association of PTSD with problem drinking and substance abuse.

0821

DRINKING TO COPE, ANXIETY AND ALCOHOL-RELATED PROBLEMS AMONG HIGH-SCHOOL STUDENTS

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Previous studies have shown that drinking motives, in particular drinking to cope, have a positive relationship with both negative affect and alcohol use disorders (Carpenter et al., 1999). Furthermore, previous studies have found that coping motives are associated with alcohol-related problems among young adults (Lyvers et al., 2010) and among adolescents (Kuntsche et al., 2005). Additionally, comorbidity between anxiety and alcohol use disorders is well known (Smith et al., 2010). As shown by Lewis et al. (2008) and Morris et al. (2005), alcohol-related problems are associated with social anxiety among college students and adolescents (Blumenthal et al., 2010). However, little research has explored the role of anxiety in the relationship between coping motives and alcohol-related problems in a sample of young adults. The current study adds to the previous literature by exploring if the relationship between drinking to cope and alcohol-related problems is moderated by clinical anxiety in high school students. The sample included 204 high school seniors (58.8% female, age M = 17.34) participating in a longitudinal study about alcohol use trajectories. Measures of anxiety (DASS; Lovibond & Lovibond, 1995), drinking to cope (DMQ; Cooper et al., 1992; Cooper, 1994), and alcohol-related negative consequences (RAPI; White, & Labouvie, 1989) were given as part of a larger assessment battery. As expected, multiple regression analyses revealed a significant relationship between drinking to cope and alcohol-related problems β = .42, R^2 = .18, p < .001. Additionally, we found a significant interaction such that the relation between drinking to cope and negative consequences was stronger for those with higher anxiety; β = .30, R^2 = .61, p < .001. These results provide additional support to a growing literature linking coping motives with alcohol-related problems and indicate that anxiety plays an important role in this link among high school students. Clinical interventions should pay close attention to anxiety when evaluating this relationship. This research was supported by NIAAA #U01 AA018276 awarded to Drs. Larimer & Berglund.

0822

AN EVALUATION OF THE STRESS-NEGATIVE AFFECT MODEL IN EXPLAINING ALCOHOL USE: THE ROLE OF COMPONENTS OF NEGATIVE AFFECT AND COPING STYLE

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According to the stress-negative affect model, negative affect mediates the relation between stressors and alcohol use as an individual drinks alcohol in an attempt to alleviate the negative affect resulting from stressful negative life events (Wills & Shiffman, 1985). The current study used a comprehensive approach to evaluate the stress-negative affect model in two samples at different developmental stages. The potential mediating role of components of negative affect (i.e., sadness, guilt, fear, and anger) intervening in the relation between negative life events and alcohol use were examined in the context of different coping styles. Methods: Survey data from a sample of 1,057 drinking adults (M_{age}=44.45) and a sample of 352 drinking college students (M_{age}=19.07) were examined separately in a structural equation modeling framework with components of negative affect and alcohol use represented with latent variables. Two coping groups were identified in each sample using latent profile analysis of approach and avoidant coping scores from the Brief COPE: a high approach-low avoidant group and a moderate approach-moderate avoidant group. Using a multiple-group analysis framework with coping style as the grouping variable, a stress-negative affect models for alcohol use were estimated, in which negative life events were modeled to be related to four components of negative affect, which, in turn, were modeled to be related to alcohol use. Results: Stress-related drinking only occurred in the adult sample and the mediation pathways differed based on coping style. Specifically, individuals who rely on approach coping strategies but rarely use avoidant coping strategies appear to drink more following sadness (mediated effect = .12, SE = .05, p < .05) but drink less following anger (mediated effect = -.03, SE = .02, p<.05). In contrast, individuals who rely moderately on both avoidant and approach coping strategies drink in response to guilt (mediated effect = .04, SE = .03, p < .05). For the college student sample, stress-negative affect model for drinking was not supported. Conclusion: The pattern of findings demonstrates the importance of considering individual differences in examining the stress-negative affect model and when designing interventions to reduce stress-related drinking.

0823

INTERACTIONS BETWEEN COPING STYLE AND DRINKING TO COPE IN PREDICTING NATURALISTIC DRINKING AND DRINKING FOLLOWING A LAB-BASED PSYCHOSOCIAL STRESSOR

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Using alcohol to cope (i.e., coping motivation) and general coping style both are theorized and demonstrated empirically to lead to problematic drinking. In the present study, we sought to examine whether these factors *interact* to predict alcohol use, both retrospectively reported and in the lab following a stressor task. Social drinkers (N=100, 50% women) received either the Trier Social Stress Test (TSST) or a no-stress control condition, and then consumed beer under the guise of a taste-test. A Timeline Followback interview to assess past month alcohol use, the Drinking Motives Questionnaire (DMQ), and the COPE (to assess adaptive coping) were administered prior to the laboratory challenge. Multiple regression models were used to examine DMQ coping motives, adaptive coping, and their interaction as predictors of mls of beer consumed (BEER) in a clinical laboratory setting. In the TSST group, the interaction between adaptive coping and coping motives in predicting BEER was marginal (p=.08). The association between coping motives and BEER was positive at both high and low levels of adaptive coping, but at low levels of adaptive coping, this association was stronger. Both simple slope effects were significant at the trend level (ps < .07). Among those who did not receive the stressor, no significant main or interaction effects were observed. Further, in the whole sample, there was no interaction between adaptive coping and coping motives in predicting quantity and frequency of drinking in the prior month. Findings suggest that when an individual is lacking in adaptive coping strategies, stronger coping motives for drinking predict greater alcohol consumption following a stress provocation. However, coping factors were not ‘‘activated’’ in the no-stress condition, and therefore, participants may not have felt the need or desire to drink. In addition, the lack of an interaction effect in predicting retrospectively-reported drinking speaks to the need to examine not just self-reports of past alcohol use when interested in the influence of affect-relevant predictors (e.g., coping), but to also examine these predictors in a controlled context in which negative affect is elicited. As both general coping skills and coping motives for alcohol use are responsive to intervention, study of the conditions under which they exert unique and interactive effects is important. This research was supported by NIAAA grants R21 AA016289 and T32 AA07474.

0824

THE UNIQUE ASSOCIATION OF SUICIDAL IDEATION WITH DRINKING TO COPE AMONG COLLEGE BINGE DRINKERS

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Suicidal ideation and attempts among college students are associated with binge drinking and alcohol-related problems. Consistent with learning theory-based motivational models of alcohol use, drinking to cope (DTC) is a significant intervening variable in the association between suicidal ideation and alcohol use and problems among students (Gonzalez et al., 2009). This study explored whether the relationship between severity of suicidal ideation and DTC was accounted for by several factors theorized or shown to contribute to both suicidal ideation and DTC, including impulsivity, negative mood regulation expectancies (NMRE), and avoidant coping. The associations of depression and hopelessness with DTC also were examined. Participants were 109 emerging adult (18- to 25-year-old) college students who reported at least one episode of binge drinking during a typical month in the past year. Regression analyses, controlling for gender, revealed that suicidal ideation (ΔR^2 = .27, p < .001), depression (ΔR^2 = .16, p < .001), and hopelessness (ΔR^2 = .12, p < .001) were moderately to strongly associated with DTC prior to including other variables in the model. A hierarchical multiple regression analysis revealed that impulsivity variables (Step 1) accounted for 21% of the variance in DTC; however, only negative urgency (β = .45, p < .001) was uniquely associated with DTC. Lower NMRE were significantly associated with DTC (Step 2, ΔR^2 = .07, p = .002), while coping skills were not (Step 3, ΔR^2 = .001, p = .97). Suicidal ideation remained significantly associated with DTC (Step 4; ΔR^2 = .06, p = .003), even when controlling for depression (ΔR^2 = .05, p = .007). In contrast, depression (ΔR^2 = .02, p =.12) and hopelessness (ΔR^2 = .004, p =.44) were no longer significantly associated with DTC once other variables were accounted for. These findings support a motivational model of alcohol use and suggest that suicidal ideation and DTC are not merely related due to shared associations with negative urgency, low NMRE, or maladaptive coping. However, given that the association of suicidal ideation with DTC was substantially attenuated when negative urgency and NMRE were included in the model, it appears that these variables may contribute to the association between suicidal ideation and drinking to cope. Therefore, negative urgency and low NMRE may be useful targets for treatments aimed at reducing alcohol misuse among emerging adult students who experience suicidal ideation.

0825

MULTILEVEL ANALYSIS OF LONGITUDINAL ALCOHOL AND MARIJUANA USE AS A FUNCTION OF GENDER, NEGLECT, AND VIOLENCE IN ADOLESCENTS

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Evidence indicates that alcohol and marijuana abuse is influenced by multiple contextual factors including adverse childhood events. The goal of this study was to examine the relationship between the growth of alcohol and marijuana use and covariates of adverse events (neglect and violence). We also measured how gender moderates these relationships. Multilevel Modeling (MLM) was used to analyze growth trajectories in cohort sequential longitudinal data from adolescents (N=1054) (grades 9 to 11). The dependent variables were recency of alcohol and marijuana use (i.e. when was the last time used, never, more than a year ago, in the past year, in the past month, and in the past week). Time-invariant variables were gender (male, female), violence, and neglect. Violence and neglect were measured once with a twelve item questionnaire given in the final year of the study (grade 9, 10 and 11). The neglect item was reversed scored. These measures have good internal consistency, convergent validity, and concurrent validity as predictors of substance use. Results confirm positive growth in recency of both alcohol (β=0.62, t=13.499, df=1302, P<.05) and marijuana consumption (β=0.36, t=8.766, df=1302, P<.05) as a function of time. Neglect was positively related to the recency of alcohol and marijuana consumption (β= 0.36 and 0.26, respectively, p<.05), but only the growth of marijuana consumption was impacted by neglect (β = 0.06, p<.05). Violence was positively related to both recency of alcohol and marijuana consumption (β= 0.26 and 0.21, respectively, p<.05); however, violence only impacted the relationship between time and marijuana consumption (β= 0.10, p<.05). Gender moderated the relationship between time and both alcohol and marijuana consumption (β=–0.05 and –0.08, respectively, p<.05) with male students revealing higher growth of alcohol consumption and higher growth of marijuana consumption than females. However, gender did not interact with the effects of neglect or violence in this analysis. Our results suggest mild or moderate violence and neglect (physical or emotional) in childhood are important factors to predict early alcohol and marijuana abuse over time. Gender differences should also be considered in this relationship.

0826

DAILY STRESSORS AND ALCOHOL IN FIRE SERVICE

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Firefighters are at high risk to develop stress-related disorders (e.g., Post-traumatic Stress Disorder; Laposa & Alden, 2003), which are often comorbid with alcohol use disorders (Back et al., 2005). This study examined the association between stress and alcohol reported in daily diary logs of 84 urban fire service members. The majority of the sample was male (75%), line firefighter (80%), non-Hispanic Caucasian (69%), and married (55%). Average age was 29.4 years (*SD* = 8.95), education 15.1 years (*SD* = 2.19 years), income $60K-89,999, and time in fire service 11 yrs. 3 months (*SD* = 7 yrs, 6 mo.). Participants completed an average of 17.5 (*SD* = 5.8) of 21 days of the diary (1449 days total). Descriptives examined number of drinks, drinking urge intensity, reports of drinking to cope, work-related stress, family stress, partner stress, and financial stress. Hierarchical linear modeling predicted same day drinking urges (Model 1) and drinking to cope (Model 2). Level 1 variables for both models included stress from emergency calls (work-related), partner stress, family stress, and financial stress. Level 2 variables included age, gender, education, years in fire service, and income. Over a quarter (27.7%) of the sample did not report any alcohol use. Of those who drank, average number of drinks per day was 1.27 (*SD* = 2.67). The mean rating of drinking urge intensity was 1.63 (*SD* = 1.17), where 1 = ''Not at All'' and 7 = ''Extremely Strong''; mean rating of drinking to cope was 2.09 (*SD* = 1.49), where 1 = ''Not at all'' and 7 = ''A Great Deal''. Mean ratings of stress were 3.35 (*SD* = 1.48), 1.86 (*SD* = 1.29), 2.19 (*SD* = 1.58), and 3.05 (*SD* = 1.77) for work-related, family, partner, and financial stress, respectively, where 1 = ''Not at All'' and 7 = ''Extremely''. Work-related stress was not significantly related to drinking urge intensity or drinking to cope. Partner stress showed a trend-like association with same day drinking urges (*B* = 0.072, *p* = 0.054), in which more partner stress was related to more intense drinking urges. Family stress exhibited a trend-like relation with same day drinking to cope (*B* = –0.918, *p* = 0.057), in which more family stress resulted in less drinking to cope, and financial stress was significantly related to more drinking to cope (*B* = 1.113, *p* = 0.033). Results underscore the importance of assessing and targeting home stressors in fire service.

0827

EMOTION REGULATION AND DAILY ARGUMENTS INTERACT TO PREDICT ALCOHOL CONSUMPTION IN PARTNERED SOCIAL DRINKERS

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Although previous research has demonstrated that the ability to self-regulate is an important predictor of alcohol consumption, little is known about the effects of self-regulation on alcohol consumption within an intimate relationship context. The current research examines the interaction between emotion regulation and daily interactions with the partner to predict alcohol consumption in a community sample of partnered social drinkers. Participants in the current study (n = 96) consisted of married or cohabiting couples, ages 21–45, who were recruited from the community. To be eligible, both partners had to drink 3–4 drinks or more on an occasion at least once a month, and at least one partner had to drink at least once a week; however, they were screened out if they met criteria for alcohol dependence. Participant couples completed a series of background questionnaires, including Deficits in Emotion Regulation (DERS, Gratz & Roemer 2004). Both partners then made daily reports of mood, conflict, intimacy, and alcohol consumption using interactive voice response technology (IVR) for 56 consecutive days. Multilevel models were estimated using the Actor-Partner Interdependence Model (APIM). Replicating previous research regarding conflict and alcohol consumption, analyses revealed that arguing with the partner on one day predicted quantity of alcohol consumed the next day. As hypothesized, this effect was qualified by a significant interaction with deficits in emotion regulation. Among those who were relatively poor at regulating emotion, arguing with the partner on one day was significantly associated with alcohol use the next day. Among those who were good at regulating emotion, however, this association was not significant. These effects were not moderated by gender, and the interaction remained significant controlling for daily feelings of stress, overall marital satisfaction, and partner effects. These results suggest that marital conflict is a unique stressor that predicts alcohol consumption in people who have trouble regulating their emotions. These results have implications for the Tension Reduction Model of alcohol consumption and for interventions that involve the partner and/or marital therapy in the treatment context.

0828

MODERATORS AND MEDITATORS OF ALCOHOL USE IN ADOLESCENT SMOKERS

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Smoking among adolescents is still a considerable health problem and is most often accompanied by alcohol use - indeed, the relationship between smoking and drinking alcohol has only grown stronger over the past decade. While smoking is often motivated by the desire to reduce negative affect, it is unclear whether a similar mechanism underlies alcohol use and whether the effects of negative mood are mediated by related beliefs and self-image. The purpose of the current study was to examine potential moderators and mediators of alcohol use within a group of adolescent smokers. Participants are drawn from a program project which examined the social and emotional contexts of smoking in adolescents using various methodologies (i.e., self-report questionnaires, ecological momentary assessment, lab-based measures, and observational coding). A group of 1263 students from Chicago-area high schools was recruited via survey and enrolled in the project during their first and second years of high school. Of these, 551 had smoked within the past month and so comprise the present sample. Outcome measures of interest include quantity and frequency of alcohol use within the past three months. The effects of depressive symptomatology and perceived stress on alcohol use were thought to be mediated by negative mood regulation expectancies and self-esteem. Basic demographics (e.g., gender and race) were considered potential moderators of these pathways. Among those who had smoked at least one cigarette in the past month, regular alcohol consumption was relatively common, as 38% drank between once a week and once a month. Depressive symptomatology and perceived stress were variously predictive of alcohol use, depending on the moderators and mediators of interest. These results indicate that alcohol use among adolescent smokers may be motivated by a desire to alleviate negative affect, though more adaptive coping strategies could provide a buffer against continued alcohol consumption. Future research examining these mechanisms will help inform prevention efforts moving forward. This research was supported by a grant from the National Cancer Institute (5PO1 CA98262).

0829

DRINKING CONTROL & REASONS FOR DRINKING AS MEDIATORS IN THE DEPRESSION PATHWAY TO DRINKING QUANTITY/FREQUENCY & ALCOHOL-RELATED PROBLEMS

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Lacking control over one's own drinking has been identified as an under-addressed risk factor for problem drinking among emerging adults (Leeman, Patock-Peckham, & Potenza, 2011). Drinking control reflects the ability to stop drinking alcohol at will (Heather, Tebbutt, Mattick, & Zamir, 1993). Most studies regarding drinking control to date have been focused upon externalizing pathways to alcohol-related problems via behavioral under-control constructs such as impulsiveness (Patock-Peckham, King, Morgan-Lopez, Ulloa, Filson Moses, 2011; Patock-Peckham & Morgan-Lopez, 2006). However, to date studies regarding drinking control have been limited concerning internalizing pathways to alcohol-related problems such as through depression. Specifically, we sought to examine if drinking control would serve as a partial mediator in the depression to drinking quantity/frequency and alcohol-related problems pathways while a well-known mediator, pathological reasons for drinking (PRD; i.e. drinking to cope with negative affect), was also included in the model. A structural equation model (SEM) utilizing a latent variable model for depression was examined with 377 college students (184 women/ 193 men) who all reported being drinkers of alcoholic beverages. Tests of structural invariance revealed no variant paths among male and female groups, therefore the base model was retained which did not allow for moderation by gender. Two path mediation tests showed that even with PRD in the model, higher levels of depression were indirectly linked to both increased drinking quantity/frequency and alcohol-related problems through reduced drinking control among both genders. Furthermore, examination of three path mediation tests showed higher levels of depression were indirectly linked to more alcohol-related problems through reduced drinking control and increased drinking quantity/frequency of alcohol use among both genders. These findings highlight the importance of a lack of drinking control (i.e. impaired control) in the depression pathway to alcohol-related problems over and above using alcohol as a means to cope. This adds to the literature by showing that drinking control is an important variable in internalizing as well as previously explored externalizing pathways to alcohol-related problems in emerging adulthood.

0830

THE RELATIONSHIP BETWEEN DEPRESSIVE SYMPTOMS AND ALCOHOL DEMAND

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Demand curve indices of the reinforcing efficacy (RE) of alcohol are associated with various alcohol-related outcomes. Using hypothetical demand curve measures, substance consumption can be plotted across a range of prices, allowing for the measurement of individual differences in RE. These curves provide several measures of the RE of drugs, including maximum consumption at the lowest price (demand intensity), maximum expenditure (O_{max}), price at which demand becomes elastic (P_{max}), the lowest price at which consumption equals zero (breakpoint), and overall price sensitivity (elasticity). Prior studies have demonstrated that greater RE is associated with increased alcohol problems, craving, and poor response to intervention (MacKillop et al., 2010). The purpose of the present study was to extend this research by examining whether individual differences in alcohol demand are related to mood. Research has demonstrated that depression is associated with alcohol dependence (Covey et al., 1993; Grant et al., 2004), increased daily consumption, compulsive drinking (Pedrelli et al., 2011), and predicts poor response to treatment (Kodl et al., 2008). We hypothesized that students with depressive symptoms would have greater demand for alcohol. Participants were 255 college students (73.3% female; M_{age}=20.55, SD=4.30) who were enrolled in a psychology course and reported consuming alcohol in the past 30 days. The sample was ethnically diverse; 60% self-identified as Caucasian, 34% African-American, and 6.4% other. To assess depressive feelings, participants completed the Center for Epidemiologic Studies Depression Scale. Additionally, they completed a modified version of the Alcohol Purchase Task that asked students to report how many drinks they would consume at various prices if they had no next day responsibilities (Skidmore & Murphy, 2011). After controlling for alcohol consumption, gender, and ethnicity, hierarchical regression analyses revealed that higher levels of depression significantly predicted higher demand intensity (R^2=.454, ΔR^2=.03), F(4, 234) = 47.89, p=.001), but was not associated with the other demand indices. These results suggest that young adult heavy drinkers with higher levels of negative affect have increased demand for alcohol, particularly in situations when alcohol is free. The association with RE may be one mechanism by which depression confers risk for substance-related problems and poor response to treatment.

0831

DOES DIFFERENTIAL ENDORSEMENT OF DIMENSIONS OF SEXUAL ORIENTATION RELATE TO PROBLEMATIC DRINKING AND DEPRESSIVE SYMPTOMS?

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The current work proposes that persons who endorse discrepant responses with regard to three dimensions of sexual orientation (self-identification, sexual attractions, sexual behaviors) will report higher levels of problematic alcohol use than those who endorse consistent responses. Data were drawn from a longitudinal study of incoming first-time college students at a large, public university (n = 2,854). Using yearly assessments, individuals were assigned to *a priori* groups according to discrepancies from self-identification categories with regard to sexual attractions and behaviors. Specifically, individuals were coded as incongruent if either their sexual attractions or sexual behaviors did not match the corresponding response category for each respective self-identification category. This time-varying covariate was included in linear growth models to examine associations with alcohol use behaviors (measured biannually) as well as depressive symptomology during the college years. Results show that women who were incongruent with regard to their endorsements of sexual orientation dimensions reported elevated levels of alcohol-related negative consequences, alcohol dependence (AD) symptomology, and depressive symptomology, as well as more frequent heavy episodic drinking and drunkenness at each assessment, compared to their congruent counterparts. Men who endorsed incongruent sexual orientation dimensions reported similar frequencies of heavy episodic drinking and drunkenness, compared to their congruent counterparts, and relatively higher levels of alcohol-related negative consequences and AD symptomology, primarily between their 2nd and 3rd year and at the end of their 4th year of college. Critically, men with an incongruent sexual orientation also reported higher levels of depressive symptomology over time. Findings suggest that individuals, particularly women, who endorse discrepant responses with regard to their self-identification, sexual attractions, and sexual behaviors, may be at heightened risk for depression and problematic alcohol use, compared to those who endorse consistent responses across sexual orientation dimensions. This work may contribute to a better understanding of trajectories of problematic alcohol involvement during sexual identity development.

0832

PRINCIPAL COMPONENT ANALYSIS OF BEHAVIORAL AND SELF-REPORTED IMPULSIVITY IN THE BARCS STUDY

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Behavioral studies suggest that impulsivity is a multidimensional construct comprised of various behaviors affected by several underlying neural systems. Debate continues as to which domains best capture aspects of impulsive behavior and whether behavioral and self-report impulsivity measures assess the same domains. Our objectives were to: (a) characterize multidimensional aspects of impulsivity; (b) assess whether behavioral and self-report aspects of impulsivity separated into distinct factor components; and (c) observe differences in impulsivity factor scores between college students meeting criteria for alcohol/substance use disorders and psychiatric diagnosis, such as major depression and anxiety, when compared to respective healthy controls. We examined 889 college freshmen (485 female) participating in the NIAAA-funded Brain and Alcohol Research in College Students (BARCS) study. We obtained self-reported trait impulsivity with the Zuckerman Sensation Seeking Scale, version 5 (SSS); Behavioral Inhibition/Activation System (BIS/BAS); Barratt Impulsiveness Scale (BIS-11); sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ); and the Padua Inventory. Behavioral impulsivity was assessed from the Balloon Analog Risk Task (BART). Mental diagnoses and alcohol/substance use disorder criterion were obtained from the Mini-International Neuropsychiatric Interview (MINI). Exploratory factor analysis using the Anderson-Rubin method and varimax rotation was conducted. Finally, ANOVAs were conducted to assess factor score differences between diagnosis groups. Four primary factor components were extracted, accounting for approximately 90% of the variance in impulsivity scores: SSS, BIS-11, and BIS/BAS loaded onto ''Self-Reported Impulsivity''; SPSRP loaded onto ''Self-Reported Reward/Punishment''; Padua loaded onto ''Self-Reported Compulsivity''; and BART loaded onto ''Behavioral Risk-Taking''. Significant differences ($p < 0.05$) were observed for one or more factors between each diagnostic group and its corresponding controls. These preliminary findings suggest (a) that the multidimensional nature of impulsivity in college-aged individuals can be captured through four components; (b) there is overlap between self-reported impulsivity measures, (hence these measures may be capturing the same domain); and (c) impulsivity components differ between psychiatric diagnostic groups and controls in a teenage sample.

0833

THE ROLE OF IMPULSIVITY ON ALCOHOL-TOBACCO USE AND CO-USE IN COLLEGE STUDENTS WITH RECENT SMOKING INITIATION

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Alcohol and tobacco use are the leading causes of preventable mortality and they are responsible for approximately 500,000 deaths each year and the economic and societal costs related to these issues are overwhelming. Previous research using large-scale epidemiological samples as well as diverse clinical samples have shown high prevalence rates between alcohol and tobacco use and problems and alcohol-tobacco co-use may facilitate progression toward dependence on both substances.

The current study uses a sample of undergraduates who were recruited during freshman year and initiated smoking within 12 months following study enrollment (n=56; 47% male). Baseline measures included the UPPS Impulsiveness Questionnaire and frequency of days using alcohol and tobacco were assessed via timeline follow-back at the quarterly followup during which smoking was initiated (Time 1) and the followup 3 months later (Time 2). A series of longitudinal Poisson models examined the relations between the four subscales of impulsivity on frequency of smoking, drinking, and co-use.

Drinking and smoking frequency did not change significantly across time, whereas co-use frequency increased from Time 1 to Time 2. Drinking frequency increased from Time 1 to Time 2 for those individuals high on sensation-seeking. Lack of premeditation predicted greater smoking frequency, and smoking frequency nearly tripled over time for individuals reporting high levels of urgency. Sensation-seeking, as well as earlier onset of smoking initiation, predicted greater frequency of alcohol-tobacco co-use three months following initiation of smoking.

Overall, these findings provide preliminary evidence for the unique impact of impulsivity on alcohol-tobacco co-use in young adults who recently initiated smoking. Such findings may help inform early intervention efforts to limit the progression from initiation and early use to dependence levels for both alcohol and tobacco.

0834

THE MOTIVATION FOR ALCOHOL REWARD: PREDICTORS OF PROGRESSIVE-RATIO INTRAVENOUS (IV) ALCOHOL SELF-ADMINISTRATION IN SOCIAL DRINKERS

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Computer-Assisted Self-infusion of Ethanol (CASE) is a method of IV alcohol administration that allows individuals to self-administer alcohol in a laboratory setting, while controlling the breath alcohol concentration (BrAC) using a physiologically-based pharmacokinetic (PBPK) model-based algorithm. The objective of this study was to examine alcohol intake behavior and the motivation for reward using subjective measures of alcohol effects and personality measures in a progressive ratio (PR) schedule of IV alcohol self-administration in social drinkers. Healthy social drinkers (N=28) underwent a PR self-administration session which consisted of a 25-min priming phase where subjects were prompted to push a button to receive individually standardized alcohol infusions, followed by a 125-min PR phase during which they had to push a button an increasing number of times for each subsequent infusion. Self-administration measures included number of button presses (NBP), peak (PEAK) and average (AVG) BrAC, time to peak BrAC (TP), total rewards earned (TRE), total ethanol (ETOH) and average button-press rate (ABPR). Subjective measures, obtained repeatedly during the study session, included Drug Effects Questionnaire (DEQ), Alcohol Urge Questionnaire (AUQ) and Biphasic Alcohol Effects Scale (BAES). Recent drinking history was measured using Time-Line Follow Back (TLFB) and personality using NEO-PI-R and Barratt's Impulsivity Scale (BIS). Results indicated that TRE was significantly associated with TLFB drinking days. AVG and PEAK were negatively associated with BIS measures of attention, attentional impulsivity and cognitive instability. The NEO openness facet was negatively correlated with PEAK, AVG, TRE and total ETOH. Maximum scores for DEQ measures of "feeling" and "liking" drug effects as well as "high" and "intoxication" were positively associated with NBP, while the ABPR was associated with feelings of "high" and "intoxication". AUQ maximum measures were significantly associated with total ETOH and NBP. BAES sedation measure after priming was strongly associated with PEAK, AVG, and TRE. PR measures were significantly associated with measures of recent drinking history, impulsivity and the NEO openness personality trait. Subjective measures of alcohol effects and urges after priming were associated with alcohol intake. These results demonstrate that the PR paradigm is sensitive to the rewarding and motivational properties of alcohol in social drinkers.

0835

TRAITS OF PEOPLE DIFFER BY THEIR PERFORMANCE ON FREE-ACCESS AND PROGRESSIVE-WORK ALCOHOL SELF ADMINISTRATION PARADIGMS

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People can express their enjoyment of drinking by the preferred level of breath alcohol concentration (BrAC) they establish in a free-access (FA) alcohol self-administration paradigm. They can also express their desire for alcohol compared to money by the amount of work they are willing to perform to achieve that preferred level in a subsequent progressive-work (PW) alcohol self-administration paradigm. Traits of interest are gender, personal recent drinking history (RDH), family history of alcoholism (FHA) and personality indices. We tested 40 young adult non-dependent drinkers in both FA and PW paradigms using the Computer-assisted Alcohol Infusion System (CAIS) that eliminates the substantial variability in the trajectory of BrAC when alcohol rewards are ingested. A cognitive task that requires the constant attention of the subject to perform correctly was employed in the PW paradigm. Preliminary analysis of the current sample population (eventually 60) showed that, compared to women, men reach higher peak BrAC and preferred levels ($p<.025$) in the FA paradigm, but work less for alcohol ($p<.04$), preferring to work for money (at $.049 per reward) in the PW paradigm. Subjects with a positive FHA, compared to those with none, expressed similar preferred levels in the FA paradigm, but worked harder ($P<.04$) and longer for alcohol ($P<.03$), and less ($p<.01$) and for less time ($p<.03$) for money, in the PW paradigm. When the sample was divided into quadrants by performing median splits on the FA preferred level and the PW cumulative work for ethanol, several traits showed interesting significant differences (all $p<.05$ on 2-tailed student T tests): people who both ENJOY and WANT alcohol (high preferred level, high cumulative work for alcohol) have a greater personal drinking history (30 day Time Line FollowBack) than those who are both INDIFFERENT and who FOREGO work (low preferred level, low cumulative work for alcohol); people who ENJOY alcohol, but FOREGO working for it, have fewer externalizing behaviors on the SSAGA than others (they are also the only group to load negatively on a principal components analysis factor that emphasizes Zuckerman Thrill-Seeking and Venturesomeness); subjects who FOREGO work for alcohol work hard for money. We conclude that CAIS alcohol self-administration paradigms are useful for phenotyping non-dependent drinkers. Supported by U01 AA017900 and P60 AA07611.

0836

ALCOHOL AND CONTEXT EFFECTS ON RISK TAKING USING THE BALLOON ANALOAGUE RISK TASK BART

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Prior studies have found that alcohol consumption leads to difficulty inhibiting behavioral responses, and engagement in a range of behavioral risks (e.g. aggression, sexual behavior). However, lab-based studies of risk taking often rely on the assessment of intentions or responses to hypothetical risk scenarios (e.g. vignettes of sexual situations). Thus, there is limited research examining alcohol effects on actual behavioral indices of risk-taking. The Balloon Analogue Risk Task (BART: Lejuez et al., 2002), provides a means to more directly study these effects. One recent study found that BART performance in early trials (but not later trials) was impaired by alcohol relative to placebo (Euser et al., 2011), whereas another recent study failed to find significant alcohol effects (Ravenzwaaij et al., 2011). Given the conflicting findings, the current study examined alcohol effects on BART performance using a larger sample (N = 115) of emerging adults (mean age = 22.81 (SD = 2.73), 32.5% female), while also examining the impact of the physical context in which drinking occurred. Although prior studies have demonstrated significant effects of physical context on alcohol expectancies and response latencies to expectancy related content (Wall et al., 2001), they have not examined the effects of context on behavioral tasks like the BART. Participants were assigned to one of four conditions, crossing beverage content (alcohol targeting a BrAC of .08 g% or placebo) and physical context (simulated bar or experimental lab). Results of ANOVAs indicated that participants consuming alcohol did not differ from participants receiving placebo on either the average number of pumps, or the number of explosions (p values > .94). There were, however, effects of context on both outcomes, with participants in the bar lab (regardless of beverage condition) demonstrating greater risk taking than participants in the experimental lab ($p = .04$ for pumps, $p = .006$ for explosions). No interactions between beverage and context were found. These results suggest that certain drinking contexts (e.g. bars, parties) may facilitate risk taking more so than the pharmacological alcohol effects. The findings have important implications for understanding risk-taking during developmental periods of high risk (e.g. adolescence and emerging adulthood), as young people are more likely to find themselves in drinking contexts that are conducive to risk behavior (e.g. bars and parties).

0837

ALCOHOL AND GROUP FORMATION: A MULTIMODAL INVESTIGATION OF THE EFFECTS OF ALCOHOL ON EMOTION AND SOCIAL BONDING

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Forming social bonds is a fundamental human motivation, and people value behaviors that facilitate interpersonal relationships. Given the widespread use of alcohol in social situations, it is notable that alcohol researchers generally have neglected the effects of alcohol on social bonding. Drinkers expect alcohol to enhance their social interactions and these beliefs predict actual alcohol use, yet, surprisingly, little research has examined alcohol consumption in social settings. The relative neglect of social context in alcohol research may help to explain the equivocal findings regarding alcohol's ability to relieve negative affect and enhance positive affect. This study integrates research on emotion and small groups to address a fundamental question facing alcohol researchers: What are the specific mechanisms by which drinking is reinforcing? In one of the largest alcohol administration studies yet conducted, we employed a novel group formation paradigm to evaluate the socio-emotional effects of alcohol. Method: Social drinkers (n= 720) were assembled into 240 3-person groups and randomly assigned to drink over 36-min a moderate dose of alcohol (males: 0.82 g/kg; females: 0.74 g/kg), a placebo, or a non-alcohol control drink. Their social interaction was video-recorded, and the duration and sequence of facial expressions were systematically coded using the Facial Action Coding System (Ekman et al. 2002). After drinking, participants completed the Perceived Group Reinforcement Scale.
Results: Using multi-level modeling that accounted for the nested structure of the group data, we found that alcohol consumption enhanced social experience at both an individual-level (e.g., increased the duration of positive affect-related facial expressions) and a group-level (e.g., coordination of smiling), and elevated self-reported bonding.
Discussion: During group formation, alcohol-consuming groups experienced heightened social bonding compared to groups consuming non-alcoholic beverages. This paradigm provides a group-level perspective on the hedonic effects of alcohol, which differs from past work relying on the individual as the unit of analysis. Through transdisciplinary methods integrating social psychology, emotion science, and addiction theory, we demonstrated the socially reinforcing effects of alcohol during group formation in men and women.
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0838

INTEGRATING LABORATORY AND BRIEF INTERVENTION METHODS TO ENHANCE BEHAVIOR CHANGE IN NON TREATMENT-SEEKING BINGE DRINKERS WHO SMOKE: A PILOT STUDY

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Alcohol acutely increases smoking urge and behavior, and young adult hazardous drinkers have high rates of smoking co-use, often with little motivation to change. While brief interventions have been developed for at-risk college drinkers, there is little research on post-college heavy drinkers who are co-users of alcohol and tobacco. Further, novel translational approaches are needed to improve brief intervention outcomes and target those most likely to respond. Thus, we conducted a pilot study in fifteen heavy-drinking nondependent smokers (8 men) in order to establish feasibility of combining laboratory alcohol challenge and brief intervention modalities. Participants attended a single-blinded beverage administration session (0.8g/kg alcohol) and then were randomized to attend two feedback sessions of either a brief alcohol-smoking feedback intervention (BASFI) or an attention control intervention (ACI). BASFI was recently developed by our group and included information on participants' drinking and smoking compared to age-relevant norms, personal feedback on alcohol response, and goal-setting to reduce alcohol harm, if appropriate. ACI was similar in format but focused on nutrition and healthy eating. The sample's average age was 24.2 ±2.6 SD yrs with an average AUDIT score of 14.8 ±3.9, 9.8 ±4.5 heavy drinking days, 23.8 ±5.5 cigarette smoking days, and 15.3 ±5.6 co-use days in the past month. Stage of change assessment revealed more interest in changing smoking than drinking (57% vs. 14% action stage). Feasibility was established with 93% of enrollees attending all study visits with 100% retention for one-month follow-up. As expected, alcohol increased positive-like subjective effects (stimulation, liking, wanting) and smoking urge. Follow-up TLFB results revealed that BASFI produced more behavior change than ACI, with reductions in drinks per drinking day (29% BASFI vs. +5% ACI), heavy drinking days (−53% vs. −25%, respectively), smoking days (−37% vs. +3%) and co-use days (−54% vs. −8%). Effect sizes (Cohen's d) ranged from 0.48 to 1.32 (>medium effect). Moreover, greater positive-like alcohol effects in the lab predicted larger drinking reductions in BASFI (rs=+.29-.66). In sum, results of this pilot study were promising: while larger studies are needed, young adult hazardous drinkers may be particularly responsive to targeted interventions using personalized alcohol challenge feedback to motivate change.

0839

BOYS WILL BE BOYS: INCREASES IN SENSATION SEEKING IN EARLY ADOLESCENCE MAY BE GENDER SPECIFIC

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Although researchers debate whether basic temperament and personality change over time, research indicates that some personality characteristics may become amplified during adolescence. While sensation seeking (SS) has demonstrated an association with emergent alcohol use in adolescence (e.g., Sher et al., 2000), little is known about individual change in (particularly increases in) SS and risk-taking propensity in early adolescence. Previous longitudinal studies examining sensation seeking in early adolescence had few assessment points or used very few items to measure the construct. Extending prior research, the current study employed latent growth curve analysis to model systematic change over time in SS in a sample of 204 individuals ranging from 9–13 years old enrolled in a 5-year longitudinal study. Unlike more traditional methods (e.g., repeated measures ANOVA) which focus on average change over time, the latent growth curve approach, by including random coefficients, explicitly models individual change over time. SS was assessed using the Sensation Seeking Scale for Children (SSSC; Russo et al., 1994), a 26-item scale measuring diverse aspects of SS. Preliminary analyses of the first two years of collected data (5 assessment points) for all participants revealed both a significant intercept and slope in SS, indicating that the construct is increasing over time for these individuals. Additional latent growth curve analyses accounting for gender revealed that the boys in the study were significantly higher in SS than the girls at baseline, and only the boys exhibited a significant increase in SS over time. These results suggest that within the developmental time period assessed by the current study, SS appears to remain stable over time for girls, while boys are initially higher in SS than girls *and* increase significantly in this propensity over time. While the data collection is not complete for the 5-year longitudinal study, these preliminary findings point to a critical need to move beyond treating sensation seeking and other risk variables for emergent alcohol use as static risk factors and start considering these variables as dynamic constructs within a developmental framework. Attaining more knowledge about dynamic changes in risk variables over time will allow researchers to better understand risk factors for increases in drinking during adolescence.

0840

SEXUAL ASSAULT, DRINKING NORMS, AND DRINKING BEHAVIOR IN LESBIAN AND BISEXUAL COLLEGE WOMEN

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Sexual assault has been associated with increased alcohol use and problems in women. One mechanism proposed is that sexual assault history leads to higher coping drinking motives thereby leading to more problematic drinking behavior. Perceived descriptive drinking norms, defined as perceptions of drinking behavior of your peer group, have also been associated with alcohol use and problems. Individuals tend to perceive that others drink more than they actually do, and the magnitude of this discrepancy predicts higher individual use and consequences. However no research has examined the role of perceived descriptive drinking norms as a mediator of the sexual assault – alcohol use relationship. To examine if descriptive drinking norms mediates the relationship between sexual assault history and alcohol use, we assessed a sample that is at high risk for drinking and sexual assault: lesbian and bisexual college women. A random sample of lesbian and bisexual women aged 18 to 25 were recruited through advertisements placed on the social networking website Facebook. Individuals were invited to take part in an initial 20-minute Web-based screening survey for a national study on the sexual behavior or lesbian and bisexual women. 1,090 completed the baseline survey. 59% of the sample indicated that they identified as Bisexual, with 41% identifying as Lesbian. Participants completed questionnaires assessing history of CSA and ASA, drinking norms for lesbian and bisexual women, and their drinking behaviors. A structural equation model supported the hypotheses: (a) CSA (child sexual abuse) predicted intoxicated ASA (adult sexual assault) (b) both CSA and intoxicated ASA predicted drinking norms and drinking behavior and (c) drinking norms partially mediated the relationship between drinking sexual assault history and drinking behavior. The model suggests that descriptive drinking norms may be a mechanism through which sexual assault is related to drinking behavior.

0841

U.S. TRENDS IN PERCEPTIONS OF SITUATIONAL NORMS FOR DRINKING AND INTOXICATION OVER THREE DECADES BASED ON SEVEN NATIONAL ALCOHOL SURVEYS

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Objective: Individuals' perceptions of social acceptability of drinking and intoxication have been viewed as important mediators of a nation or a group's drinking patterns. We studied for the last 30 years how the U.S. population's perceptions about injunctive drinking norms in four situations changed over time and consider how these trends may be reflective of shifts in US drinking culture, alcohol-related policies, and social discourse about situations in which drinking or intoxication is permissible.
Methods: Data come from 7 National Alcohol Surveys of US adults (age 18+) conducted by the Alcohol Research Group at approximately 5-year intervals from 1979 through 2010 (total N = 36,476; range of survey Ns: 1,723 to 7,427; mean N = 5,211 cases). Four identical measures asked how much drinking was acceptable: When with friends at home, at someone else's party, for a man at a bar with friends and for a woman at a bar with friends. Responses were none, some alcohol but not enough to feel the effects, enough to feel the effects but not be drunk, enough to feel drunk. Analyses for the population used Chi-square and logistic regression, with results weighted.
Results: Intoxication (feeling effects or feeling drunk) for men at bars has become less acceptable (37.7% to 31.3%, $p < .001$) while for women at bars it has become slightly more acceptable (24.8% to 27.3% $p < .001$), remaining below men's throughout but showing a marked gender convergence. Intoxication at other people's parties has become somewhat less acceptable over time (32.3% to 28.6%; $p < .01$). Only the situational norms for drinking with friends at home show considerable loosening, the population percentage who accept being intoxicated in this private setting almost doubling from 1979 to 2010 (19.6% to 39.0%, $p << .001$).
Conclusions: Study findings make clear that the percentages endorsing intoxication in specific social-situational contexts during the past 3 decades have fluctuated quite widely with major changes in the 1980s, some instability in the 90s and a steady rise in the new millennium, especially in endorsing alcohol intoxication as acceptable with one's friends at home. We discuss factors affecting these long-term shifts in US drinking culture, especially the alcohol policy environment and specific demographic and birth cohort subgroup norms. Supported by NIAAA Center grant P50 AA005595.

0842

CULTURAL NORMS REGARDING ALCOHOL USE AMONG TWO GENERATIONS OF CAMBODIAN AMERICANS

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Our purpose was to assess cultural norms regarding alcohol use and misuse among first- and second-generation Cambodian Americans. Previous ethnographic and mixed methods research by the team had indicated problematic patterns of alcohol use and misuse among Cambodians in Northern California including heavy drinking among youth and increasing alcohol use among women. Prior studies have linked substance abuse among Cambodians with poor mental health stemming from war and refugee traumas together with poor living conditions in the U.S. During a two-year community-based participatory research project, in extended focus group discussions a group of Cambodian community women identified alcohol use as a key health issue in their community. The group associated problematic drinking with Cambodian cultural norms. We fielded a brief anonymous survey at a Cambodian New Year celebration, the largest gathering of Cambodians in Oakland (attendance estimated at 400). The survey included items recording agreement with a set of normative statements on alcohol use. The items were developed collaboratively by the community work group and researchers. The survey was available in either English or Khmer (Cambodian language). All protocols were IRB approved. The 172 Cambodians who responded to the survey included females (63%) as well as males, and second-generation youth and young adults (aged 18–24, 30%) as well as first-generation adults (aged 25–59, 58%) and seniors (aged 60–84, 12%); 44% of respondents responded to the Khmer version. Results were analyzed in SPSS. Respondents overwhelmingly disapproved of kids drinking (91%) and drunkenness by youth (84%) and 81% of respondents disagreed that Cambodians drink more than other ethnic groups. However, younger respondents were significantly more likely than older respondents to support occasional male drunkenness (p=.040). There was also a reasonably strong correlation (p=.071) between younger age and support of occasional female drunkenness. Males were significantly more likely than females to support occasional drunkenness by both men and women (p=.025 and p=.053, respectively). The results provide minimal support of associations between cultural norms and problematic drinking by U.S. Cambodians, but stronger evidence of such norms among younger and male community members. In addition to other social-environmental influences, alcohol prevention and treatment programs for U.S. Cambodians should address drinking norms.

0843

DIMENSIONS OF ACCULTURATION AND ACCULTURATIVE STRESS: ASSOCIATIONS WITH HAZARDOUS ALCOHOL USE AMONG ASIAN AMERICAN COLLEGE STUDENTS

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We examined a bidimensional model of acculturation (which includes both heritage and U.S. practices, identifications, and values; Schwartz, Unger, Zamboanga, & Szapocnik, 2010) and its association with dimensions of acculturative stress (including heritage and English language competency pressures, pressures against acculturation, and pressures to acculturate) and hazardous alcohol use. The data analytic sample consisted of 1,058 Asian American students (M=19.80, SD=2.14; 34% immigrants, 66% U.S.-born) from 30 colleges and universities across the U.S. Participants completed online measures of acculturation, acculturative stress, and hazardous alcohol use. Results showed that none of the acculturation dimensions were directly associated with hazardous alcohol use. However, indirect relationships emerged through increased pressures for English language competency, and these mediated patterns were different for two dimensions of acculturation. In particular, increased involvement in American practices was associated with decreased pressures for English language competency, whereas increased involvement in heritage practices was associated with more pressures for English language competency, and such pressure in turn was related to higher levels of hazardous alcohol use. The overall patterns of associations observed in this study were generally consistent across immigrant and U.S.-born Asian American students. Taken together, these results help broaden researchers' understanding of the mechanisms that underlie the complex association between acculturation and hazardous alcohol use among Asian American college students. The present findings also have practical implications in that practitioners might consider including multidimensional measures of acculturation and acculturative stress in their assessment of hazardous alcohol use in this student population.

0844

ACCULTURATION, PEER DRINKING, PROTECTIVE BEHAVIORS, AND ALCOHOL-RELATED PROBLEMS IN ASIAN AND PACIFIC ISLANDER AMERICAN COLLEGE STUDENTS: A PATH MODEL

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Asian and Pacific Islander American (APIA) students represent a growing presence in U.S. colleges, with increasing rates of problematic drinking. Acculturation and peer drinking have been identified as predictors of alcohol use among APIA adolescents and young adults. However, less is known about how these factors relate to experiencing alcohol-related problems. Examining these factors in relation to alcohol protective behavioral strategies (PBS) may provide further insight into the drinking behavior and subsequent consequences among this group. Practice of PBS has emerged as a predictor of reduced drinking and fewer alcohol-related consequences in U.S. college students. The current study assessed relationships between acculturation, peer drinking, and use of alcohol protective behavioral strategies as potential pathways to alcohol use and related problems among APIA college students.
Participants were recruited from undergraduate psychology courses, and reported consuming at least 1 alcoholic drink per week (N = 449). Students completed a battery of online measures on acculturation, weekly drinking quantity, estimated peer drinking, alcohol related problems and three subscales of the Protective Behavioral Strategies Scale (Martens et al., 2005): stopping/limiting drinking, manner of drinking, and serious harm reduction. Relationships between variables were tested using path analysis with manifest variables. Several key findings emerged: (1) greater weekly drinking predicted greater alcohol-related problems, $\beta = .51$, $p < .05$; (2) greater peer drinking was related to increased weekly drinking, $\beta = .43$, $p < .05$; (3) higher acculturation scores, i.e. orientation towards U.S. culture, had a positive relationship with use of harm reduction strategies, e.g. using a designated driver, $\beta = .16$, $p < .05$, and an inverse relationship with drinking moderation strategies; e.g. avoiding shots of liquor, $\beta = -.12$, $p < .05$; and (4) use of drinking moderation strategies was related to decreased weekly drinking, $\beta = -.40$, $p < .05$, which in turn would predict decreased alcohol-related problems. Fit indices indicated good model fit, $\chi^2(df = 5) = 9.29$, $p = .43$; $RMSEA = .05$, $CFI = 1.00$. Similar patterns emerged when testing the model in specific APIA subgroups. The results provide further insight into social and cultural factors in drinking behavior among APIA students, and may have implications for the development of culturally sensitive treatment and prevention programs.

0845

ALCOHOL CONSUMPTION, COPING, AND SEXUAL BEHAVIORS AMONG UNIVERSITY MEN IN VIET NAM: IMPLICATIONS FOR INTERVENTION

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Recent data suggest that rapid socio-economic changes in Asia are precipitating changes in social behaviors of adolescents and emergent adults. Limited data are available regarding alcohol consumption patterns among university populations. Attendance at university is associated with increasingly independent living conditions and greater autonomy from family. In Viet Nam, university is also associated high parental expectations regarding both conduct and academic achievement. The current project was designed to assess mediating and moderating factors in relation to drinking patterns and the relationship between alcohol consumption and risky sexual behaviors among 18 to 24 year old men in Khanh Hoa Province Viet Nam. A randomly selected sample of 500 students from a population of 2,664 freshmen and sophomore men at a mid-sized university were invited to participate. A longitudinal survey was conducted at three data collection points at six-month intervals. Preliminary analyses are presented. At twelve-month data collection, retention was over 91%. Over 99% reported ever consuming alcohol at baseline. More than 56% reported intoxication in the past six months. Mean drinks per episode was 2.0 (range 0.25 to 13) and days drinking in past 30-days was 2.9 (range 1 to 23). Respondents' reporting ever engaging in vaginal sex was 22% at baseline and 29% at 12 months. Forty-eight percent of sexually active respondents report using condoms less than half the time. Two separate linear regression analyses were conducted using age, Epidemiological Studies Depression scale scores, Perceived Stress scores and Adolescent Coping for Problem Experiences subscale scores (sub-scales: self-reliance, social support, venting, avoidance) to predict the number of drinking days and number of drinks respectively. Self-reliant coping was negatively associated with drinks per episode ($t = -3.739$; $p<.001$) and days drinking ($t = -3.234$; $p<.01$). Avoidance coping was positively associated with drinks per episode ($t=5.743$; $p<.001$) and days drinking ($t=5.354$; $p<.001$). Multinomial regression analysis indicates levels of alcohol consumption and coping mechanisms are strongly associated with engagement in vaginal sex at 12 months. Findings indicate a need for recognizing mediating psychosocial factors associated with levels of alcohol consumption both in terms of interventions for alcohol risk reduction and reproductive health education in university settings in Viet Nam.

0846

INVESTIGATING FACTORS UNDERLYING RACIAL/ETHNIC DIFFERENCES IN COLLEGE STUDENT DRINKING

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Racial and ethnic variation in alcohol consumption and associated problems exists; yet race is a social construct that confers no inherent meaning and is unlikely to be directly responsible for these differences. Because of this, researchers must go beyond attributing differences in alcohol use to an individual's race or ethnicity and consider what factors contribute to differential mean levels of alcohol use and consequences between groups. This study examines such factors (spirituality/religiosity, perceived discrimination, and cultural values) and their relation to alcohol use among a diverse group of college students attending a large Southwestern university. The 167 participants (54% female) self-identified as non-Hispanic White (NHW; $n = 78$), Hispanic/New Mexican ($n = 44$), Hispanic/Mexican ($n = 32$), and American Indian/Alaska Native ($n = 13$). Participants were recruited from undergraduate psychology courses and completed questionnaires at a single time point. Relevant measures included: the machismo, familism, and filial piety subscales of the Multiethnic Cultural Values Scale (MECVS; Unger et al., 2002), the perceived discrimination subscale of the Scale of Ethnic Experience (SEE; Malcarne et al., 2006), two items inquiring about the importance of religion/spirituality, and the Graduated-Frequency past-year alcohol consumption measure (GF; Clark & Midanik, 1982). No differences were found in GF total by race/ethnicity. Regarding cultural values, both groups of Hispanic students reported significantly higher levels of filial piety than NHW students, with no differences in machismo or familism between the four groups. Machismo was significantly associated with greater alcohol consumption. NHW participants rated religion and spirituality as significantly less important than did the Hispanic students; religion and spirituality were not related to past-year alcohol consumption. SEE perceived discrimination was significantly lower for NHW students compared to all other groups; perceived discrimination was unrelated to GF total. These findings highlight the complexity of racial/ethnic identification and suggest potential factors, such as machismo, that warrant more detailed exploration in relation to alcohol use. In contrast to other studies, alcohol consumption did not vary across racial/ethnic groups, which could be a function of the small sample size. Supported by 1T32AA018108-01A1.

0847

ALCOHOL RISK BEHAVIORS AMONG HISPANIC EMERGING ADULTS: THE ROLE OF ACCULTURATION CATEGORIES AND ALCOHOL EXPECTANCIES

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Acculturation is a multidimensional process whereby identifications,values,and practices change through contact with a new culture.Acculturation subsumes both receiving-culture (American) acquisition and heritage-culture (Hispanic) retention.Acculturation categories represent permutations of American and Hispanic culture:Biculturalism corresponds to retention of Hispanic and American culture, assimilation indicates rejection of Hispanic culture and retention of American culture and separation implies retention of Hispanic culture and rejection of American culture.Among Hispanics, acculturation has been shown to play an important role in determining vulnerability to alcohol risks behavior(ARB). Similarly, alcohol expectancies (AEs) defined as anticipated beliefs about the effects of alcohol use and their valuations-individual evaluation (good or bad) regarding an effect associated with drinking have been shown to explain the mechanism by which distal processes like acculturation is associated with ARB.The current study used an integrative approach to examine the mediating role of AEs and valuations in the association between acculturation categories and ARB.The data consisted of 1,527 Hispanic emerging adults.Participants completed measures of Hispanic and American cultural practices;AEs and valuations; and five ARB.Zero-inflated Poisson modeling was used to test the hypothesis that AEs and their valuations would mediate the relationship between acculturation categories and ARB.Results indicated that acculturation categories were differentially associated with ARB. Separated bicultural and low bicultural categories were inversely related to all of the ARB except for riding with a drunk driver.Negative expectancy valuations were positively associated with binge drinking and drunk driving.Negative expectancies were negatively associated with binge drinking, drunk driving and riding with a drunk driver.With the exception of sexual activity under the influence of alcohol, the associations between acculturation categories and ARB were partially mediated by positive alcohol expectancies.The current findings support the notion that positive alcohol expectancies serve as a ''common pathway'' through which distal processes like acculturation categories influence ARB among Hispanic emerging adults.These findings are informative for preventive interventions aimed at reducing ARB among Hispanic emerging adults.

0848

ALCOHOL-RELATED PROBLEMS AND PROTECTIONS AMONG MALE AND FEMALE HIGH SCHOOL AND UNIVERSITY STUDENTS IN MEXICO

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Purpose: To examine alcohol use, age of onset and alcohol-related problems among high school and university students in Mexico.
Methods: From 2008 surveys administered to entering high school and first year students in the National Autonomous University of Mexico (UNAM) system 14,974 10^{th} grade students and 21,546 first year university students were identified as ever drinkers. Multiple logistic regression models examined associations between potential risk and protective factors and alcohol related problems.
Results: Male and female students showed similar age of onset patterns. Among male and female high school students, 70% reported drinking onset by age 15, while among those entering college, 43% reported age of onset by age 15. Males were more likely to report alcohol related problems than females. High school students ages 15 and 16 were more likely to have problems than 14 year olds and university students aged 18–21 were more likely to have problems than 17 year olds . Compared with those who began drinking at age14 or older, male and female high school students who began drinking at ages 10–13 had greater odds of experiencing problems, e.g., onset age 12 v 14 AOR 1.8 (1.6,2.0). Similarly, compared with those who began drinking at age 15 or older, male and female university students who began drinking at ages 10–14 had greater odds of experiencing problems (e.g., onset age 13 v 15 AOR 2.0 (1.7,2.2). Although high school students who drank liquor consistently had greater odds of alcohol-related problems compared to beer drinkers. AOR 1.4 (1.3,1.5), there was little difference between liquor and beer drinkers in the college sample. Both high school and college students who reported low parental monitoring had greater odds of experiencing alcohol-related problems than those who reported high parental monitoring, high school AOR 2.5 (2.3,2.7) and college AOR 2.5 (2.3,2.8).
Conclusion: Male and female Mexican students report early age alcohol use. Studies are needed to determine risk and protective factors for alcohol-related problems among Mexican students including whether type of alcohol alone or in combination with other factors heightens risk, and whether protective factors including culture specific factors protect against problems.

0849

PROTECTIVE CULTURAL FACTORS AND ALCOHOL USE AMONG MALE AND FEMALE STUDENTS IN MEXICO

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Purpose: To investigate patterns of alcohol use and cultural attributes that may modify or prevent the likelihood of harmful drinking among students in Mexico City.
Methods: We conducted 120 qualitative interviews of heavy, regular, occasional and non drinking first year university students in Mexico City. The interview protocol was developed in collaboration with Mexican collaborators and interviews were conducted by Mexican university students.
Results: Both male and female first year university students reported first drink by age16. Male and female heavy drinkers and non drinkers reported different drinking practices than their parents while occasional and regular drinkers described similar drinking patterns as their parents. Heavy drinkers discussed reducing their alcohol use because of parents' concerns about their drinking. Occasional, regular and non drinkers referred to traditional values about drinking as impacting their alcohol use, and all the students acknowledged prescriptive Mexican drinking norms including appropriate gender and family roles.
Conclusion: Results of this qualitative study indicate that male and female Mexican students initiate early age alcohol use but parents and traditional values may protect against misuse. Studies are needed to determine other culture specific norms that may protect against harmful drinking among Mexican and Mexican American young people in order to provideguidelines for culturally relevant prevention programs for Mexican, Mexican American and other young people in the U.S.

0850

THE PROTECTIVE EFFECTS OF ETHNIC IDENTIFICATION ON ALCOHOL INVOLVEMENT IN A SAMPLE OF ALASKA NATIVE AND NON-NATIVE COLLEGE STUDENTS

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Alcohol use disorders represent a significant minority health disparity, with indigenous populations suffering at disproportionate rates. Recently, ethnic self-identification has been the subject of much health disparities research, as the ways in which people self-identify may lead to differences in health outcomes. However, little is known about the effects of ethnic identification on alcohol involvement. This exploratory study examined data from Alaska Native (n = 51) and non-Native (n = 247) students at a minority-serving university in Alaska. Participants completed a questionnaire including items about race, alcohol use, ethnic identity (Multigroup Ethnic Identity Measure; MEIM), drinking motives (Drinking Motives Questionnaire; DMQ-R), consequences (Young Adult Alcohol Consequences Questionnaire; YAACQ), and alcohol dependence (Short Alcohol Dependence Data Questionnaire; SADD). In this sample, Alaska Native and non-Native college students had equal rates of lifetime and past 30-day alcohol and drug use, and there were no significant between-group differences in frequency of binge drinking or number of drinks consumed on a typical drinking day. Although there were age and gender effects, ethnicity did not predict alcohol outcomes. Ethnic identity, however, appeared to be protective. Controlling for age, gender, past 30-day alcohol use, and ethnicity, greater total MEIM scores predicted less drinking to cope (β = -.15, p < .05; full model R^2 = .133), less alcohol dependence (β = -.15, p < .05; full model R^2 = .154), and fewer alcohol-related consequences (β = -.22, p < .01; full model R^2 = .099), regardless of ethnicity. Similarly, high scores on the MEIM Ethnic Identity Achievement subscale predicted lower drinking to cope (β = -.17, p < .05), less drinking for conformity reasons (β = -.14, p < .05), lower alcohol dependence (β = -.17, p < .05), and less alcohol-related consequences (β = -.21, p < .01), regardless of ethnicity. Finally, the MEIM Ethnic Affirmation and Belonging subscale predicted less drinking to cope (β = -.19, p < .01), regardless of ethnicity. These findings suggest that having a strong ethnic identity is protective for students of all ethnic backgrounds. These data may be especially relevant for the development of prevention efforts and strength-based interventions for minority student drinkers. Further, the findings stress the need to evaluate ethnic identity as well as race in minority health disparities research.

0851

NOT ACCORDING TO PLAN: DISCREPANCIES BETWEEN ANTICIPATED AND ACTUAL SPRING BREAK DRINKING

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Event-specific drinking has been the focus of recent research and media attention, suggesting there are known times for increased risk, such as college Spring Break (SB). Behavioral intentions are key components of many theories of health behaviors and are often highly correlated with actual behavior. Research for other high-risk drinking events such as 21st birthdays has also documented that there are several factors that may influence that relationship and lead to inaccuracies between intentions and behavior. This study was designed to examine the discrepancies between intended drinking during college SB compared to actual drinking reported after SB, as well as examining correlates of underestimating drinking. Web-based survey responses prior to, and after, SB assessed students' (N = 262) intended and actual drinking, contextual factors during SB (e.g., going on a trip), SB-specific drinking motives, drinking pacts with friends, and other related measures. Findings indicate that, in general, students who intended to drink less during SB, had a pact to get drunk with friends, or went on a SB trip with friends and/or family drank more than they had anticipated prior to SB. Among students who indicated going on a trip with friends, the number of friends on the trip was also an important determinant of whether the student underestimated their level of drinking. Findings highlight the importance of SB trips and behavioral intentions as correlates of underestimated drinking and could be targets of prevention and intervention strategies.

0852

UNDER-AGED YOUTH EXPOSURE TO ALCOHOL ADVERTISING IN CANADA

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Alcohol marketing is present in many venues available to under-aged youth. The widespread marketing of alcohol products has the potential to create unrealistic representations of drinking for youth and may contribute to the excessive levels of under-aged drinking. To assess exposure to and impact of these advertisements in youth, this study first monitored placement of alcohol advertisements shown in the Canadian television market during summer and fall 2010 and early spring 2011. This placement was compared to television viewing patterns reported by under-aged group of youth (15–16 year olds in Grade 10) and drinking aged youth (19+ in University) in the province of British Columbia where the study took place. In addition, both groups were shown eight advertisements from those shown during the monitoring period. After viewing each ad, each participant was asked how many times they had seen the ad and how much they liked it. In addition, we asked a series of questions that assessed compliance with the Canadian Radio and Television Commission (CRTC) guidelines for alcohol advertising. The pattern of alcohol advertisements was heavily associated with sports programming, but also comedy shows. The prevalence of alcohol ads was high for shows routinely watched by many youth. The memory frequency results indicated that over 50% of under-aged respondents reported seeing seven of the eight alcohol ads on at least 10 or more occasions. These ratings were at least as strong, if not stronger, than those of drinking age respondents. Under-aged youth also had higher levels of likeability scores on several commonly shown ads. Finally, for many of the ads, both groups reported that the ad portrayed characteristics in violation of one or more guidelines set by the CRTC. These potential violations were confirmed by an expert panel who also rated the ads. These findings suggest that current regulatory practices do not control content or restrict exposure of alcohol advertisements to populations under the legal drinking age in any meaningful way.

0853

DOES PERCEIVED ACCESS TO ALCOHOL RELATE TO AGE OF FIRST DRINK AND NEGATIVE CONSEQUENCES IN HIGH SCHOOL SENIORS?

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Underage drinking is associated with many negative outcomes including increased binge drinking and health and behavioral consequences (Weschler et al., 2000, Weschler et al., 2002). Furthermore, research on adolescent access to alcohol shows that access to alcohol predicts earlier onset of alcohol use (e.g., Komro et al., 2007). Given these relationships, limiting access to alcohol is offered as one way to reduce negative consequences related to alcohol (e.g., Harrison et al., 2000). However, it has not been shown that access to alcohol itself predicts alcohol-related negative consequences. Thus, the present study explored the relationship between perceived access to alcohol, age of first alcohol use, and alcohol-related negative consequences in adolescents who reported drinking alcohol at least once in their lifetime. Washington state high school seniors (N = 289, 51.6% Female, 85.5% Caucasian) participating in a pilot study investigating alcohol use trajectories were included in the sample. Participants completed a survey including questions about how easy (impossible to very easy) it would be to obtain either beer, wine, spirits, or any type of alcohol; age of first alcohol use; and alcohol-related negative consequences as measured by the Rutgers Alcohol Problem Index (White & Lobouvie, 1989). First, regressions were run to assess the relationship between access to beer, wine, spirits, or any type of alcohol and negative consequences. No significant results were found. Next, regression analyses assessed if the access to beer, wine, spirits, or any type of alcohol was related to age of first drink. Results revealed a significant inverse relationship between access to beer and age of first drink such that the easier perceived access of beer younger the age of first drink, β = -.53, R^2 = .05, p = .01. These results do not provide support for the hypothesis that perceived alcohol access is related to negative consequences. However, these results suggest that access to beer as an adolescent may facilitate a younger age of first drink. Future research should continue to explore the variables that contribute to negative alcohol related outcomes in adolescents. This research was supported by NIAAA # 1U01AA018276 awarded to Drs. Larimer & Berglund.

0854

GETTING INTO THE SPIRIT: ALCOHOL-RELATED INTERPRETATION BIAS IN HEAVY DRINKING STUDENTS

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The aim of the present study was to advance our current understanding of the role of alcohol-related, implicit memory associations in adolescents' alcohol use. Findings from this area of research reveal that spontaneously activated memory associations can lead to a biased interpretation of ambiguous, alcohol-related cues. In addition, the degree of this bias is positively related to alcohol use.

Towards this aim, heavy and light drinking students were required to create continuations for ambiguous, open-ended scenarios that provided either an alcohol-related or neutral context. So, unlike previous studies, we used ambiguous, alcohol-related scenarios instead of single word cues. The scenarios described emotional, cognitive and social themes that are associated with excessive alcohol consumption, and as such comprised a high ecological validity.

Results revealed that heavy drinking students exhibited an interpretation bias towards the ambiguous, alcohol-related scenarios. They produced more alcohol-related continuations than light drinking students. This result was independent of the coding method employed, with an interpretation bias found when continuations were coded by either participants themselves or by two independent raters using two different coding methods.

These findings clearly extend our knowledge regarding the role of implicit memory associations in adolescents' alcohol use. Due to the novelty of this scenario-based approach in the context of alcohol research our results might provide an inspiring starting point for further investigations.

0855

MEASURING COLLEGE STUDENTS' MOTIVES BEHIND PREPARTYING DRINKING: DEVELOPMENT AND VALIDATION OF THE PREPARTYING MOTIVATIONS INVENTORY

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Drinking motives are vital in identifying risk factors and better understanding alcohol-related outcomes. However, context-specific motivations could provide greater motivational perspective on high-risk context-specific alcohol use behaviors such as prepartying (consuming alcohol prior to attending one's intended destination) than general motivations. Prepartying provides a setting that can lead to heavy drinking via rapid consumption while prepartying and, often, continued heavy drinking throughout the night. Students who preparty experience more alcohol-related consequences and reach higher blood alcohol levels during drinking events/nights which involving prepartying compared to those that do not involve prepartying. In the current study, students' reasons for prepartying were collected from a large diverse sample (n = 2497) and these reasons were coded to create a prepartying motivations inventory (PMI) that was then piloted with another unique sample (n = 1085). A split-half validation procedure was used for the purpose of both generating and confirming the PMI's factor structure. Exploratory and confirmatory factor analyses yielded a final 12-item measure consisting of four distinct, but inter-related, factors: Interpersonal Enhancement (IE), Situational Control (SC), Intimate Pursuit (IP), and Barriers to Consumption (BC). Internal consistency reliability, discriminant validity, and predictive validity were empirically demonstrated. The IE subscale contains items pertaining to prepartying as a means to loosen up before going out and because it makes talking to new people easier. The IP subscale contains items pertaining to increasing the likelihood of 'hooking up' and meeting potential dating partners. The SC subscale refers to having control over the alcohol that is consumed and not having to drink at the ultimate destination. The BC subscale concerns reasons related to not being able to obtain alcohol at the later function and avoid getting in trouble with authorities. Results support the notion that individuals preparty for a variety of reasons that are distinct from general motives. Findings can be used to more fully understand preparty behavior and its psychosocial correlates and connections to consequences and other risk behaviors, as well as to help hone and target context-specific intervention strategies. Researchers are encouraged to use the PMI in future research with young adults to provide further understanding of prepartying behavior.

0856

GENDER DIFFERENCES IN EXPECTANCIES, MOTIVATIONS, AND EXPERIENCED ALCOHOL-RELATED CONSEQUENCES ON SPRING BREAK

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Every year many college students go on Spring Break trips, engage in peak levels of alcohol use during Spring Break (Greenbaum *et al*., 2005), and experience an increase in alcohol-related consequences (Lee *et al*., 2009). Sixty-eight percent of Spring Break vacationers reported drinking more alcohol on their Spring Break trip than on an average week of the year (Patrick *et al.,* 2010). Gender also plays a role in alcohol use, as men consume alcohol more frequently and in larger quantities than women (Johnston *et al.,* 2011; Wilsnack et al., 2000). Although a previous study has assessed pre- and post-Spring Break surveys of intentions to consume alcohol, expected outcomes of alcohol use, and actual quantities of alcohol consumed on Spring Break, it did not include reasons to avoid drinking (Sonmez *et al*., 2006). Utilizing pre- and post-Spring Break web-based surveys, this study examined gender differences in planned drinking, negative alcohol expectancies, alcohol motivations, and actual drinking, (N=270; 45% men, 55% women; 97% retention rate as post-Spring Break survey). Men expected more negative physical/behavioral and driving consequences than women. Women had more important motivations to avoid physical/behavioral consequences, although there were no gender differences in motivations to avoid driving consequences. In regression analyses, men planned to drink more, reported a greater number of total drinks consumed, and experienced more physical/behavioral and driving-related consequences on Spring Break than women. Physical/behavioral expectancies from the pre-Spring Break survey predicted a greater number of total drinks consumed, a higher of maximum drinks, and more experienced physical/behavioral consequences on Spring Break. Greater motivations to avoid physical/behavioral consequences predicted fewer maximum drinks, but no other outcomes. Driving expectancies predicted more experienced driving consequences, but motivations to avoid driving consequences were not significantly associated with behavior or consequences. In addition, students who went on Spring Break trips drank more total drinks and maximum drinks than students who did not go on trips, although there were no differences by trip in experienced consequences. These findings could help in creating more specific interventions based on gender, drinking expectancies, and motivations to decrease negative alcohol consequences on Spring Break.

0857

DRINKING UNTIL YOU WIN: THE IMPACT OF PERCEIVED TOLERACE AND DRINKING GAME TYPE ON MAXIMUM IN-GAME ALCOHOL CONSUMPTION

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Participating in drinking games (DGs) is a particularly risky activity as DGs often facilitate heavy and rapid alcohol consumption. As such, this exploratory study investigated factors contributing to maximum DG drinking. The first goal of the study was to examine the impact of perceived tolerance to alcohol on maximum drinking game alcohol consumption. Tolerance to alcohol is important to investigate in the context of drinking games as drinking games provide a structured and measured means to convey to others how much one can drink. The second goal of the study was to investigate differences in types of DGs with respect to maximum drinks consumed by creating a novel categorization scheme based off drinking behaviors directly caused by specific DG rules and procedures. Participants were student drinkers from two west coast universities (*N*=3,546) who completed online surveys administered in the fall of 2008. Among these students, 69.2% (*n* = 2,290) reported playing a drinking game in the past month. A hierarchical linear regression model revealed that higher levels of perceived tolerance were related to increased maximal DG alcohol consumption for all participants. Gender and Greek-statues differences were also evidenced. Additionally, 100 unique drinking games provided by participants were identified, defined, and categorized into five mutually exclusive categories (i.e., targeted, communal, even competition, chance, and extreme consumption games) based on the primary way in which the game promotes alcohol consumption. ANOVAs and *z* tests of independent proportions revealed differences in the number of maximum drinks consumed by DG category and differences in percentages of players reporting which DG category resulted in their maximum DG drinking. Further ANOVAs demonstrated DG categories varied across player profiles (i.e., gender, ethnicity, and Greek-status). These results provided a better understanding of factors relating to maximum DG drinking and how these factors vary by gender, Greek-status, and race, identifying personal factors (e.g., gender) and contextual factors (e.g., type of DG) that lead to increased risk when playing DGs. Intervention and prevention programs may educate students on how perceived tolerance and the specific types of DGs contribute to increased risk when participating in DGs.

0858

A CROSS-NATIONAL STUDY OF DRINKING MOTIVES IN COLLEGE STUDENTS

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Purpose: The aims of this study were to explore cross-national similarities and differences in the structure of the Drinking Motives Questionnaire-Revised (DMQ-R), in the links between drinking motives and both heavy drinking and alcohol-related problems, and in the mean endorsement levels of social, enhancement, coping, and conformity drinking motives, among college students from 9 countries.
Methods: The 20-item DMQ-R (Cooper, 1994) and criterion measures of drinking quantity, drinking frequency, and drinking-related problems were administered to 701 Canadian (M age = 20.7, 82% F), 2923 American (M age = 18.6, 58.6% F), 1756 Swiss (M age = 22.8, 65.8% F), 961 Hungarian (M age = 22.1, 62.7% F), 496 Spanish (M age = 22.2, 64.3% F), 126 British (M age = 20.2, 85.7% F), 171 Israeli (M age = 23.8, 70.2% F), 189 Irish (M age = 19.9, 85.7% F), and 385 Brazilian (M age = 21.5, 55.3% F) college students.
Results: CFAs indicated that the four-factor structure of the measure was superior to an alternate three-factor structure across all countries surveyed, and that the four-factor model showed adequate/marginal to excellent fit in all countries. Further, across the majority of countries, the internal motives (coping and enhancement) were predictive of drinking levels and alcohol problems. However, in some countries, social motives were predictive of drinking outcomes (i.e., Israel and Brazil). Similarities were found in the rank order of drinking motive endorsement across all countries tested (i.e., social > enhancement > coping > conformity) but some interesting cross-national differences emerged in the mean levels of endorsement of particular motives. For example, the internal drinking motives received higher endorsement in northern than in southern European countries, and internal motives received higher endorsement in the United States than in Canada. Furthermore, cross-national differences in gender effects emerged in the mean level of endorsement of particular motives (e.g., enhancement motives received higher endorsement among males than among females in Switzerland, Canada, and the United States but not in other countries).
Conclusions: The results have important implications for how to best prevent alcohol misuse in college students from different countries, and suggest that motives-based early interventions for alcohol misuse developed in Canada (e.g., Conrod et al., 2006) might be readily transported for use with young people in other nations.

0859

ALCOHOL AND CAFFEINE AND PERCEPTIONS OF RISK FOR DRINKING AND DRIVING

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The consumption of caffeinated drinks in combination with alcohol has become popular among college students (Malinauskas et al., 2007). Research suggests that the combination of alcohol and energy drinks reduces the subjective perception of alcohol intoxication (Ferreira et al., 2006), and in field studies, has been shown to increase intentions to drive (Thombs et al., 2010). The present study aimed to test the effects of alcohol and caffeine on perceptions of danger relating to driving after drinking (DD).
Data used for these analyses are a subset of a larger study investigating the pharmacological and expectancy effects of alcohol and caffeine. Participants were randomly assigned to receive a combination of alcohol and/or caffeine, placebo combinations of the two substances, or neither (control). They completed a packet of questionnaires and two attention-related tasks as part of the study. Following beverage consumption, participants rated their willingness to drive and perceived danger of driving at multiple points across the blood alcohol curve. These analyses were conducted using only participants (*n*=67, 52% male, mean age=22.5) in the three alcohol conditions (i.e., alcohol and caffeine, alcohol only, and alcohol and placebo caffeine). We examined perceived danger of DD both at baseline and at the highest BAC at which participants endorsed being willing to drive.
For all participants, both baseline and intoxicated perceived danger were associated with DD behavior (baseline: $\beta = .56$, $p < .001$, intoxicated: $\beta = .23$ $p < .05$). We also observed a significant interaction with condition. Probing this interaction indicated that, when alcohol was the only active substance (i.e., alcohol only and alcohol and placebo caffeine conditions), both baseline and intoxicated perceived danger were predictive of DD behavior (baseline: $\beta = .40$, $p < .01$, intoxicated: $\beta = .33$ $p < .001$). However, for participants who received alcohol and caffeine, baseline but not intoxicated perceived danger was associated with DD behavior (baseline: $\beta = .80$, $p < .001$, intoxicated: $\beta = .01$, *ns*).
These results suggest a pharmacological effect of alcohol and caffeine on DD judgments. For participants who consume alcohol alone, their perceptions of risk of DD are strongly related with their behavior. However, the addition of caffeine alters these perceptions in such a way that these perceptions are no longer consistent with their DD behavior outside of the lab.

0860

THE ROLE OF ALCOHOL EXPECTANCIES IN DRINKING BEHAVIOR AMONG WOMEN WITH AUD AND PTSD

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Alcohol use disorders (AUD) are highly comorbid with posttraumatic stress disorder (PTSD). One hypothesis seeking to explain the rate of co-occurrence is the self-medication hypothesis, which proposes that individuals use alcohol to cope with symptoms and triggers related to PTSD and distress associated with the trauma memory. The aim of the present study was to examine the role of alcohol expectancies, psychological symptoms, and distress in drinking behavior in a comorbid sample. Participants were women (n = 40) who had experienced intimate partner violence (IPV) seeking integrated AUD and PTSD treatment in an outpatient community co-occurring disorders program. The women were, on average, 42 years old (SD = 10.48), with 60% White, 25% Hispanic, 12.5% African American, and had an average of 12 (SD = 2.81) years of education. All participants had lifetime AUDs, with 67.5% meeting current alcohol abuse/dependence criteria. 76.9% of the women met criteria for current PTSD, with the rest having subthreshold PTSD. Pearsons correlations were examined with baseline measures of alcohol use (Addiction Severity Index), alcohol expectancies (Alcohol Expectancies Questionnaire) and PTSD symptoms and distress (PTSD Checklist, Clinician Administered PTSD Scale, Trauma-Related Guilt Inventory). Only positive alcohol expectancies significantly correlated with drinking behavior. Expectancies that alcohol would increase sexual enhancement ($r = .419$, $p = .024$) and increase social disinhibition ($r = .403$, $p = .034$) were positively correlated with numbers of years drinking alcohol excessively. Expectancies that alcohol would improve mood ($r = .374$, $p = .050$), increased sexual enhancement ($r = .520$, $p = .005$), increased social disinhibition ($r = .466$, $p = .016$) and increased relaxation ($r = .544$, $p = .005$) were associated with greater alcohol severity on the ASI. Expectancy that social behavior would be enhanced was associated with greater number of days drinking in the past 30 days ($r = .405$, $p = .019$). Psychological symptoms and distress related to past trauma were not significantly related to drinking behavior. These results suggest that among a highly co-morbid population, expectancies about alcohol's positive effects may be more salient for coping with situational triggers (i.e., drinking to get through social situations) as opposed to PTSD symptom management. More work on the relationship between self-medication and alcohol expectancies in comorbid samples is needed.

0861

DYSFUNCTIONAL INTERPERSONAL BEHAVIOR, EMOTION DYSREGULATION, AND DRINKING SEVERITY IN A SAMPLE OF INDIVIDUALS WITH BORDERLINE PERSONALITY DISORDER

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Research has linked emotion dysregulation, dysfunctional interpersonal behavior, and Borderline Personality Disorder (BPD) each independently to problem alcohol use. It is hypothesized that each of these variables may constitute measurement of similar underlying factors, though perhaps at progressively higher levels of analysis and at varying levels of complexity and scope.

This study examined the relationships among dysfunctional interpersonal behavior, emotion dysregulation, and alcohol problems in two samples of individuals entering clinical trials for alcohol use disorders: 1) 125 men and women with BPD and opiate dependence in a trial comparing Dialectical Behavior Therapy (DBT) to standard drug counseling (Sample 1); 2) 99 women in a component analysis of DBT (Sample 2). At baseline, the Difficulties with Emotion Regulation Scale (DERS) was used to assess emotion dysregulation, the Inventory of Interpersonal Problems (IIP) was used to assess dysfunctional interpersonal behavior, and the Addiction Severity Index was used to assess alcohol related problems (ARP).

In both samples, ARP was associated positively with DERS total score, and the Goal and Impulse subscales. In sample 2, ARP was additionally associated with Nonacceptance, Clarity, and Strategies. In sample 1, ARP was associated with IIP Sensitivity and Aggression, while in sample 2 ARP was not associated with any of the IIP variables.

Within two independent samples of individuals with BPD, a strong association was found between emotion dysregulation and alcohol problems such that participants with higher levels of emotion dysregulation also had higher levels of problem alcohol use. However, the same strong pattern of relationships was not found across both samples between dysfunctional interpersonal behavior and problem alcohol use; drinking was only associated with dysfunctional interpersonal behavior in the opiate-dependent sample. These findings suggest that emotion dysregulation is an underlying process likely to predict problem drinking independent of the categorical BPD diagnosis, whereas the relationship of dysfunctional interpersonal behavior and problem alcohol use found previously may be accounted for by BPD diagnosis.

*Data will also be presented on drinking frequency and intensity.

0862

COGNITIVE FUNCTIONING, IMPULSIVITY AND RISK-TAKING: RELATIONSHIPS WITH MEASURES OF CLINICAL SYMPTOMOLOGY IN VETERANS WITH PTSD AND AUD

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Background: Cognitive dysfunction is commonly observed in individuals with substance use disorders and PTSD, and may be conceptualized as a trans-disease phenomenon. Previous research suggests that individuals with lower executive functioning (EF) and higher trait impulsivity are at increased risk for engaging in risky behavior (e.g., problematic substance use) and may have poorer treatment outcomes. Little is known though about how these constructs co-vary with trauma-related symptoms, substance use and other related clinically important outcomes.

Objective: To examine associations, pre-treatment, between cognitive functioning, impulsivity, risk-taking and clinical assessments.

Method: A series of correlational analyses were conducted with baseline data from a pilot controlled trial of topiramate augmentation for veterans with PTSD and alcohol dependence. Trails B was administered as an index of EF and the Hopkins Verbal Learning Test (HVLT) was employed to assess learning and memory. Risk-taking was measured with the Balloon Analogue Risk Task (BART) and the Short Inventory of Problems - Impulsivity Subscale. A delay discounting (DD) task was given to assess impulsivity. Data were also collected on PTSD symptom severity (CAPS), drinking goals, global impairment, alcohol craving, alcohol obsessions and compulsions (OCDS) and alcohol problem severity (AUDIT).

Results: Lower performance on Trails B was associated with higher estimates of patient-rated impairment, more ambitious drinking reduction goals and greater alcohol problem severity. On the HVLT, poorer recognition accuracy, single-trial and multiple trial learning were correlated with worse re-experiencing symptoms. Delayed recall was lower for participants with higher craving for alcohol. Riskier, more impulsive behavior while drinking was associated with stronger pre-occupations with drinking. Discounting of future rewards was positively associated with poorer resistance to drinking urges, craving and re-experiencing symptoms. No relationships emerged with BART scores.

Conclusions: Findings highlight the relationship between EF and perceived impairment and treatment need and suggest that learning and memory capacity may be reduced among patients with elevated PTSD symptoms and craving for alcohol. Additionally, capacity to delay gratification on a DD task was negatively associated with severity of alcohol craving symptoms and ability to resist using and thinking about alcohol.

0863

RISK-TAKING, IMPULSIVITY, MEMORY & EXECUTIVE FUNCTIONING AS OUTCOME PREDICTORS IN A TRIAL OF TOPIRAMATE FOR ALCOHOL DEPENDENCE IN VETERANS WITH PTSD

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Background: PTSD and alcohol dependence frequently co-occur among veterans. Cognitive dysfunction, impulsivity and risk-taking are common features of both disorders. However, the role of these cognitive problems in predicting treatment outcomes is not well characterized in patients with both PTSD and alcohol dependence.

Methods: Participants were the first 27 subjects entering a pilot controlled trial of topiramate treatment of co-occurring alcohol dependence and PTSD. The study was 12 weeks in duration with a Week 16 follow-up visit (4 weeks after end of medication). Pretreatment measures of risk-taking (Balloon Analog Risk Task [BART]), impulsivity (Delay Discounting), learning and memory (HVLT) visuomotor processing speed (Trails A) and executive functioning (Trails B), were analyzed for correlations with treatment outcome variables including completion of the 12-week study, Week 16 follow-up alcohol use (Timeline Followback [TLFB]), alcohol craving (Penn Alcohol Craving Scale [PACS]) and obsessive thinking about alcohol (Obsessive-Compulsive Drinking Scale [OCDS]).

Results: Subjects' mean age was 50 years, 93% were male, and 63% were white. Mean Clinician Administered PTSD Scale (CAPS) score was 77. Frequency of alcohol drinking days at baseline was 79%, with a mean of 11 drinks per drinking day. Significant positive correlations were found between pre-treatment scores on Trails A & B and likelihood of completion of the 12-week trial ($p = .004$ and .015, respectively). Significant positive correlations also emerged between pre-treatment BART risk-taking scores and Week 16 follow-up TLFB percent of drinking days ($p=.04$) and number of drinks per drinking day ($p=.02$) as well as PACS alcohol craving ($p=.008$) and OCDS alcohol obsessions ($p=.008$). No significant correlations were noted between measures of learning and memory, or impulsivity, and treatment outcomes.

Conclusions: Among alcohol dependent veterans with PTSD entering a topiramate treatment trial, better pre-treatment visuomotor processing speed and executive functioning were associated with treatment completion. Moreover, severity of pretreatment risk-taking was correlated with post-treatment alcohol craving, alcohol obsessions, and alcohol use amount and frequency.

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0864

COGNITIVE PROCESSING BIASES FOR ALCOHOL-RELATED STIMULI AMONG ALCOHOL-DEPENDENT ADULTS ATTENDING RESIDENTIAL TREATMENT

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This study examined cognitive processing biases for alcohol-related information among alcohol-dependent individuals recently admitted to residential treatment. Participants completed a computerized attentional task wherein they classified a centrally-presented digit as odd or even. On some trials, an alcohol word, neutral word, or anagram was presented along with the digit. On these dual trials participants first classified the digit and then classified the other stimulus as a word or nonword. Participants took significantly longer to classify digits that appeared with alcohol (M = 1314 ms) as opposed to neutral words (M = 1238 ms); suggesting the alcohol words distracted them from processing the digit. In the word/non word task, participants took longer to classify alcohol words (M = 600 ms) than neutral words (M = 565). Performance in the attentional task was generally unrelated to self-report approach and avoidance tendencies for alcohol, though patients with an avoidant profile took significantly longer to classify alcohol words than neutral words for the initial presentations of each word type. Following the attentional task participants completed a recognition memory test consisting of words that had appeared in the task (old words) and words that had not previously appeared (new words). Participants showed significantly higher hit rates (i.e., correctly classifying an old item as old) and false alarm rates (i.e., incorrectly classifying a new item as old) to alcohol words (95% vs. 22%) compared to neutral words (85% vs. 14%) and also showed a more liberal response bias to alcohol words. The findings suggest that alcohol-dependent individuals exhibit a variety of cognitive processing biases for alcohol-related information, and these biases may be related to avoidant tendencies.

0865

NEUROCOGNITIVE IMPAIRMENT INTERACTS WITH 12-STEP AFFILIATION AND DEPRESSION TO PREDICT FUTURE DRINKING IN DEPRESSED, SUBSTANCE-DEPENDENT VETERANS

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Many patients with an alcohol or substance use disorder (ASUD) enter treatment with neurocognitive impairment (NCI). Direct links between NCI and substance use have been inconsistent, but some studies show indirect effects through self-efficacy. Level of NCI has also moderated effects of self-efficacy and 12-step affiliation on substance use. Patients with comorbid major depression (MDD) are prevalent and may have relatively greater levels of NCI that interact with other correlates of drinking (e.g., depressive symptoms). In patients with ASUD and MDD, we examined if self-efficacy, 12-step affiliation, and depression mediated the effects of NCI, and whether NCI moderated relations with future drinking.

Veterans (N=208) meeting DSM-IV criteria for alcohol (89%), cannabis (29%), or stimulant dependence (54%) and MDD received group Twelve-Step Facilitation or Integrated Cognitive Behavioral Therapy. In 6 months of treatment and 12 months of follow-up these variables were collected every 3 months: twelve-step affiliation (TSA), depressive symptoms (DEP), self-efficacy, and percent days drinking (PDD). An intake NCI score (0–8) summed domains in which patients were severely impaired. Hierarchical linear models (HLMs) tested effects of NCI on mediators and PDD, and cross-level interactions between NCI and lagged (i.e., prior time-point) process variables tested moderation, controlling for session attendance, race, sex, age, and years of education, and baseline level of outcome.

Most patients (63.5%) were impaired on ≥1 domain. The effects of intake NCI on future drinking were mediated by self-efficacy, as greater NCI predicted lower self-efficacy (p<.01), and lower self-efficacy predicted greater future PDD (p<.001). Intake NCI did not moderate effects of self-efficacy on PDD, but NCI did moderate effects of TSA on future PDD (p<.01), with stronger effects of TSA for impaired individuals. However, this was qualified by a significant 3-way interaction between NCI, lagged TSA, and lagged DEP (p<.05), such that greater TSA predicted lower future PDD to a greater extent for impaired patients, but only when depression was high.

For patients with comorbid ASUD-MDD, greater neurocognitive impairment may impact alcohol use primarily by inhibiting self-efficacy for abstinence. The benefits of 12-step affiliation are increasingly important for cognitively impaired patients during periods of elevated depression, possibly due to lacking alternative methods of coping.

0866

APPROACH AND AVOIDANCE DIMENSIONS OF CRAVING PREDICT DRINKING FOLLOWING TREATMENT INITIATION IN PATIENTS DIAGNOSED WITH A SEVERE MENTAL ILLNESS AND ALCOHOL USE DISORDER

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Despite the emergence of well validated treatments for alcohol use disorders (AUDs), AUDs continue to be a widespread problem in the United States. Among the most negatively affected are individuals diagnosed with co-occurring severe mental illnesses (SMI: i.e., schizophrenia, bipolar disorder). Specifically, those diagnosed with SMIs experience greater negative consequences associated with their use, have a poorer treatment response and higher relapse rates following treatment. Greater understanding of factors that predict drinking among individuals diagnosed with SMIs and AUDs has the potential to improve both treatment responder and long-term success rates. Using the Ambivalence Model of Craving (Breiner et al., 1999), which defines craving as the relative activation of both desires to consume (approach inclination) and desires to avoid consuming (avoidance inclination) alcohol, we investigated the dynamic relationships between craving and alcohol use in patients diagnosed with a SMI-AUD. Participants (n= 278) diagnosed with SMI-AUDs were recruited from a community mental health center and were followed over the course of 6 months, during which they completed a battery of self-report measures bi-monthly including the Approach and Avoidance of Alcohol Questionnaire. Multilevel modeling techniques were used to estimate the time-lagged bidirectional associations between approach and avoidance inclinations and drinking. Results indicated that avoidance inclinations moderated the effect of approach inclinations on number of drinks consumed and drinks per drinking day, such that avoidance inclinations buffered the effect of approach inclinations on heavier drinking levels, differences which remained constant over time. Results also indicated that drinks per drinking day predicted approach inclinations differentially over time, such that lower levels of drinking predicted decreases in approach inclinations, whereas an opposite pattern was found following higher drinking. Decreases in drinking also predicted increases in avoidance inclinations, which were maintained over time. These findings highlight the complexity of craving and the importance of measuring both the desire to consume and desire to avoid consuming alcohol simultaneously when assessing subjective craving experiences. Among those diagnosed with SMIs, avoidance inclinations may be an important component of strategies to increase abstinence rates in this difficult-to-treatment population.

0867

AFFECT AND CRAVING: POSITIVE AND NEGATIVE AFFECT ARE DIFFERENTIALLY ASSOCIATED WITH APPROACH AND AVOIDANCE DIMENSIONS OF CRAVING

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With nearly 9% of the U.S. population age 12 or older diagnosable with Substance Use Disorders (SUDs) – most notably alcohol and tobacco use problems – SUDs are undeniably a major public health concern. The high rates of comorbidity of SUDs with anxiety and mood disorders serves to complicate this problem, but also directs attention to the need for a better understanding of links between affect and compulsive use of popular psychoactive substances. Despite apparently strong links between affect and addictive behaviors, research on cue reactivity (conditioned responses to psychoactive substance stimuli) or cue elicited craving (craving specifically elicited by such stimuli) have typically either neglected affective state altogether or focused rather narrowly on the role of negative affect in craving. The present study sought to elucidate the links between affect and craving for alcohol and tobacco by incorporating evaluation of the potential role of positive as well as negative states in the affect-craving nexus. Specifically, we applied the multidimensional Ambivalence Model of Craving (Breiner et al., 1999) to explore the possibility that positive versus negative affect might be differentially associated with inclinations to approach (use) or avoid (not use) the psychoactive substances depicted in cue presentations. Participants were 144 men and women recruited from an inpatient detoxification unit. Affect was indexed by the Positive and Negative Affect Schedule and self-reported inclinations to approach (use) and avoid (not use) alcohol, cigarettes, and non-psychoactive control substances (food and beverages) were recorded when images of substance cues were presented. Participants with elevated negative affect reported significantly higher approach ratings for cigarette and alcohol cues, whereas those high in positive affect showed significantly higher levels of avoidance inclinations for both alcohol and cigarette cues and also significantly lower approach ratings for alcohol cues, all relative to control cues. Results highlight the importance of both negative and positive affect in substance dependent individuals' inclinations to both consume and avoid consuming problem substances and underscore the utility of a multidimensional conceptualization of craving in the analysis.

0868

AFFECTIVE AND ANXIETY DISORDERS MODERATE THE EFFECTS OF EFFORT TO REGULATE ALCOHOL USE ON LONG-TERM REMISSION FROM ALCOHOL DEPENDENCE

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Little research has examined whether recovered alcoholics' effort to regulate alcohol use effectively increases the likelihood of maintaining recovery from alcohol dependence. The self-control strength model suggests that one's capacity to regulate alcohol use may be depleted under conditions of high-self control demands. Given that both affective and anxiety disorders are associated with depletions in self-control resources, these disorders may moderate the association between effort to regulate alcohol use and the likelihood of maintaining remission from alcohol dependence. Using longitudinal data from a high-risk community sample, the present study tested whether past-year DSM-III-R affective or anxiety disorders interacted with recovered alcoholics' effort to regulate alcohol use to influence their likelihood of maintaining long-term remission from alcohol dependence.

The present study utilized a subsample of participants who showed evidence of recovered alcoholism and also had long-term follow-up data to allow tests of maintenance of recovery. At baseline, all participants (n= 82; 73% male; 67% children of alcoholics; 70% non-Hispanic Caucasian; M_{age} at baseline= 21.7; M_{age} at follow-up= 32.9) met lifetime DSM-III-R criteria for alcohol dependence but did not have any past-year symptoms of abuse or dependence. Participants who had not experienced any consequences or symptoms due to alcohol use within the past 5 years at the 10-year follow-up were considered to have maintained long-term remission (n= 37; 45%). All analyses controlled for age, gender, parent alcoholism, whether participants used alcohol at the baseline assessment, and treatment history (only age had a significant effect).

Results from logistic regressions showed that effort to regulate alcohol use had a significant main effect on maintenance of remission, such that those who tried harder to limit their alcohol use were more likely to maintain long-term remission. Affective and anxiety disorders at baseline did not have significant main effects on maintenance of remission. However, both disorders significantly moderated the influence of effort to regulate alcohol use such that the protective effect of effort to regulate use was only significant for those without an affective or anxiety disorder. These findings suggest that affective and anxiety disorders may undermine the protective effect of effort to regulate alcohol use on maintaining long-term remission from alcohol dependence.

0869

WAS IT WORTH IT? PERCEPTIONS OF POSITIVE AND NEGATIVE CONSEQUENCES IN DISCRETE DRINKING OCCASIONS

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Although positive outcomes of drinking are experienced more often, negative outcomes are readily acknowledged. Continued drinking despite negative outcomes may occur when negative aspects of heavy drinking occasions are seen as "worth it" given the positive consequences that are almost universally experienced. We sought to investigate the influence of positive and negative consequences on perceptions about whether discrete drinking experiences are "worth it."
Data are from an ongoing longitudinal study in which college students complete computerized telephone interviews each day on mobile telephones. Participants report whether they drank alcohol the previous day (if so, how many drinks were consumed) and are asked if they experienced any of a checklist of 15 positive and negative drinking consequences. Each consequence that was experienced is then rated on a scale of 1=extremely bad to 9=extremely good. Finally, participants rate whether the overall drinking experience was "worth it" given the good and the bad consequences (1=not at all; 9=extremely).
Participants reported drinking on 415 (45%) of the 922 days with complete data; the mean number of drinks consumed was 5.9 (range 1–24), and more than 5 drinks were consumed on 46% of occasions. 93% of drinking occasions resulted in at least one reported positive consequence, compared to 47% of occasions that resulted in at least one negative consequence. No drinking occasions resulted in solely negative consequences; all negative consequences were accompanied by positive consequences.
Drinking occasions were generally seen as "worth it" (mean rating 6.49), with only 12% of occasions rated below the midpoint of the 9-point scale. In a multivariate regression analysis using multilevel modeling, these ratings were predicted by the number of drinks consumed (b=.08) and the occurrence of one or more positive consequences (b=1.2), but not by the occurrence of negative consequences.
Using data from daily reports in which drinkers reported on consequences of discrete drinking occasions, we found that drinkers perceived the positive consequences of the occasion as worth the negative consequences. These results may reflect the commonplace nature of most negative consequences or a bias toward the positively reinforcing nature of pleasant states.

9. CONSEQUENCES OF ALCOHOL CONSUMPTION IN HUMANS

0870

RELATIONSHIPS BETWEEN SPECIFIC COPING STRATEGIES AND VIOLENCE AMONG ALCOHOL AND DRUG USERS IN RESIDENTIAL TREATMENT

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Objective: This study evaluated associations between coping styles, alcohol and drug use, and violence perpetration among 321 individuals entering a residential substance use disorder (SUD) treatment program.
Method: Participants completed measures of demographics, recent alcohol and drug use, violence perpetration toward partners and non-partners, and three different coping styles: emotion-focused, problem-focused, and avoidant. Using scores from a modified Conflict Tactics Scale, participants were categorized into the following groups 1) no past year violence perpetration, 2) only past year violence perpetration against a partner, 3) only past year violence against a non-partner, or 4) any past-year violence against both a partner and a non-partner. Multinomial logistic regression models examined the relationships between demographic characteristics (race/ethnicity, gender, age), frequency of alcohol, heroin, cocaine, and marijuana use, and frequency of use of three coping styles with violence type (no violence perpetration was treated as the reference group). Parallel analyses were conducted with each coping style entered as a predictor in three separate models. Results: Bivariate associations were observed between gender, age, heroin use, and avoidant coping with violence perpetration type. In multivariate analyses, problem-focused coping was not associated with any violence perpetration. However, both emotion-focused and avoidant coping were related to increased odds of reporting violence towards both partners and non-partners. Recent alcohol and other substance use were not associated with violence perpetration in the multivariate models.
Conclusions: The findings suggest a need for SUD interventions to target avoidant (e.g., giving up, denial) and emotion-focused coping strategies (e.g., substance use, venting, humor), especially among individuals engaging in violence toward both partners and non-partners. Interventions that aim to reduce use of substances for coping, in addition to promoting the development of skills such as emotion-regulation, mindfulness, and acceptance might play a role in helping substance users cope more effectively with stressful situations. These findings suggest the need for future research to evaluate the prospective association between the use of emotion-focused and avoidant coping skills and violence perpetration.

0871

NEIGHBORHOOD CHARACTERISTICS, EMOTION AND SOCIAL NORMS: RELATIONSHIPS WITH HEAVY DRINKING AND NEGATIVE ALCOHOL-RELATED CONSEQUENCES

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Background: Theories suggest pathways from neighborhood disadvantage to alcohol problems involve distress and social norms supporting heavy drinking. In contrast, the relationship between neighborhood affluence and alcohol outcomes may involve positive affect and norms discouraging heavy drinking.
Methods: Using data from the 2000 and 2005 National Alcohol Surveys (N = 7,912 current drinkers; 49% female) and the 2000 Decennial Census, we examined simultaneous multivariate path models of relationships between neighborhood disadvantage and affluence operating through distress, positive affect and pro-drinking norms on heavy drinking and negative drinking consequences among past-year drinkers. We used multiple groups analysis to assess differences by sex and race. Covariates included neighborhood immigrant concentration and individual-level demographics.
Results: In the full sample, neighborhood disadvantage had a significant direct path to increased negative consequences, with no indirect paths through either distress or pro-drinking norms. Counter to expectations, neighborhood affluence had significant indirect paths to increased negative consequences through both pro-drinking norms and increased heavy drinking. Distress and pro-drinking norms each were positively associated with heavy drinking and negative consequences. Sub-group analyses revealed that overall findings were most consistent with results for white men. There was an additional significant indirect path from neighborhood disadvantage to increased consequences for non-white men that was partially explained by both pro-drinking norms and increased heavy drinking. There were limited neighborhood effects for both white and non-white women.
Conclusions: Existing theories of neighborhood effects are insufficient when considering alcohol outcomes in diverse groups. Interventions targeting drinking norms in both affluent and disadvantaged areas are necessary to reduce alcohol-related problems, particularly among men.

0872

POVERTY AND ALCOHOL/DRUG USE DISORDERS AS PROSPECTIVE PREDICTORS OF FIRST-TIME HOMELESSNESS

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Aim: Poverty, alcohol/drug use disorders, and homelessness are important public health concerns. No study has prospectively examined the joint influences of poverty and alcohol/drug use disorders on first-time adult homelessness in national data.
Method: Longitudinal data were used to examine whether baseline poverty and alcohol/drug use disorders interacted to predict first-time homelessness over 3-year follow-up. Participants ≥18 years were interviewed in Waves 1 (2001–2002) and 2 (2004–2005) of the NESARC. Those analyzed were those never homeless at Wave 1 (N=30,558). DSM-IV alcohol/drug use disorders were assessed with the AUDADIS. Baseline poverty was calculated using 2001 federal poverty guidelines, adjusted for household size. First-time homelessness at Wave 2 was defined as having no place of one's own to live for ≥1 month since Wave 1. Risk ratios (RR), adjusted for demographics, psychiatric disorders, and region, were obtained and tested using the average marginal predicted risk from logistic regression using SUDAAN.
Results: At Wave 2, 4.2% reported first-time homelessness since Wave 1 (N=1,222). Rates were higher among those in poverty (7.9%), with alcohol use disorders (8.6%), with drug use disorders (16.3%), and with a combination of poverty and an alcohol and/or drug use disorder (21.0%). Both baseline poverty (RR=1.54; CI=1.30,1.84) and alcohol/drug disorders (RR=1.49; CI=1.23–1.80) independently increased the risk for first-time homelessness. Adjusted for controls, alcohol/drug use disorders significantly increased risk of homelessness both for those not in poverty at baseline ($p<.01$) and among those in poverty at baseline ($p<.01$). The effect of alcohol/drug use disorders was significantly moderated by poverty ($p=0.04$).
Conclusion: This is the first study to prospectively examine the joint influences of alcohol/drug use disorders and poverty on adult first-time homelessness in national data. The combination of alcohol/drug use disorders and poverty created significantly greater risk for the first-time incidence of homelessness than the sum of risks associated with these factors considered separately. Given the present economic climate, this study reinforces the importance of prevention and treatment of alcohol and drug disorders, and can serve as a benchmark for future studies on the etiology of homelessness.

0873

PSYCHIATRIC CORRELATES OF PERCEIVED ALCOHOL STIGMA IN A NATIONALLY REPRESENTATIVE SAMPLE

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Introduction: The construct of perceived alcohol stigma (PAS) reflects the extent to which individuals expect that negative evaluations and behavioral reactions occur towards persons with current or prior alcohol use disorders (AUDs). Research has found that perceived stigma of alcohol and substance use disorders (SUDs) is associated with lower mental health functioning and higher depression scores among those with SUDs. However, we are aware of no work that has examined the relationship between PAS and the presence of DSM-IV psychiatric disorders, including AUDs. Thus, we examined the relationship between PAS and lifetime DSM-IV psychiatric disorders in a sample of persons with and without lifetime AUDs.
Method: We analyzed data from 34,653 respondents of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) who completed Wave 1 and Wave 2 interviews. Wave 2 included the 12-item alcohol-adapted Perceived Devaluation-Discrimination (PDD) scale to assess PAS (α=0.82). DSM-IV lifetime psychiatric and SUDs (excluding AUD) were collapsed into four categories of internalizing only (IO), externalizing only (EO), both internalizing and externalizing (BIE), and neither internalizing nor externalizing (NINE) disorders. AUD status was represented by a separate hierarchical variable that captured lifetime AUD, alcohol consumption, and alcohol treatment history. We used linear regression to examine the relationship between PAS (dependent variable) and disorder status variables while controlling for sociodemographic characteristics, family alcohol problem history, and closeness to persons with alcohol problems.
Results: Persons with IO (b=0.77) and BIE (b=0.68) had significantly higher levels of PAS than persons with NINE (p<0.01), whereas persons with EO did not have higher PAS. Lifetime abstainers had higher levels of PAS than those who drank but never met AUD criteria (b=1.63), whereas recovered persons (b=–0.77) and those with prior alcohol treatment (b=–1.57) had lower PAS.
Conclusion: The positive association between PAS and internalizing disorders is consistent with common clinical presentations among those with mood or anxiety disorders (e.g. rumination, excessive concern about others' perceptions). The relationship between PAS and AUD/drinking status requires further consideration; for example, lifetime abstainers may perceive more stigma due to religious concerns, personality characteristics, or family experiences.

0874

SOCIAL NETWORKS OF PERSONS WITH ALCOHOL USE DISORDERS, MOOD DISORDERS AND CO-OCCURRING DISORDERS

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Aims: Social networks are an important tool in illness management and health recovery. Here, we examine the social network index measure (SNI) among persons in the National Epidemiologic Survey of Alcohol Related Conditions (NESARC).
Methods: Data is from Wave 2 of the NESARC. From the structured diagnostic interview (AUDADIS-IV), those with a 12-month alcohol use disorder (AUD), a 12-month mood disorder (MD) (Grant et al., 2004), and a 12-month co-occurring AUD and MD were examined, in comparison to the remainder of the NESARC sample. The SNI examined the frequency of persons seen or spoken to every 2 weeks, and sociodemographic variables. Analyses were completed in STATA (v12), with Taylor series estimation methods using sampling weights provided in the NESARC to obtain standard error estimates for the population.
Results: Poisson regression analysis showed the SNI of persons with 12-month AUD (M=20.57, S.E.=0.5) was significantly higher than the general NESARC sample (M=19.5, S.E.=0.2). Further, persons with 12-month MD (M =16.3, S.E.=0.4) reported a significantly lower SNI than both the general NESARC sample and persons with 12-month AUD. Persons with co-occurring 12-month AUD and MD (M=15.3, S.E.=1.1) reported a significantly lower SNI than both the general NESARC sample and persons with 12-month AUD. When examining predictors of SNI among persons with co-occurring 12-month AUD and MD, those with no high school education reported a lower SNI, compared to those with more than high school education, (b = −0.5, S.E.=0.2). Women reported a lower SNI compared to men (b = −0.3, S.E.=0.1). Finally, those reporting $40K-69K of annual income (b =0.4, S.E =0.1) and those reporting over $70K annual income (b = 0.5, S.E.=0.2) reported a higher SNI compared to those reporting $0–19K annual income.
Conclusions: Persons with MD and co-occurring AUD and MD reported the lowest SNI among our sample. Additionally, among persons with a co-occurring AUD and MD, those with lower education, women, and low annual income reported a significantly lowered social network index. Results suggest that with a focus on systems-thinking approaches to mental health, further attention is needed to increase potential for families, friends and groups to better assist vulnerable individuals in recovering from or coping with mental illness and addiction, especially among those with MD and co-occurring AUD and MD.
This project was supported by Grant T32 AA007477-21 from the NIAAA and NIH.

0875

TESTING A GENERAL MODEL OF EMPLOYEE ALCOHOL USE AND WORKPLACE PRODUCTIVITY AMONG U.S. WORKERS

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To extend past research that has persistently oversimplified the process linking employee alcohol use and workplace productivity, the present study provides the first test of a detailed model developed by Frone (2004, 2012). The model simultaneously considers (a) the distinction between alcohol use and impairment, (b) the context of alcohol use and impairment (off-the-job vs. on-the-job), (c) the distinction between outcomes of off-the-job alcohol impairment (absenteeism, tardiness) and outcomes of on-the-job alcohol impairment (leaving work early, task performance, job dedication, coworker assistance), and (d) the broad role of possible confounding factors (demographics, deviance proneness). Mplus was used to test the model using a national probability sample of 2,364 employed adults. Three models were estimated. Model 1 contained the hypothesized direct and indirect relations among the alcohol use and productivity variables. Model 2 controlled for eight demographic covariates. Model 3 controlled for the demographic covariates and deviance proneness. The results supported the hypothesized links in Model 1. Off-the-job use was positively related to off-the-job impairment. Partially supporting the model, off-the-job impairment was positively related to tardiness, but was unrelated to full-day absenteeism. Further supporting the model, on-the-job use and off-the-job impairment were positively related to on-the-job impairment. Finally, on-the-job impairment was positively related to leaving work early and negatively related to task performance, job dedication, and coworker assistance. These relations were still significant after controlling for the demographic variables. However, when deviance proneness was added to the model, the relations of on-the-job impairment to all three job performance outcomes (task performance, job dedication, coworker assistance) were no longer significant. The present results largely supported the model in terms of employee alcohol use and work attendance. However, the relations between employee alcohol use and job performance were spurious due deviance proneness. This study suggests that developing an understanding of the processes linking employee alcohol use to workplace productivity needs to consider multiple dimensions of alcohol use and impairment, multiple dimensions of productivity, the contextual match between alcohol impairment and specific productivity outcomes, and the confounding influence of employee personality.

0876

PRESSURE TO REDUCE DRINKING AND REASONS FOR SEEKING TREATMENT

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Objective: Individuals with alcohol problems often receive interpersonal or legal pressure to change their drinking. However, it is unclear how often such pressures influence individuals to enter treatment.
Method: A secondary analysis was conducted using four National Alcohol Surveys (NASs) collected at 5-year intervals between 1995 and 2010. Individuals who sought alcohol treatment (N=476) were interviewed about heavy drinking over their lifetime, whether they ever received pressure from six different sources (spouse, family, friends, doctor, work and police), and queried about six potential reasons for seeking treatment (legal/felt forced, quit/cut down, resolve work/finances, to improve relationships, well-being, health). Respondents were asked to indicate all reasons for treatment seeking and to choose a primary reason.
Results: Over 90% of the sample received pressure about their drinking from at least one source. The reasons cited for seeking treatment did not change significantly over time with the exception of increases in the desire to resolve employment issues and to cut down on drinking. Overall, thirty-four percent identified legal/felt forced as their primary reason for seeking treatment. Other primary reasons included a desire to improve relationships (25%) and health (15%). When asked to indicate all reasons for entering treatment, 46% endorsed five or more reasons and legal/felt forced was included as a reason by 74%. Although pressure from physicians and work was common, such pressures were rarely reported to be the primary reason for seeking treatment. When pressure was received from police it tended to be identified as the primary reason for seeking treatment.
Conclusions: Study findings make clear that external pressure is an important reason why individuals seek treatment. Thus, public policies or advocacy that can encourage pressure to facilitate help seeking are to be recommended. Additionally, our results suggest that individuals report multiple reasons for seeking treatment and future research should assess pathways between receipt of pressure from different sources, recognition of different types of problems, and reasons given for seeking treatment. Supported by grants P50 AA005595 and R21 AA018174

0877

DUI OFFENDERS: WHO IS OVERLOOKED IN MANDATING OFFENDERS TO TREATMENT?

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Aim: Driving under the influence (DUI) of drugs is increasing, but little is known about the ways in which DUI offenders who are dependent on alcohol or drugs are identified and referred to substance abuse treatment.
Methods: This is an analysis of 42,763 unduplicated admission records of individuals who reported past-year DUI arrests entered treatment programs funded by the Texas Department of State Health Services between 2005 and 2009. Statistical methods include t-tests and chi squares, with significance set at .05.
Results: Primary referral sources included DUI probation (44%), non-DUI probation or court services (17%), self-referral (10%), and family and friends (3%). The referral source varied by substance problem: 54% of those with alcohol problems were referred by DUI probation as were 29% of marijuana, 25% of powder cocaine, and 23% of methamphetamine clients. Other court sources and non-DUI probation referred 45% of marijuana, 27% of powder cocaine, and 23% of methamphetamine clients. In comparison, 34% of heroin, 24% of other opiate, and 20% of crack cocaine clients were self-referred. The impaired drivers differed not only on the way they came to treatment, but also by socio-demographic characteristics and levels of severity based on their Addiction Severity Index scores. .
Conclusions: While impaired drivers with a primary problem with alcohol were most likely to be referred by DUI probation officers, those with problems with drugs other than heroin, other opiates, and crack cocaine were referred through other court and probation programs, which could indicate they were handled for crimes such as drug possession or crimes to support their habits rather than for DUI and that their drug problems were not identified during their DUI adjudication. Heroin, other opiates, and crack cocaine clients were most likely to be self-referrals. The characteristics of these non-DUI referrals may indicate the individuals with problems with drugs other than alcohol are not being screened for drug problems at their DUI arrest. This could occur if the screening and assessment instruments focus on alcohol problems. With the increasing prevalence of drugged driving, it is important for the justice system which handles DUI offenders to use instruments which assess both alcohol and drug problems.

0878

AL-ANON NEWCOMERS' REASONS FOR INITIATING ATTENDANCE: CONCERNS ABOUT THE PROBLEM DRINKER

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Al-Anon Family Groups is a 12-step mutual-help program used frequently by people who are concerned about a loved one's alcohol use. While there are 24,000 Al-Anon groups worldwide, little is known about the specific concerns that motivate people to initially attend Al-Anon meetings. The current study seeks to examine the reasons individuals first attend Al-Anon.
A sample of 372 new Al-Anon members (attending for six months or less) was recruited from 236 Al-Anon groups across the U.S. to complete a survey. The sample was 83.3% female and 93.5% white, with a mean age of 46.8 years (SD=13. 5). The survey contained 16 potential problems pertaining to the Al-Anon trigger (the problem drinker); respondents indicated whether each influenced their decision to attend Al-Anon meetings.
Participants' Al-Anon triggers were 71.5% male, with a mean age of 43.1 years old (SD=15.0). The most frequently endorsed concern about the trigger that prompted Al-Anon attendance was the trigger being depressed or moody (81.1%), followed by the trigger missing what is important in life (79.6%), and being stressed, tense, anxious, or unable to relax (77.7%). Concerns specific to the trigger's drinking behaviors were endorsed somewhat less often as a reason for initiating Al-Anon attendance, and included the trigger's drinking causing problems for loved ones (64.5%), the trigger drinking too much, too often (63.2%), and drinking such that serious harm could happen to him or her (58.3%) or to someone else (58.3%).
These findings suggest that while the trigger's drinking behavior does influence Al-Anon newcomers' decision to attend meetings, the trigger's emotional well-being may be of even greater concern. This research is helpful to understanding more about newcomers' state of mind when first attending Al-Anon meetings and can be used to further tailor Al-Anon's approach to new members. Additionally, treatment providers should consider that emotional concerns about a loved one who has alcohol problems are common among Al-Anon newcomers, and research about Al-Anon can encourage them to make referrals to local groups.

0879

INVESTIGATING THE LINK BETWEEN AL-ANON FAMILY GROUP MEMBERSHIP AND INTIMATE PARTNER VIOLENCE VICTIMIZATION

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Intimate partner violence (IPV) victimization is often reported by the spouses and significant others (SO's) of problem drinkers. Al-Anon Family Groups (AAFG) is a self-help venue in which SO's may seek support related to the drinking behavior of their family member or loved one. This study investigated the mental health correlates of IPV victimization among SO's in AAFG reporting past versus current physical, emotional, verbal, and/or sexual IPV perpetrated by the drinker for whom they were attending meetings; as well as the link between AAFG membership and current IPV victimization. First, we hypothesized that individuals no longer experiencing IPV would report more years of membership in AAFG. Second, because previous research suggests that IPV victimization is correlated with mental health problems, we hypothesized that those reporting current IPV victimization would be more likely to report depression and a lifetime alcohol or substance use diagnosis, compared to SO's with no current IPV. The data were collected as part of a national survey conducted by Al-Anon Family Groups World Service Office in 2009. The sample consisted of 1082 individuals (84.7% female; mean age = 55.21), experiencing past (86%) or current (16%) IPV. A regression analysis revealed that, after controlling for prior treatment history, participants reporting current IPV had fewer years of AAFG membership compared to those with past IPV (β= -.15; $p < .01$). A chi-square test revealed a significant association between current IPV and having had a substance or alcohol use diagnosis in the past ($\chi^2 = 5.5$; $p = .02$). Results also revealed that 73% of participants currently experiencing IPV also reported feelings of depression before attending AAFG, whereas a significantly smaller percentage (64%) who reported feelings of depression before AAFG were no longer experiencing IPV victimization. Overall, attendance in AAFG may be effective at reducing SO's risk of experiencing IPV perpetrated by the problem drinker in their life. Findings also suggest a link between current IPV victimization and negative mental health correlates experienced before attending AAFG. More research is needed to identify the components of AAFG membership that are beneficial to members and their association with the occurrence of IPV victimization.

0880

THE RELATIONSHIP BETWEEN ALCOHOL USE AND INTERPERSONAL STRESSORS IN DAILY LIFE

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Though people with borderline personality disorder (BPD) tend to experience daily events as especially stressful, interpersonal relationships may constitute their main source of stress. The relationship between BPD and interpersonal dysfunction is reflected in the diagnostic criteria *unstable interpersonal relationships* and *frantic efforts to avoid abandonment*, but has been under-studied. BPD is also characterized by impulsive behaviors (APA, 2000). One indicator of impulsivity is excessive alcohol use. Individuals with BPD may drink alcohol in in such a way that interpersonal stress is exacerbated or they may engage in impulsive behaviors as a result of interpersonal stress. This study investigates the relationship between alcohol use and interpersonal stressors using Ecological Momentary Assessment (EMA; Stone & Shiffman, 1994). EMA yields data based on subjects' assessment of environmental phenomena as they occur. BPD outpatients were given electronic diaries for 28 days. The participants were signaled 6 times per day to report on interpersonal events, alcohol use, and other behaviors. Fifty-two female BPD participants consumed alcohol during the study period. These participants reported a mean of 6.81 drinking days, 6.94 disagreement days, and 6.73 rejection days. A series of HLM analyses demonstrated that lagged number of drinks and current alcohol use disorder diagnosis are associated with rejection experiences reported by an individual over and above time, measured as hours since waking. Disagreement experiences were not associated with alcohol use. Though these analyses demonstrate that drinking behavior is associated with rejection, it is still unclear what may drive this relationship among individuals with BPD. Future research examining interpersonal dysfunction associated with alcohol use should also measure alcohol use of close others or the broad social network. Dyadic EMA studies have become increasingly common in the last decade. These kinds of studies can shed light on interpersonal processes in psychopathology.

0881

DISTAL AND PROXIMAL RISK FACTORS FOR NON-PARTNER VIOLENCE IN A SUBSTANCE USE DISORDER TREATMENT SAMPLE

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The majority of studies of violence in substance use disorder (SUD) treatment settings focus on partner violence although there is evidence that non-partner violence (NPV) is also a common problem. This study examines the role of parental history of alcohol use problems, childhood violence perpetration and victimization with peers, symptoms of psychiatric distress and alcohol and drug use in non-partner violence perpetration (NPVP) and victimization (NPVV) among a SUD treatment sample.

This sample included 193 participants reporting past year violence who were recruited from SUD treatment programs (ages 17–63; 76% female; 49% Caucasian, 37% African American). This study focused on baseline measures of proximal (e.g., alcohol use, marijuana use, cocaine use, and symptoms of psychiatric problems) and distal risk factors (e.g., history of parental alcohol misuse, childhood violence perpetration and victimization) in addition to past year NPVP and NPVV. Multivariate, multiple mediation analyses were conducted using Hayes and Preacher's (2011) approach (SPSS MEDIATE macro) in order to examine the influence of distal risk factors on proximal risk factors in non-partner violence.

In terms of direct effects of proximal and distal risk factors, heavy drinking ($p<.05$) and childhood aggression ($p<.001$) were positively associated with NPVP. Indirect effects were found with history of alcohol misuse by fathers positively associated with cocaine use, which was associated with more NPVP. Childhood aggression was associated with more psychiatric problems which was in turn associated with more NPVP. Parallel direct effects for NPVV were found for heavy drinking ($p<.01$) and childhood victimization ($p<.01$). History of father's alcohol misuse was again associated with more cocaine use, which was associated with more NPVV. Finally, childhood victimization, non-violent childhood conduct problems and history of mother's alcohol misuse were all associated with more psychiatric distress, which was associated with more NPVV.

The findings revealed similar patterns of predictors for NPVP and NPVV. For SUD samples, assessing family history of alcohol problems as well as childhood aggression and victimization could be useful in identifying those at risk for NPV. Further, the results suggest that the treatment needs of those involved with NPV include addressing psychiatric distress in addition to substance use (alcohol and cocaine). (Supported by NIDA R01 DA017295 & T32 DA007267)

0882

GENDER DIFFERENCES IN SUBSTANCE USE AND SEXUAL HARASSMENT PERPETRATION AMONG AFRICAN AMERICAN ADOLESCENTS

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Aim: The current study examined gender differences in substance use and sexual harassment perpetration among African American adolescents.

Methods: We analyzed data from the Secondary Student Life Survey, a school-based study of 2,744 middle- and high-school students. This study utilizes Wave 2 of this dataset, occurring when the participants were ages 11–19 years (M age = 14.9, SD=1.67). The analytic sample was comprised of those who self-reported their race as African American (20.4% of full sample), yielding a total of 840 respondents (51.7% female). Sexual harassment perpetration was defined as committing at least one incidence of unwanted heterosexually-related touching, name-calling, commenting, or teasing in the previous 12 months. Alcohol use was assessed with items asking participants if they ever had more than a few sips of alcohol in their lifetime, in the previous year, and/or the past 30 days. Cigarette use was assessed by asking participants if they ever smoked a cigarette in their lifetime, in the previous year, and/or in the previous 30 days.

Results: Chi square analyses indicated that for all measures of cigarette use, no significant differences were found between males and females. However, more females (46.6%) reported lifetime alcohol use than males (34.9%, $p< .01$). Considering sexual harassment perpetration, 21.5% of male respondents reported perpetrating at least one incident of unwanted sexual harassment in the previous 12 months; 15.3%, of females reported the same. Logistic regression analyses showed that female perpetrators were over three times more likely than perpetrating males to report ever having smoked cigarettes (OR = 3.6, 95% CI = 1.67–7.94). Conversely, male perpetrators were almost two times as likely as female perpetrators to report any lifetime alcohol use (OR = 1.9, 95% CI. 1.11–3.48). No other significant associations emerged.

Conclusions: Gender differences in lifetime substance use are more pronounced among African American adolescent perpetrators of sexual harassment. Specifically, African American males who perpetrate had higher odds of lifetime alcohol use than females, while their female counterparts report higher lifetime cigarette use. It may be that lifetime cigarette and alcohol use are gender-specific markers for the constellation of risk and troubled behavior among male and female adolescents.

This research was supported by NIDA Training Grant T32-DA-007267-16.

0883

RELATIONSHIP BETWEEN IMPULSIVITY, AGE OF ONSET OF ALCOHOL USE, AND ALCOHOL-RELATED SEXUAL CONSEQUENCES IN HIGH SCHOOL SENIORS

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Age of onset of alcohol use has been previously identified as a strong predictor of alcohol use and related consequences among adolescents and young adults (Grant et al., 2001; Hingson et al., 2006). Additionally, studies have found impulsivity to be positively related to worse alcohol outcomes (Balodis et al., 2009; Henges & Marczinski, 2011) and earlier onset of drinking (Anderson & Brown, 2010; Malmberg et al, 2010). Previous research has also found a relationship between impulsivity and non-alcohol related risky sex (Deckman & Dewall, 2011). However, little research has examined the relationships between age of onset of alcohol use, impulsivity, and alcohol-related sexual consequences in a pre-college age group. The present study examines these relationships in a sample of high school seniors (n=289). It was hypothesized that impulsivity would be positively related to alcohol-related sexual consequences, and that this would be moderated by age of onset of alcohol use, such that individuals with an earlier age of onset and higher impulsivity would report more alcohol-related sexual consequences. Participants (age range: 17–18, 52% female) completed self-report measures of age of onset of alcohol use, impulsivity and alcohol-related sexual consequences as part of a larger baseline assessment during the fall of their senior year of high school. Multiple regression analyses found a significant main effect for impulsivity, such that individuals with higher impulsivity scores experienced more alcohol-related sexual consequences (b=.12, p=.001). No main effect was found for age of onset of alcohol use on alcohol-related sexual consequences. Additionally, results showed a significant interaction between impulsivity and age of onset of drinking (b=-.05, p<.05) in the prediction of alcohol-related sexual consequences. Specifically, the positive relationship between impulsivity and alcohol-related sexual consequences was stronger for participants with an earlier age of onset of alcohol use. These results suggest that age of onset of alcohol use and impulsivity are important factors to consider when addressing alcohol-related sexual consequences in this age group. This research was supported by NIAAA award #U01 AA018276 awarded to Dr. Mary Larimer & Dr. Mats Berglund.

0884

ALCOHOL AND SEXUAL AGGRESSION IN MALE COLLEGE STUDENTS

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Male college students who perpetrate sexual aggression consume more alcohol than their non-aggressive peers. However, it is not clear whether alcohol plays a causal or facilitative role. The relationship between alcohol and sexual aggression may reflect a common third variable (e.g., antisocial behavior) or the fact that alcohol tends to be present in situations in which sexual aggression is more likely to occur. The present analyses considered 1) whether the alcohol-sexual aggression relationship results from an underlying personality factor, 2) whether alcohol use in general or within various contexts (e.g., parties, dates) predicts perpetration of aggression, and 3) whether expectancies about alcohol and sex predict perpetration. Freshman males (N =997, 69% response rate) were recruited via email to complete a web-based survey. As expected, men who perpetrated sexual aggression during the fall semester (N=59, 6%) differed significantly from non-perpetrators on frequency of heavy episodic drinking, frequency of attending parties, drinking at parties, drinking on dates, hookups, antisocial behavior, self-control, sex-related alcohol expectancies (disinhibition and enhancement) and hostility toward women; they were not more likely to date or be in a relationship. Multivariate analyses revealed significant effects of antisocial behavior and (low) self control on sexual aggression, which reduced the effects of heavy episodic drinking, party attendance and party consumption to non-significance. However, quantity of alcohol consumed in dating situations remained a significant predictor of perpetration. Moreover, regardless of which alcohol variables were considered, the expectancy that alcohol disinhibits sex (but not expectancies regarding sexual enhancement) predicted sexual aggression. Findings suggest that underlying personality factors account for much of the relationship between college men's alcohol use and sexual aggression; however, drinking on dates and believing that alcohol disinhibits sex, had unique effects on the likelihood of perpetration.

0885

AN EVENT-LEVEL ANALYSIS OF THE RELATIONSHIP BETWEEN ALCOHOL USE AND SEX-RELATED CONSEQUENCES: DOES IT VARY BY GENDER OR PREVIOUS SEXUAL VICTIMIZATION?

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Heavy drinking among college students has been linked to numerous consequences, including risky sexual behaviors. While the link between drinking and sex-related consequences has been demonstrated consistently at the global level, less is known about how the relationship between drinking and sex-related consequences functions across specific drinking occasions. Furthermore, there is a gap in the literature with respect to how between-person factors, such as gender and previous sexual victimization, affect event-level associations between drinking and sexual consequences. The current study used multilevel modeling to assess the event-level covariation between alcohol use and sex-related consequences while accounting for gender and past year sexual victimization. First-year students (n = 290) provided diary data on weekend drinking and sex-related consequences on Friday and Saturday nights over six weekends during their first semester on campus, resulting in 12 measured drinking occasions. Both between- (β = .02, p < .001) and within-person associations (β = .02, p = .03) between alcohol use and sex-consequences were significant, such that higher consumption was associated with more consequences on average and across drinking occasions. Previous victimization also was significantly associated with experiencing more sex-related consequences (β = .23, p = .01). The interaction of between- and within-person effects was not significant, suggesting that the relationship between alcohol use and consequences on a given event was similar, regardless of one's typical drinking pattern. Neither gender nor previous victimization moderated the association between drinking and consequences. Findings suggest that typical heavy drinking behavior, event-level heavy drinking occasions, and previous sexual victimization are associated with increased sex-related consequences over time. Taken together, these findings suggest valuable entry points for prevention efforts, supporting a continued focus on heavy episodic drinkers and an increased focus on recent victims of sexual assault.

0886

GENERAL MOTIVATIONAL ORIENTATION AND ITS ROLE IN IPV AND ALCOHOL CONSUMPTION

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Considerable research has demonstrated a link between intimate partner violence (IPV) perpetration and victimization and alcohol consumption. Problem drinking and IPV perpetration are most prevalent among young adults in their early to mid 20s. More specifically, IPV perpetrators are five times more likely to use alcohol, when compared to nonperpetrators. The present research was designed to evaluate the relationship between personality characteristics, reasons for drinking, alcohol consumption, and perpetration/victimization of IPV. Specifically, we were interested in examining the influence of motivational orientation (SDT) on alcohol consumption and IPV perpetration. Participants included 780 undergraduates who completed self-report alcohol related measures (quantity and frequency, RAPI, as well as drinking motives), a measure assessing IPV perpetration/victimization, as well as measures regarding general motivational orientation on five different occasions. Exploratory analyses suggest that IPV victimization at wave one was correlated with alcohol related measures at each subsequent wave. Further, exploratory analyses propose that there may be a relationship between individuals with a controlled personality orientation, alcohol consumption, and the perpetration of IPV. A controlled motivational orientation was strongly related to alcohol consumption at all time point as well as perpetration of IPV at all time points. These preliminary findings have the potential to contribute to the growing body of literature dedicated to better understanding factors that influence alcohol consumption and IPV perpetration. This research demonstrates a step toward understanding an individual's personality orientation, instances of IPV, and alcohol consumption.

0887

DESCRIPTIVE CHARACTERISTICS OF A SAMPLE OF NON-TREATMENT-SEEKING FEMALE RAPE VICTIMS WITH AND WITHOUT AN ALCOHOL USE DISORDER

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This study descriptively reports on the baseline characteristics of a sample of non-treatment-seeking female rape victims with and without a DSM-IV alcohol use disorder (AUD),who are part of an ongoing prospective (6-month) assessment of help-seeking outcomes. We examined associations among assault-related factors, drinking behavior, coping mechanisms, depression, and PTSD severity. Seventeen non-treatment-seeking women who reported a rape in the past five years (Mean age = 30) completed the Beck Depression Inventory (BDI), the Post-Traumatic Stress Disorder Checklist (PCL-C), the Coping Strategies Scale (CSS), the 90-day Timeline Follow-Back, the alcohol module of the SCID, and an assessment of the most recent rape. Sixty percent of the sample met criteria for a DSM-IV AUD. Women with an AUD consumed, on average, 5 drinks per drinking day and engaged in heavy alcohol consumption (5+ drinks in one day) on 17% of the days. Women with no AUD consumed2 drinks per drinking day and engaged in heavy drinking less than 1% of the time. In terms of assault-related characteristics, 66% experienced at least one unwanted sexual intercourse episode in their lifetime after consuming too much alcohol. Half of the sample reportedly consumed alcohol at the time of the most rape incident. Pearson correlations showed that quantity of alcohol consumed in the past 90-days was significantly correlated with level of incapacitation due to alcohol at the time of the most recent rape (r = -.57, p < .05). Women with an AUD reported higher PTSD (M = 56) and depression (M = 27) severity than women with no AUD (M = 51 for PTSD; M = 21 for depression), although levels of psychiatric severity were high regardless of AUD diagnosis. Women with an AUD were more likely to use emotion-focused coping (M = 3.21) relative to women with no AUD (M = 1.96), and emotion-focused coping was significantly and positively related to drinking frequency (r = .65, p < .01). In terms of post-rape outcomes, regardless of AUD status, the majority of women acknowledged the most recent incident as a rape (62%) and very few (10%) reported the incident to police. Findings suggest there may be links between alcohol use and emotional reactivity among female rape victims with a co-occurring AUD and that intensity of drinking may place a woman at greater risk for experiencing an alcohol-related sexual assault and negative psychological consequences thereof.

0888

THE 'DOUBLE-WHAMMY' EFFECT OF COMBINED SMOKING AND DRINKING UPON EVERYDAY PROSPECTIVE MEMORY

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The combined effect of drinking alcohol and smoking has been found to produce greater deficits in memory, when compared to those who just consume alcohol alone, or non-drug users. No research to date has compared whether polydrug (combined alcohol and smoking) users perform more poorly than an alcohol only group on everyday prospective memory (PM: memory for future intentions/actions).
The current study explored this by comparing a group of polydrug users (those who smoked and drank alcohol) with a single use group (those who used only alcohol) on the Cambridge Prospective Memory Task (CAMPROMPT) which is a standardised measure of both event-based and time-based PM. An in-house Recreational Drug Use Questionnaire measured recreational drug use; the Hospital Anxiety and Depression Scale measured generalised anxiety and depression; and the National Adult Reading Test measured IQ. After screening out those who used any illegal substance (e.g. cannabis, ecstasy) and after controlling for any between-group differences in terms of age, the amount of alcohol used per week, the total number of years spent drinking, time since last drink consumed (hours), anxiety and depression, and IQ, the results revealed that the polydrug use group performed significantly worse on the CAMPROMPT when compared with the single-drug group. It is concluded that the combined effect of drinking and smoking damages PM to a greater extent than just drinking alcohol alone.

0889

THE IMPACT OF BINGE DRINKING UPON EVERYDAY PROSPECTIVE MEMORY
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Binge drinking (BD: defined as males drinking 8/more units and females 6/more units on at least one session per-week) has been associated with everyday memory problems in the past, such as prospective memory deficits (PM: memory for future intentions/actions). This may be an important finding and requires replication using a standardised measure of PM. The current study compared 28 BDs and 28 non BDs on their scores on the Cambridge Prospective Memory Task (CAMPROMPT) which is a standardised measure of both event-based and time-based PM. Drug use was assessed using an in-house Recreational Drug Use Questionnaire; the Hospital Anxiety and Depression Scale measured generalised anxiety and depression; a strategy-scale measured strategy use; and the National Adult Reading Test measured IQ. After controlling for any between-group differences in terms of age, the total number of years spent drinking, time since last drink consumed (hours), anxiety and depression, strategy-use and IQ, the results revealed that BDs exhibited reduced function on time-based PM, but not event-based PM, when compared with NBDs. BDs exhibit selective impairments on time-based PM; this deficit is a new finding in terms of the neuropsychological sequelae associated with BD.

0890

DISRUPTION OF SLEEP RELATED MEMORY CONSOLIDATION BY AN ALCOHOL BINGE SUBSEQUENT TO LEARNING, IN LIGHT DRINKING COLLEGE STUDENTS
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Sleep is critical for the consolidation of memory and newly learnt tasks. Alcohol ingestion disrupts sleep and also disrupts memory processes, specifically when the learning of tasks occur whilst intoxicated. This study sought to examine if alcohol consumption after learning a motor task disrupts sleep related consolidation, after a night of sleep and once alcohol had been eliminated from the system. It was hypothesized that while there would be no difference in motor (procedural memory) task performance prior to alcohol consumption, alcohol would reduce the sleep related memory consolidation when tested the following morning once alcohol had been eliminated. Seven low drinking (2.71±2.27 drinks/week in the previous month) participants (18.86±0.90 years; 3 female) spent an adaptation night in the sleep laboratory at The University of Melbourne followed by an experimental night in one of two counterbalanced conditions. In the first condition they learned a procedural motor task 2 hours prior to consuming an alcoholic beverage which was consumed over 30 minutes 4 hours after a standard meal. Alcohol was dosed by body weight and percentage body water to a peak blood alcohol concentration (BAC) of 0.09%. In the second condition they received a placebo beverage with the same timeline. Participants were retested on the motor task after an eight hour sleep opportunity at which time BAC had returned to 0.00%. Performance on the procedural task used has previously been shown to be enhanced by sleep following the learning phase (Walker et al. *Learn Mem.* 2003, 10:275–284). Participants had a BAC of 0.076±0.01% in the alcohol condition compared to 0.000% in the placebo condition at lights out, 30 minutes after finishing the beverage. There was no difference in performance after the motor task learning phase between alcohol or placebo conditions (p=0.993). Sleep increased performance in both placebo (p=0.003) and alcohol (p=0.008) conditions, however the performance increase after sleep was lower after alcohol consumption compared to placebo (p<0.05). These preliminary data indicate that alcohol consumption prior to sleep may disrupt the beneficial effect of sleep on procedural memory.
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0891

BINGE DRINKING COLLEGE STUDENTS SHOW ENHANCED IMPLICIT AND EXPLICIT MEMORY FOR ALCOHOL COMPARED TO NEUTRAL WORD CUES
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It is well established that acute alcohol challenge significantly impairs explicit memory while sparing implicit memory processing for neutral word cues in experimental paradigms wherein both learning and retrieval of stimuli took place under the same intoxication state (Ray & Bates, 2006; Tracy & Bates, 1999). Few studies have examined the effects of alcohol on explicit memory for emotional stimuli and those that did varied state (no-alcohol, alcohol) between learning and retrieval conditions (Knowles & Duka, 2004), and showed that alcohol impaired explicit memory. The present study examined how explicit and implicit memory for alcohol, emotionally positive, negative and neutral word cues was affected during acute alcohol intoxication where both learning and retrieval took place during alcohol intoxication. Participants were 75 (38 women) undergraduate students whose average quantity of alcohol consumed per drinking occasion met binge drinking criteria (NIAAA, 2004). Participants were randomly assigned to an alcohol-challenge, a placebo-challenge, or a told and received no-alcohol beverage group. Each participant took part in a word cue study phase and a memory test phase that consisted of four tasks: explicit free recall, explicit recognition memory, implicit repetition priming, and implicit or explicit category exemplar generation. Here we focus on the free recall and repetition priming tasks performance. Compared to the no-alcohol and placebo-challenge groups, individuals in the alcohol-challenge group showed impaired free recall (p<.01), but not repetition priming of alcohol, emotional and neutral word cues. Free recall was enhanced for the alcohol-related words compared to the emotional and neutral words (ps < .01). Repetition priming was enhanced for the alcohol-related words compared to the neutral words (p< .01). No gender differences in memory performance were observed. Results suggest that in binge-drinking college students, alcohol-related verbal information was more salient in semantic memory than emotional or neutral verbal information, and that this processing advantage of alcohol information was present in both explicit and implicit memory systems. Future studies are needed to examine alcohol-related memory in students with varying drinking patterns. This research was supported by NIAAA grants R01 AA015248 and K02 AA00325.

0892

RELATIONSHIP BETWEEN PRIOR BRAIN INJURY AND ALCOHOL CONSUMPTION IN COLLEGE STUDENTS
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This study examined whether the occurrence of a prior brain injury was related to current patterns of alcohol consumption, and whether the existence of a prior brain injury exacerbated the effects of alcohol on cognition. Participants were college students ages 18–21 (N=50; 52% female; 80% Caucasian). Prior brain injury was identified via the HELPS screening tool (Picard, Scarisbrick, & Paluck, 1991). Binge drinkers were identified with the Timeline Follow-Back (TLFB; Sobell et al., 1992) . Participants were administered a neuropsychology battery using the Cogstate™ (CogState Ltd.) and JAva NEuropsychological Test (JANET) (Glahn et al., 2007). The Cogstate consisted of: the One Back; the Two Back; the Groton Maze Learning task; Visual Paired Associate Learning. The JANET included the following tests: the Digit Symbol task; the Balloon Analogue Risk Task (BART); the Penn Conditional Exclusion Test (PCET).
Cognitive measures were categorized a priori as those requiring complex attention/speed of processing (One Back; Two Back; Digit Symbol; PCET), those requiring learning/memory (Groton Maze Learning Test; Visual Paired Associate Learning), and those requiring impulse control (BART). Two by two by three analysis of variance (ANOVA) (brain injury, not brain injury) x (binge, no binge) x cognitive domain revealed that: (a) students who reported prior brain injury (N=20) performed more poorly than those no brain injury on measures of attention and impulse control; (b) students who binge (N=18) performed more poorly in all cognitive domains than those who do not binge, and (c) binge drinking students with a previous brain injury showed a greater decrement on tests of attention than those with binge drinking only and those without brain injury. A similar pattern was found for impulse control. No such interaction was found for learning and memory.
These data suggest that individuals with a history of brain injury may be at particular risk for increased cognitive decrements if they also binge. The synergistic effects of brain injury and binge drinking on cognitive functioning has received relatively little attention in college age samples (Graham & Cardon, 2008). The relations among prior brain injury, impulsivity and binge drinking are worthy of further investigation, along with documentation of the natural history of their temporal ordering.

0893

COGNITIVE PROCEDURAL LEARNING IN ALCOHOLISM AND KORSAKOFF'S SYNDROME: ERRORLESS VERSUS ERRORFUL LEARNING

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Errorless learning (EL) has inconsistently been found advantageous in patients with Korsakoff's syndrome (KS), depending on the nature of the processes involved in the task and the to-be learned information. The goal of the present study is to compare errorful (EF) and EL learning of a cognitive procedural task (tower of Toronto task) in alcoholics with and without Korsakoff's syndrome (AL).
Sixty-five control subjects (EF: 36; EL: 29), 32 AL (EF: 16; EL: 16) and 20 KS (EF: 11; EL: 9) matched for age and education performed 40 trials of the tower of Toronto task during 4 daily learning sessions. In the EF condition, participants were required to solve the puzzle as quickly and with the fewer number of disks moves as possible (no cue provided). In the EL condition, the goal and instructions were provided throughout the task. During the three first learning sessions, subjects had to watch the experimenter solve the task while imitating him/her and listening to verbal explanations of the resolution. In the course of the learning sessions, cues and aids vanished so that participants performed the fourth learning session under the same condition as those in the EF condition. Number of moves and solving time were recorded and compared between groups and learning conditions.
There was no effect of learning condition but a group effect on episodic memory (KSWhile EL has been shown to improve the learning of face-name associations or word lists in KS, our results showed no beneficial effect of EL learning of a cognitive procedural task compared with EF learning. Rather, the use of EL learning was to the detriment to KS, who performed lower in the EL condition than in the EF one. These findings suggest that EL learning may not be suitable for new complex procedural learning in KS.
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0894

STUDY OF BRAIN ATROPHY LINKED WITH COGNITIVE PROCEDURAL LEARNING IMPAIRMENT IN PATIENTS WITH CHRONIC ALCOHOLISM

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Cognitive procedural learning is characterized by three phases (cognitive, associative and autonomous), each involving distinct processes. We showed a deleterious effect of episodic and working memory deficits on the cognitive procedural learning dynamics in alcoholism (Pitel et al., 2007). In a PET study conducted in healthy subjects, we demonstrated the involvement of a frontoparietal network including especially the angular region during the cognitive phase (Hubert et al., 2007). Chronic alcohol consumption resulting in frontoparietal brain abnormalities, the present study aims to examine the relationship between brain macrostructural abnormalities and cognitive procedural learning impairment in alcoholism.The tower of Toronto task (TT task) was performed by alcoholic patients (N=31) and age-matched healthy controls (N=31) to measure cognitive procedural learning abilities. The learning of the task was carried out during 4 daily learning sessions (10 trials in each). The subjects' performance on the TT task was assessed in terms of completion time and number of moves needed to complete it. For each variable, learning scores corresponded to the sum of the ten trials in each session. Alcoholics also underwent a Magnetic Resonance Imaging (MRI 1,5T) and brain data were compared to controls using SPM5 software. Correlations were then conducted in the whole brain between completion time on the cognitive procedural learning task and gray matter volume.For the TT task, results showed a significant difference between alcoholics and controls in terms of time and moves. Patients had lower gray matter volume compared to controls in the prefrontal, parietal, temporal, cingulate and occipital cortices, and in subcortical regions and cerebellum. Moreover, we found significant correlations between procedural learning results and gray matter volumes in the prefrontal cortex, postcentral and angular gyri, and in the cerebellum (session 1); in the postcentral, angular and fusiform gyri, thalamus, caudate and putamen nuclei (session 2); and in the angular gyrus, caudate and putamen nuclei (sessions 3 and 4).Our results confirm that alcoholism affects the cognitive procedural learning dynamics (Pitel et al., 2007). Brain data suggest that this deficit is related to abnormalities in the angular gyrus, which was demonstrated as a signpost of cognitive phase of procedural learning (Hubert et al., 2007).

0895

EVIDENCE OF VISUOSPATIAL COMPROMISE OVER 5 YEARS IN ALCOHOLISM-HIV INFECTION COMORBIDITY; RELATION TO DISEASE PROGRESSION

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Visuospatial construction and memory are both compromised with alcoholism; these processes show further impairment in alcoholics who are also HIV infected. Little is known, however, regarding how these functions change over time with continued drinking or changes in immune function (T-cell count) in either single-diagnosis or cormorbid patients. Participants (31 ALC+HIV, 12 ALC, 30 HIV, and 16 healthy controls) in a longitudinal study involving 4 visits spanning 5 years were administered the Rey-Osterrieth Complex Figure (ROCF) test consisting of copy, recall, and recognition measures. Repeated-measures analyses of covariance, with education as a covariate, examined ROCF performance across all subjects and visits. ALC+HIV had significantly worse visuoconstructional scores than all other groups across all visits. In all groups, ability to copy the complex figure initially worsened but then returned to baseline levels at the 5-year test. Deterioration in visuoconstructional ability over 5 years was related to decline in T-cells in ALC+HIV but not in HIV only. While HIV and controls recalled increasingly more figure components over 5 years (evidence of visuospatial learning), ALC and ALC+HIV did not. Decline in visuospatial memory over 5 years was associated with greater alcohol consumption over that interval in ALC but not ALC+HIV. Recognition memory by ALC+HIV was significantly poorer than HIV and controls, with ALC falling in between; no group improved significantly over time. In conclusion, declining immune function over a 5 year interval was associated with increasing compromise in visuospatial construction skills in alcoholism-HIV comorbid patients, whereas continued drinking over that interval was associated with increasing compromise in visuospatial learning in patients with alcoholism alone. That patients with HIV infection alone showed relative lack of compromise in these functions highlights the exacerbating effect of alcoholism in patients with HIV infection.
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0896

FRONTOCEREBELLAR DAMAGE AND EXECUTIVE IMPAIRMENTS IN ALCOHOLICS

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Alcoholism is associated with cognitive deficits and structural brain damage. Previous studies have shown that alcoholism-related brain abnormalities in frontal and cerebellar regions underlie a wide range of neuropsychological impairments. For example, executive deficits, frequently reported in alcoholic subjects, have mainly been related to frontal lobe damage. However, several studies indicated that volume deficits in other nodes of the frontocerebellar circuit may also underlie executive dysfunctions. The goal of the present study was to investigate the role of compromised frontocerebellar pathway on dissociable components of executive functions.
Thirty-two alcoholics performed executive tasks, which evaluated memory search strategies, inhibition, flexibility and manipulation of information. Executive performances in patients were compared with those of 33 control subjects matched for age and education. Patients also underwent structural MRI (1.5T) and volumes of the prefrontal cortices, cerebellum (including both hemispheres and vermis) and thalami were compared with those of a sample of 25 age-matched control subjects drawn from our database using SPM 5. In the alcoholics group, a multiple regression analysis was conducted between executive measures and gray matter volumes in the target regions at $p<0.005$ uncorrected for multiple comparisons and $k=50$ voxels.
Compared to the control group, alcoholics exhibited impaired manipulation of information in working memory and inhibition. Flexibility and memory search strategies were preserved. Furthermore, alcoholics had decreased gray matter volumes in the prefrontal cortices, thalami and cerebellum. On the overall, executive impairments (composite score) correlated with decreased gray matter volumes in the prefrontal cortices. When analyzed component-by-component, flexibility and memory search strategies were linked to gray matter volume in the prefrontal cortex. Impairments in inhibition and manipulation of information in working memory correlated with cerebellar alteration in addition to prefrontal volume deficits.Chronic alcoholism adversely affects executive functioning. The present data confirm that executive impairments arise not exclusively from prefrontal lesions but also from damage of other nodes of the frontocerebellar circuitry.
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0897

ALCOHOL MOOD AND COGNITIVE PERFORMANCE: A PILOT FIELD STUDY
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The effects of alcohol intoxication on aspects of cognitive performance and information processing are well documented. Given the widespread use of alcohol, and current concerns regarding its social impact, there is a surprising paucity of field research in this area. The current pilot study aimed to assess the effects of drinking in a natural setting on aspects of performance. Thirty individuals were approached and tested individually in a bar on the university campus. Each was breathalysed before and following completion of a computerised test battery. Participants provided details regarding alcoholic drinks consumed and length of time since their first drink. They were also invited to record information regarding other recreational drug use. A short test battery was administered on a handheld Newton computer (www.penscreen.com). The battery consisted of a series of psychomotor and cognitive tests previously shown to be sensitive to ethanol intoxication in laboratory studies. This included a maze, handwriting, Serial Sevens and a test of 'self calibration' (the General Knowledge Adaptive test). Visual analogue scales (VAS) were also presented. There were highly significant inter-correlations between measured blood alcohol concentrations, estimated units of alcohol consumed and scores on a 'sober-drunk' VAS ($p < 0.001$ in all cases). The level of intoxication followed similar patterns to those found in laboratory studies, leading to a characteristic shift in the speed/accuracy trade-off which was reflected as production of significantly more errors with no effect on speed across several measures (including maze performance and Serial Sevens). Individuals who were more intoxicated were also significantly less alert. The data suggest that controlled laboratory tests into the effects of alcohol intoxication may have ecological validity. Such findings emphasise the ramifications for alcohol consumption in real-life settings.

0898

DEFICITS IN PROCESSING EMOTIONAL INFORMATION IN LONG-TERM ABSTINENT ALCOHOLICS
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Background: Although research consistently shows that alcoholics have difficulty processing emotional information relative to non-alcoholics, it is unclear whether, and to what degree, this deficit resolves with extended abstinence. We studied the processing of positive, negative, and neutral emotional words in the Affective Go/No-Go (AGN) task in age and gender comparable groups of 35–60 year old non-alcoholic controls, short-term (6–15 week) and long-term (> 1.5 year) abstinent alcoholics.
Method: Signal detection analysis was used to estimate performance on the AGNG task, separating out signal detection sensitivity (d') from decisional response bias (*C*). Two-hundred and ninety three adults (age=47.7 + 7.0; 45.7% Female) were classified into 3 groups: non-substance abusing controls (NSAC; n=82), short-term abstinent alcoholics (STAA; 6–15 weeks abstinent; n=101), and long-term abstinent alcoholics (LTAA; > 1.5 years abstinent; n = 110).
Results: LTAA and STAA had lower signal detection sensitivity (d') than NSAC, but did not differ from each other on d'. There were no differences between the groups on decisional response bias (*C*). Individual differences in d' and *C* were not associated with family history of alcoholism nor lifetime alcohol use density, frequency, or duration.
Conclusions: Chronic alcoholics have impairments in processing emotionally laden information, which do not resolve over years of abstinence. This deficit reflects a general impairment in processing the affective valence of emotionally laden stimuli, and is not a decisional bias toward responding to information of a particular affective valence.

0899

THE EFFECTS OF ALCOHOL AND ENERGY DRINK ON COGNITIVE PERFORMANCE AND MOOD
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The combination of alcohol and energy drink has become increasingly popular, particularly amongst young adults. Many consumers believe that by mixing caffeine with alcohol, the negative effects that occur with intoxication, such as tiredness and impaired cognition, will be masked as the stimulant effects of the caffeine counteract the depressant effects of the alcohol. There is an increased concern that these antagonising effects lead to young people underestimating their level of intoxication and hence drinking greater amounts of alcohol than would be consumed when using non-caffeinated mixers, although, this idea is yet to be supported by research. The purpose of this study was to investigate the effects of alcohol, energy drink, and an alcohol and energy drink combination, in comparison to placebo, on cognitive performance and mood. Cognitive performance was measured using a computerised battery of alcohol sensitive psychomotor and cognitive tasks while mood was measured using a validated mood questionnaire and visual analogue scale measuring mood on three categories plus level of drunkenness. The design of the current study was a randomised, double-blind, placebo-controlled and 4-arm trial administering 0.6g/kg alcohol and 250ml energy drink. Participants were randomly allocated to a treatment sequence with a seven-day washout period between each condition. Alcohol intoxication was associated with the predicted pattern of cognitive and mood effects, these were differentially reversed by the energy drink. This pattern is to be discussed in context of the current patterns of alcohol and energy drink consumption and implications for real life behaviours. Results from this study may help guide policy and preventative health and safety practices in consumers.

0900

IMPULSIVITY AND RISK OF ALCOHOL USE AND SEXUAL BEHAVIORS: THE ROLE OF SEX-RELATED ALCOHOL EXPECTANCIES
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Previous research has shown that positive urgency, a form of impulsivity that refers to the tendency to act impulsively in response to extreme positive emotions, prospectively predicts increases in alcohol consumption, in part through formation of alcohol expectancies (Settles et al., 2010). It also appears that positive urgency might have a role in sexual behaviors (Zapolski et al., 2009), although it is unclear whether or not this is related to increased sex-related alcohol expectancies. The goal of this project is to determine how positive urgency might influence the development of sex-related alcohol expectancies and alcohol use, and how these might, in turn, increase sexual behaviors. Six hundred eleven college students at a public mid-western university participated in the study (78% female, 22% male). They were all sampled through online survey during the school year of 2010 to 2011; their age ranged from 18 to 51 (mean = 21.2, SD = 5.403) and most participants were Caucasian (77%). We conducted a series of hierarchical regressions, as well as a product of coefficients test of mediation to test study hypotheses. Results showed sex-related alcohol expectancies, positive urgency, lack of planning, and sensation seeking were all significant predictors of sexual behaviors. Mediation tests indicated full mediation of the relationship between positive urgency and sexual behaviors by sex-related alcohol expectancies ($z = 4.66$, $p < .001$) and alcohol use ($z = 5.03$, $p < .001$). Although cross-sectional in nature, the data is consistent with the theory that positive urgency predicts increased behavioral risk, in part through expectancy formation. This study should be replicated with prospective analyses.

0901

DIFFERENT LOBAR WHITE MATTER AND CSF VOLUMES IN PATIENTS WITH POLY-SUBSTANCE USE AND ALCOHOL USE DISORDER

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Neuroimaging has demonstrated that chronic alcohol misuse is associated with gray and white matter (GM and WM) volume losses (particularly in the frontal, parietal and temporal lobes) and corresponding CSF increases. Frontal lobe atrophy has also been shown in stimulant abusers and in poly-substance users (PSU). In this report, we assessed the differences in GM and WM volumes of the frontal (f), parietal (p), occipital (o) and temporal (t) lobes as well as ventricular and lobar CSF between abstinent PSU (mostly cocaine and alcohol dependent) and alcohol dependent individuals (ALC) using quantitative magnetic resonance imaging (MRI).

1.5 Tesla T1-weighted images obtained from 80 ALC (53 smokers) and 19 age-matched PSU (12 smokers) were segmented into GM, WM and CSF. The segmented maps were then parcellated into lobar volumes by overlaying the segmented maps on a T1 template. The ALC sample was put into 4 groups of 20 (3 groups contained 13 smokers each and the 4th group contained 14 smokers) and each group compared separately with the 19 PSU. 20 age-matched light drinking individuals (LD, incl. 7 smokers) were used as controls.

ALC and PSU had similar duration of abstinence from alcohol and/or all substance use (ALC 31.9 ± 7.7 days, PSU 30.5 ± 8.8 days). Drinking severity was lower in PSU than ALC (PSU: 275.0 ± 269.9 drinks/mo over 1 year, ALC: 456.8 ± 226.9 drinks/mo over 1 year). 3-group multivariate analysis of variance showed significant effects for fGM and oGM, as well as fWM, pWM, and tWM. Follow-up analyses showed that PSU tended to have less fGM and oGM than LD and larger WM volumes in all lobes compared to both ALC and LD. ALC had less fGM and oGM than LD but had similar pGM, tGM and WM volumes in all lobes to LD. Also, fCSF and tCSF volumes were significantly smaller in PSU and tended to be smaller in LD than ALC.

PSU show little GM loss and greater lobar WM volumes compared to both LD and ALC at one month of abstinence. Larger WM volumes in PSU may suggest an inflammatory tissue state early during abstinence.

0902

ADAPTING TO UNCERTAIN HIGH-RISK CONDITIONS IN ALCOHOL DEPENDENCE

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Alcohol dependent patients have been proposed to be impaired at flexibly adapting their behavioral strategies to match a social context. Behavioral therapies focus on helping patients to adapt new behavioral strategies to cope with high-risk situations without using alcohol. Because cognitive processes contributing to coping strategies are incompletely understood, we devised a task involving high-risk cognitive conditions. Participants were 20 alcohol dependents (ALC; age=47.6) and 20 age- and education-matched healthy controls (HC; age=47.2). Solid-colored circles emulating scattered coins were presented for 2000 ms; participants answered whether the number of coins was ODD or EVEN. The task consisted of two conditions: a) *certain* condition- participants could readily estimate the correct answer; b) *uncertain* condition- participants could only guess because the coins overlapped making the separation ambiguous. The task was repeated twice in the same manner, with the exception that run 1 allowed only two response options (ODD or EVEN), whereas run 2 provided three response options (ODD, EVEN, PASS). Each response was immediately followed by feedback, indicating whether the response was correct or not. If the participant chose PASS, no feedback was given. The uncertain condition was high-risk because the percentage of correct feedback was fixed at 12.5%, regardless of the participant's responses. The PASS option was rarely used in certain conditions by either group (<1%). By contrast, in uncertain conditions, the percentage of PASS responses highly varied (0–100%) across participants. The groups did not differ significantly in percentage of PASS responses (ALC=47.7%, HC=49.2%) and higher percentage of PASS responses correlated with faster $RT_{uncertain}$ in both groups (HC, r=–0.80, p<.001; ALC, r=-.62, p=.004). However, higher percentage of PASS responses correlated with fewer missing responses in the HC group (r=-.57, p=.009) but not in the ALC group (r=-.267, p=.256). Use of the PASS option indicates avoidance or reluctance to engage in uncertain conditions, situations that result in slowed RT but that can be remedied through use of strategies of aversion. Although the ALC group adapted the PASS option as a new strategy to overcome uncertainty, its use was not so effective in the ALC as in the HC group in terms of reducing errors, which implies deficits in the ability to cope with high-risk situations.

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0903

ACUTE INTOXICATION ALTERS PERCEIVED DANGER OF DRINKING AND DRIVING

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Although awareness of the risks of drinking and driving (DD) has increased, DD continues to be a major public health problem. Perceptions of risk have been found to be an important predictor of a number of health risk behaviors, including DD. The goal of the present study was to test whether acute alcohol intoxication alters perceived risk of DD. Further, we tested whether risk perceptions, measured when sober and intoxicated, uniquely contribute to the prediction of DD behavior.

Participants (N = 85) attended two counterbalanced sessions (sober and intoxicated). At the sober session, participants reported recent DD behavior and rated how dangerous they believe it is to drive after consuming a set number of drinks in a 2 hour time frame. To account for gender differences in the pharmacokinetics of alcohol, women rated perceived risk of consuming 3 drinks in 2 hours and men rated 5 drinks in 2 hours. Participants' blood alcohol concentration (eBAC) for each question was estimated using their weight based on the National Highway Traffic and Safety Association's (1994) formula. At the intoxicated session, participants received a dose of alcohol based on weight and gender (.72 g/kg for men, .65 g/kg for women) and rated the perceived danger of driving at multiple points across the breath alcohol curve. Perceived risk from the intoxicated session was selected by matching observed breath alcohol concentration with eBAC from the sober session. Matching was done for both the ascending and descending limb of the breath alcohol curve.

Paired-sample t-tests compared perceptions of the dangerousness of DD when sober and intoxicated. Results indicated that participants perceived DD as less dangerous in the intoxicated than the sober session (ascending: $t(84) = 2.72$, $p < .01$; descending: $t(84) = 7.43$, $p < .001$). Logistic regression was then used to test whether sober and intoxicated perceptions uniquely predicted DD behavior. Lower perceived risk, both when sober and intoxicated, was uniquely associated with increased odds of reporting DD in the past 3 months (ORs ranged from 2.35 to 2.76, all ps < .05).

These results suggest that acute intoxication reduces one's perceived risk of DD, particularly on the descending limb. These altered perceptions may in turn increase the likelihood of DD. Intervention and prevention efforts may benefit from attention to how intoxication can alter perceptions of DD.

0904

EFFECTS OF RECENT DRINKING HABITS ON TOLERANCE TO ALCOHOL IMPAIRMENT IN NON-DEPENDENT DRINKERS

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Tolerance to the behavioral effects of alcohol develops after repeated administrations of the drug and is considered a risk factor for dependence. Laboratory work has consistently shown that heavier drinkers display reduced reactions to a dose of alcohol whereas lighter drinkers are more affected by the same dose. However, research has focused almost exclusively on the development of tolerance on motor performance and self-reported intoxication. To date, no work has examined the effect of recent drinking habits on the behavioral and cognitive mechanisms by which alcohol impairs self-regulation, which has been implicated as a risk factor for alcohol abuse. The present study examined the relationship between recent drinking habits (quantity and frequency of consumption over the past 90 days) and the degree to which alcohol impaired inhibitory mechanisms of behavioral control, motor coordination, and self-reported intoxication in a group of 52 adult drinkers in response to placebo and a moderate dose of alcohol (0.65 g/kg). Results showed that alcohol significantly impaired inhibitory control and motor coordination and increased subjective ratings of subjective intoxication. Moreover, drinking habits bore a significant relationship to the degree to which alcohol impaired motor coordination and increased ratings of intoxication such that heavier, more frequent drinking predicted less motor impairment and lower ratings of intoxication. By contrast, there was no such relationship between recent drinking habits and the degree of alcohol impairment of inhibitory control. That is, participants showed no tolerance to the disinhibiting effects of alcohol regardless of their drinking history, and despite reduced impairment of other aspects of behavior (i.e., motor coordination). Taken together, these findings might provide some account for continued alcohol consumption (i.e., excessive binge drinking) in heavier, more frequent drinkers as a result of feeling less intoxicated and showing reduced motor impairment while still being significantly disinhibited. Research supported by NIAAA grants R01 AA018274 and R01 AA012895 and NIDA T32-DA07304 training grant.

0905

DANGEROUS DESCENT: REDUCED ACUTE TOLERANCE TO ALCOHOL IN ADULTS WITH ADHD

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Humans and other animals develop acute tolerance to the behavioral effects of alcohol over the time-course of a single drug exposure. There is considerable variability in the degree to which behavioral and cognitive functions show recovery, however, and some functions (e.g., motor control) recover quickly, whereas others (e.g., inhibitory control) do not show acute tolerance. The current study sought to characterize acute tolerance processes in adults with ADHD— a group whose atypical responses to alcohol may place them at increased risk for alcohol-related problems. Adults with (n = 10) and without (n = 16) ADHD completed tasks measuring inhibitory control and motor control under two doses of alcohol (i.e., placebo, 0.64 g/kg). Participants performed the battery once during the ascending limb of the BAC curve and again at a comparable BAC during the descending limb. Alcohol disrupted performance on both tasks, ps < .05. Under placebo, there were no significant changes in task performance between limbs, ps > .152. Under 0.64 g/kg alcohol, however, the control group was similarly disinhibited during each limb, p = .261, whereas the ADHD group made more inhibitory failures during descending limb than during the ascending limb, p = .011. The control group showed acute tolerance to alcohol-induced impairment of motor control, p = .004, whereas the ADHD showed similar impairments of motor control during both limbs, p = .982. Both groups reported less subjective intoxication during the descending limb than during the ascending limb, ps <.001, and the decline was comparable between groups, p = .885. Results indicate that unlike healthy adult drinkers, adults with ADHD do not recover motor control as acute tolerance develops, and they may become acutely sensitized to the disinhibiting effects of alcohol. This atypical alcohol response may act to prolonged drinking sessions in this group, because they become more disinhibited over the time-course. Further, their reduced recovery of fine motor control may place them at increased risk for alcohol-related injuries or traffic collisions. These atypical responses may be particularly insidious because adults with ADHD show acute tolerance to the subjective effects of alcohol. Thus, affected adults may not perceive their continued impairment during the descending limb, and they may make risky decisions (e.g., driving) accordingly.

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0906

CORTICAL OSCILLATIONS ELICITED BY NOVEL & TARGET STIMULI ARE MODULATED BY ETHANOL DOSE & FAMILY HISTORY OF ALCOHOLISM DURING IV ETHANOL ADMINISTRATION

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Disturbances in cortical information processing functions have been extensively documented using event-related potentials (ERP). In addition to ERPs individual stimuli elicit event-related oscillations in cortical EEG. While ethanol dose-related effects on ERP indices have been established, the relationship between ethanol sensitivity and the transient shifts in EEG power due to changes in focus to task relevant, salient, or novel stimuli has not been well described. Methods: 105 Healthy non-smoking participants, between the ages of 21–30, without psychiatric or medical disorders participated in 3 laboratory test sessions, in a randomized, double blind fashion. Participants received alcohol intravenously using a clamp procedure to achieve 3 doses, a) placebo, b) low dose (breathalyzer reading target 40 mg/dl), and c) high dose (breathalyzer reading target100 mg/dl). The IV alcohol infusion rate was adjusted at multiple timepoints to sustain the target breath alcohol level. During the steady state portion of the infusion, event-related potentials (ERPs) were recorded from Fz, Cz, and Pz electrode sites while participants viewed centrally presented blue circles (small, 80%; large, target, 10%) and unique patterns (novel, 10%). Three components frequency bands of EEG were analyzed for target and novel stimuli at each electrode, alpha (8–12 Hz), beta (13–30 Hz), gamma (30–100 Hz). Average EEG power was calculated for time points of interest.
Results: The decrease in gamma oscillations (350–500 msec post stimulus) in response to attentional targets was greater for participants with a family history of alcoholism. This effect was found during the placebo testing session (Dose x Family History, F (2,824) = 4.7, p < 01). The event-related alpha oscillations showed an effect of dose for both attentional targets (275–375 msec post-stimulus) and novel stimuli (350–550 msec post-stimulus). Alpha power decreased across doses but, the decrease during the placebo infusion was greater than during the low dose alcohol infusion.
Conclusions: These findings indicate that a family history of alcoholism exacerbates the event-related decrease in gamma related to attentional processing. Additionally, at a low breath alcohol level (BAC =0.04) there is an attenuation of the event-related reduction in alpha power across attentional demands.

10. TREATMENT / RECOVERY

0907

EXPLORATORY FACTOR ANALYSIS OF A SCALE TO MEASURE EMOTIONAL AMBIVALENCE ABOUT REDUCING PROBLEM DRINKING

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Ambivalence about reducing problem drinking may be an important construct for explaining why some individuals make changes in their problem drinking while others do not. The resolution of ambivalence is also theorized to be a key explanation for the efficacy of motivational interviewing. Empirical support for the importance of ambivalence, whether in the context of treatment or self-change, is not possible until a valid measure of ambivalence about reducing problem drinking exists. This study is one of a series of studies designed to develop an accurate measure of ambivalence for alcohol use disorder treatment research. The version of the instrument administered in this study reflected advice given by experts that a valid measure of ambivalence must contain items that measure the emotional aspect of ambivalence about reducing problem drinking, in addition to a balance of pros and cons about quitting or drinking less. The current research was a secondary analysis of the Social Networks, Alcohol Consumption, and College Students (SNACCS) study. Participants were 196 undergraduate students who gave valid responses to the questionnaire and reported drinking alcohol once or more in the previous year. Exploratory factor analysis using maximum likelihood extraction with oblimin rotation was performed on 35 items developed to measure the emotional experience of ambivalence. There were only four items with loadings under .45, the chosen cut-off value that represents 20% of shared variance with other items of the same factor, and only two items loaded on more than one factor. The analysis revealed two factors that accounted for 55.45% of the total variance and were correlated at −0.65. The factors were labeled *conflicted* (e.g., pulled in different directions, like I should cut down but I don't want to) and *uncomfortable* (e.g., anxious, stuck). Results suggested that most items were good candidates for inclusion in the final version of the emotional ambivalence scale, but firm conclusions must wait until the instrument is administered to a larger sample and a confirmatory factor analysis can be conducted.

0908

DISTRESS TOLERANCE AS A MEDIATOR BETWEEN DEPRESSION AND POSTTRAUMATIC STRESS DISORDER SYMPTOMS IN AN ALCOHOL DEPENDENT IN-PATIENT TREATMENT SAMPLE

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Preexisting psychological problems, such as depression, have been related to increased likelihood of developing posttraumatic stress disorder (PTSD) following a traumatic event. Additionally, distress tolerance has been theorized to be related to the development of PTSD, such that the better distress tolerance a person has, the less likely s/he is to develop PTSD. Finally, it is also possible that depression affects distress tolerance, such that the more depressive symptoms a person experiences, the poorer the distress tolerance s/he will express. Considering the aforementioned relationships, distress tolerance may act as a mediator between depression and severity of PTSD. Participants were 44 men and 42 women, alcohol dependent patients at an in-patient substance abuse rehabilitation facility, between the ages of 17–65 (M = 34.99, SD = 10.12). Participants were enrolled in the residential substance abuse treatment program for 1 to 90 days (M = 20.94, SD = 18.29) and had been sober for 2–120 days (M = 45.36, SD = 56.74) at the time of data collection. Participants were given a battery of self-report measures, including the Beck Depression Inventory (BDI-II), PTSD Checklist (PCL), and the Distress Tolerance Scale (DTS). Depression was a reliable predictor of PTSD (path c; β= .85, p < .001) and distress tolerance (path a; β = -.25, p < .05). Distress tolerance was also a reliable predictor of PTSD (path b; β = -.69, p < .01). Results indicated that distress tolerance acted as a partial mediator of the relationship between depression and PTSD symptoms (path c′; β = .83, p < .001). However, the strength of the relationships between all three was small to moderate. This suggests that, while depression and distress tolerance are important components in predicting symptoms of PTSD, there are likely other factors involved.

0909

DEVELOPMENT AND PRELIMINARY VALIDATION OF A SCALE OF ATTITUDES TOWARD HARM REDUCTION AND ABSTINENCE-ONLY ALCOHOL INTERVENTIONS

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Current best practices for treating college student alcohol misuse involve harm reduction (HR) strategies. However, no research has been conducted to examine college students' attitudes toward HR versus abstinence-only approaches to alcohol treatment. Barriers to conducting research on these attitudes among potential treatment recipients include a lack of valid and reliable assessment instruments. This research involved the development and preliminary evaluation of a measure assessing attitudes toward HR and abstinence-only treatment modalities in a college student population. We generated 46 items to capture techniques that primarily are associated with either HR (e.g., ''spacing out drinks in order to drink less'') or abstinence-only (e.g., ''only spending time with friends who do not drink'') interventions. A sample of 256 college students completed the attitudes measure, rating on a Likert scale the perceived effectiveness of each technique (1 = *not all likely to be effective* to 5 = *very likely to be effective*). Participants also completed measures of alcohol dependence symptoms (YAACQ dependence subscale), alcohol consumption (AUDIT-C), and the Short Understanding of Alcoholism Scale. An exploratory factor analysis using maximum likelihood extraction and promax rotation resulted in a two factor solution with factors representing HR and abstinence-only techniques. Factor loadings ranged from .45 to .80 on the HR subscale and .40 to .89 on the abstinence-only subscale, and no items loaded on both factors. These factors were moderately correlated (r = .43) and had high internal consistency (alpha = .92 for each subscale). Consistent with previous research there were small associations between younger age and favoring HR (r = -.17, p = .007), older age and favoring abstinence-only (r = .15, p = .018), and having great alcohol dependence (r = .18) and consumption (r = -.18) and favoring abstinence-only less. Belief in a disease model of alcoholism was negatively associated with favoring HR (r = -.17, p = .009) and positively associated with favoring abstinence-only (r = .17, p = .007), providing evidence for convergent validity. These findings provide initial evidence of the reliability and validity of this newly created measure, which can be used to examine differential attitudes toward HR and abstinence-only among potential treatment recipients, as well as factors affecting those preferences in different populations.

0910

UNIQUE NEUROCOGNITION IN TREATMENT SEEKING POLYSUBSTANCE AND ALCOHOL USERS: DIFFERENCES IN DECISION MAKING, IMPULSIVITY, LEARNING, AND MEMORY

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The clinical reality in treatment centers today is that at least 50% of patients present with combinations of alcohol use disorders (AUD) and various substance use disorders (e.g., AUD + cocaine, methamphetamine, or marijuana). Research has shown that both AUD and polysubstance use disorders (PSU) are associated with cognitive abnormalities. However, studies comparing PSU and ''pure'' AUD on cognition, particularly on measures of executive domains such as impulsivity, risk taking and decision making are very limited. Developing a robust knowledge of potential neurocognitive differences is critical to better assess and direct treatment of AUD and these understudied PSU.

Treatment seeking PSU (n=30, abstinent for 30 ± 8 days), AUD individuals (n=114, abstinent 33 ± 9 days) and light drinking controls (LD, n=62) were compared on 11 traditional domains of cognition Additional comparisons were made on a sub-sample of this population who received the following executive reward/control cognitive and behavioral measures: Balloon Analogue Risk Task (BART), Barratt Impulsiveness Scale (BIS), Iowa Gambling Task (IGT). Omnibus MANOVA covaried for age, AMNART, and cigarette smoking status.

PSU exhibited poorer performance compared to AUD in the domains of auditory-verbal memory, visual spatial learning and memory, and general intellectual functioning. Unexpectedly, PSU performed better than both AUD and LD on a domain measuring traditional executive functioning. However, when the BIS, BART, and IGT were examined, PSU exhibited higher overall levels of impulsivity. Specifically, PSU had greater non-planning impulsivity than AUD and LD, as well as higher levels of motor and attentional impulsivity and poorer decision making than LD. AUD tended to have greater non-planning impulsivity than LD.

These results show that learning and memory as well as specific measures of impulsivity differentiate PSU from both AUD and LD. Addition of measures that specifically assess impulsivity/risk-taking/decision making to traditional batteries assessing executive function may enhance the ability to detect more clinically relevant cognitive dysfunction in PSU. Further analysis of these differences is warranted and may help tailor treatment to the deficits exhibited by AUD and the highly understudied PSU population.

0911

SCREENING U.S. CAMBODIANS FOR DISORDERED SUBSTANCE USE, A FEASIBILITY STUDY

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Our purpose was to assess the feasibility of screening U.S. Cambodians for disordered substance use and to compare the utility, with this population, of two brief screeners: the six-item CRAFFT (recommended for youth) and a single-item 5/4 drinks screener. Both screeners have performed well in a variety of settings. U.S. Cambodians are highly at-risk for disordered AOD use but are underserved in mental health and substance abuse treatment. Validated screeners have not been assessed with this population. In preliminary discussions for a pilot study, Cambodian service providers expressed concern that stigma associated with alcohol and drug dependence would reduce Cambodians' willingness to respond to such screeners. We conducted a brief survey with a convenience sample of 67 U.S. Cambodian, recruited over a three-week period. The sample included both first-generation adults (aged 30–70, median age 54; 70% of respondents) and second-generation youths and young adults (aged 18–29, median age 23; 27% of respondents); and females (66%) as well as males. Respondents were recruited at mental health and social service clinics as well as community venues where Cambodians congregate in Oakland, CA. Surveyors were bilingual/bicultural mental health and social service providers trained in survey administration and well-known by community members. Respondents were given a one-page anonymous close-ended survey in either English or Khmer (Cambodian language); 72% of surveys were conducted in Khmer. The survey included CRAFFT and the 5/4 drinks item. Responses were entered in SPSS and analyzed for descriptive statistics. All protocols received IRB approval. Surveyors reported low refusal. Of the 67 respondents, 100% responded to the CRAFFT items, with 61% screening positive (including 57% of females), while 63% of persons responded to the single item 5/4 drinks screener, with 37% of all respondents screening positive (including 32% of females). Of positive screens for CRAFFT, 100% were also positive using RAFFT (version validated for adults) and 84% were also positive using the 5/4 drinks screener. The screener results were not externally validated, and the sample size and opportunistic recruitment strategy do not allow for generalizability of the results to all U.S. Cambodians. Nevertheless the results are encouraging for applications in research and practice. Brief screeners may be useful in identifying at-risk U.S. Cambodians in community as well as clinical settings.

0912

MI-BASED INTERVENTION MAY DECREASE THE LIE: SELF REPORTED PRE-TREATMENT AUDIT SCORES OF COURT REFERRED YOUTH INCREASE AFTER THEY RECEIVE MI

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The purpose is to examine the effects of an MI-based group intervention on the consistency of self-reported alcohol use by court referred adolescents.

Methods: Analyses were conducted on a sub sample of court referred 16–20 year-olds recruited into a large RCT that examined the effect of a 20-hour MI-based group intervention on alcohol use and recidivism. Youth were randomized to either Community Service (CS) or to one of two versions of MI-based group intervention (MI) that included 4 MI sessions. For these analyses MI groups were combined.

Procedure: A random sample of 478 participants, who at baseline completed the AUDIT in reference to the 6 months prior to their conviction, completed the AUDIT again at treatment completion, in reference to the same 6 month baseline time period. Participants were asked to provide accurate reporting and were assured confidentiality.

Results: At the completion of their treatment, participants in the MI groups reported a significantly greater baseline AUDIT score (M=6.09) than they indicated prior to treatment (M=5.21); where as the CS group reported no change from baseline (M=5.53) to post-treatment (M= 5.58); this difference between CS and MI groups was significant (F=5.52, p=.02).

Discussion: These results suggest that MI may have an effect on the validity of self report. Overall, participants assigned to the MI groups reported significantly higher baseline AUDIT scores at post-treatment as compared to their self report at pretreatment. For the groups receiving MI their AUDIT scores were 16.9% higher when asked at post-treatment compared to no change for the control group. This may be due to more honesty because of a trusting therapeutic alliance between the participant and counselor and/or a response shift bias caused by the focus on alcohol use during the MI groups. A shift in patient report of alcohol use following a treatment that is alcohol focused may have important implications for how we interpret treatment outcome results. Specifically, does the process of MI, and for that matter perhaps other treament approaches, increase the likelihood of more accurate self reporting when compared to a no treatment control group? If this is true, research studies that rely on pre to post treatment changes in self-report may be under-reporting differences, and thus under-estimating the effects of treatment.

0913

RISKY DRINKING, TRAUMATIC EVENTS AND PTSD AMONG ADULTS PRESENTING TO AN INNER-CITY EMERGENCY DEPARTMENT

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The Emergency Department (ED) visit presents an opportunity to assess and conduct brief interventions for a variety of health related issues. Prior research has documented exacerbated rates of violence exposure and post-traumatic stress disorder (PTSD) among adults residing in the inner-city. This study examined rates and correlates of exposure to traumatic events and PTSD in relation to alcohol use among adults in an inner-city ED. For this study, adults (18–60) being treated in an inner-city ED self-administered a computerized survey with questions regarding demographics, substance use and mental health. All patients screened were asked about exposure to traumatic events. For the purpose of this analysis, the following groups were compared (1) no traumatic event (NTE), (2) a traumatic event with no PTSD (TE), and (3) a traumatic event with PTSD (PTSD). Among the screening sample (n=1617), 67% reported NTE, 17% reported TE, and 16% reported PTSD. Of those reporting PTSD, 94% reported more isolation from others and 96% reported sleep problems. Bivariate analysis of the PTSD group were significant for African American race ($p < 0.001$), some college education ($p < 0.001$), employment ($p < 0.001$), and an AUDIT score of ≥8 in the last 3-months. Compared to the NTE group, those with PTSD were less likely to be African American, have some college education and be employed; however those with PTSD were more likely to have an AUDIT score of ≥8. Binge drinking was not significantly different among the groups. After controlling for demographics, multinomial logistic regression analyses were used to predict membership with the NTE group serving as the comparison group. The PTSD group was more likely than the NTE group to have an audit score of ≥8 (AOR=1.92, CI=1.25–2.94). PTSD is underestimated in the ED setting and it associated with more chronic medical conditions and riskier negative health behaviors such as hazardous drinking. The inner-city ED provides an opportunity to assess and provide referral for PTSD as part of an SBIRT model.

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0914

PARTNER RELATIONSHIP QUALITY AND INTERPERSONAL STYLES IN THE PREDICTION OF PEER SUPPORT AMONG VETERANS IN ALCOHOL AND DRUG TREATMENT

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Objective: The overarching aim of this ongoing study is to determine whether veterans' prior relationships and interpersonal styles influence their experiences in alcohol and drug treatment programs. Here, we specifically tested (1) whether spouse/partner relationship quality at the outset of treatment predicts level of support from peers in treatment – a salient predictor of treatment engagement and outcomes (Kelly et al., 2010) – and (2) the extent to which this association is accounted for by veterans' interpersonal styles.
Method: The Inventory of Interpersonal Strengths (IIS; Hatcher & Rogers, 2009) and Inventory of Interpersonal Problems (Alden et al., 1990) were administered to participants in two residential substance abuse treatment programs within seven days of their entry date to evaluate participants' initial level of interpersonal functioning. Veterans who reported being in a significant romantic relationship during the 30 days prior to their entry date were assessed on the quality of that relationship using the Life Stressors and Social Resources Inventory (LISRES; Moos et al., 1988). The LISRES was also administered to participants 30 days after their entry date to assess their level of support from peers in treatment.
Results: A higher quality of relationship with one's partner at the outset of treatment was associated with higher levels of peer support in treatment, as well as interpersonal styles marked by being assertive and direct and forthright. Interestingly, in multiple regression analyses, these interpersonal styles were associated with *lower* levels of support from peers in treatment; however, the link between partner relationship quality and peer support remained unchanged.
Conclusions: Results indicate that a veteran's relationship quality with their spouse/partner prior to entering treatment may predict their level of support from peers in residential alcohol and drug programs regardless of that veteran's interpersonal style.

0915

PSYCHOLOGICAL AND PSYCHOSOCIAL FUNCTIONING IN PATIENTS WITH ALCOHOL-RELATED LIVER DISEASE PRE- AND POST-LIVER TRANSPLANTATION

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Orthotopic liver transplantation (OLT) for alcoholic liver disease (ALD) is subject to the many challenges associated with organ transplantation, including shortages of donor organs and a high rate of waiting list mortalities. The difficulties associated with transplantation often continue following surgery due to recognised side effects of immunosuppressant therapy and the need for life-long medical follow-up. Treatment non-compliance as a result of ongoing post-operative psychological and psychosocial distress may jeopardise transplant success. Given the shortage of available organs and the significant costs involved in the transplantation process, the emotional health of transplant recipients is a clinical priority. The impact of OLT on psychological and psychosocial functioning for ALD is currently poorly documented. This prospective study examined changes in these areas of function pre and post-OLT. Comprehensive psychological and psychosocial (State-Trait Anxiety Inventory, Beck Depression Inventory, Psychosocial Adjustment to Illness Scale*)* assessments were conducted on 92 abstinent ALD patients scheduled for OLT. Forty-two patients were available for re-assessment 12-months post OLT. Patients not assessed at follow up were either not yet due for repeat assessment (<12 months), still awaiting transplantation, deceased, or lost to follow-up [42/51 or 83% of patients who could be potentially retested provided follow-up]. Significant reductions in depression and anxiety symptomatology were observed in most patients, along with significant improvements in psychosocial adjustment to illness 12-months post-OLT. A portion of the sample continued to report emotional and psychosocial distress 12-months post-transplant. Further research attempting to identify which patients are more likely to experience ongoing psychological distress would assist health professionals to target limited resources to those most in need.

0916

VISUAL IMAGE INDUCED CRAVING FOR ETHANOL (VICE)

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Craving induction in a controlled environment proves very helpful in the research of craving mechanism and its role in development of alcohol dependence; predict treatment response and prevent relapse by clinical simulation of high risk situation while in hospital. This study describes a novel tool Visual Image induced Craving for Ethanol (VICE) - a scale which was specifically designed to measure the self-reported craving for alcohol among patients with alcohol dependence syndrome in Indian settings.
Alcohol related visual cues in 5 scenarios were created with inputs from five qualified psychiatrists. This included pictures of bars/liquor stores, alcoholic beverage containers/ bottles, pouring of alcohol into glasses, glasses filled with alcohol and scenes of people sipping alcoholic beverages and were counterbalanced with neutral pictures (involving water, milk, coffee, tea etc.,) for each image. Each picture was rated on a scale 0 to 5 with a descriptive response. Craving scores were obtained from 15 hospitalized subjects with alcohol dependence, during an initial assessment phase before active treatment commenced. Images were displayed on a 15 inch LCD monitor in a user based interface. Subjects were asked to vocally respond to the images with scores.
VICE showed a high internal consistency with Cronbach's α coefficient of 0.86 which confirmed its reliability. Construct validity of the VICE scale was demonstrated via its convergence with a commonly used measure for assessing craving (Penn Alcohol Craving Scale-PACS) with a significant correlation of total VICE scores with total PACS scores ($r = 0.605$, $df = 14$, $p = 0.008$). The pictures of bars/liquor stores, alcoholic beverage containers/ bottles and pouring of alcohol into glasses were scored the highest and had significant positive correlation with PACS craving scores. Mean craving scores reported were less than half of the scale maximum. Possible reasons for this include reduction in perceived opportunity to drink being in a controlled setting and fear that a high craving score might cause clinicians or family members to worry that the participants may fail to maintain abstinence.
To conclude, the VICE is a reliable and valid measure of alcohol craving. The predictive validity of this scale needs to be examined further. This scale will be used in future functional magnetic resonance imaging studies to identify neural substrates of cue-induced craving.

0917

URGE DISTRESS AS A DIMENSION OF CRAVING FOR ALCOHOL
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Craving, typically defined as a strong or persistent desire for a substance, is a commonly reported phenomenon in addictive behaviors. When considering alcohol dependence, urges or cravings for a drink are often thought of as a key element in maintaining problematic alcohol use. Despite this, craving remains controversial topic in addiction research. In part, this is due to how craving is defined operationally and how it is measured. While much research has investigated the association among craving and clinically significant impairment, research has been scant in investigating the level of distress associated with urges to consume alcohol. The current study sought to investigate the level of distress caused by cue-elicited cravings in individuals with alcohol use disorders (AUDs). Treatment-seeking individuals (N= 72) were recruited from the community for an AUD pharmacotherapy study, including an in-person screening session to determine eligibility. During the screen, an in-vivo exposure to alcohol cues was used to assess cue reactivity (i.e., increases in desire to drink and distress associated with these urges) when exposed to neutral cues and then, subsequently, alcohol cues. Within-subjects ANOVAs revealed a significant overall effect of alcohol cues on both subjective craving ($F=59.53$, $p<.01$) and urge distress ($F= 53.12$, $p <.01$) and there was a significant relationship between craving and urge distress ($r = .82$, $p <.01$). Correspondingly, urge distress was negatively associated with feeling relaxed ($r=–0.36$, $p<.01$) and positively related to feeling bad ($r=.56$, $p < .01$) and feeling stressed ($r=.48$, $p<.01$).To account for the overlap between craving and urge distress, within-subjects ANCOVAs, covarying craving, indicated that urge distress remained significant ($F= 5.27$, $p < .05$). These findings suggest that urge distress may be a meaningful dimension of craving for alcohol. A collateral urge distress index may contribute to a number of areas, such as predicting drinking behavior or treatment response. Future research on urge distress is needed to further validate this dimension of craving and to determine clinical applications and utility.
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0918

NEUROTICISM AND AGGRESSION IN TREATMENT-SEEKING ALCOHOLICS WITH COMORBID POST-TRAUMATIC STRESS DISORDER (PTSD)
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Our previous studies demonstrated differences in personality, specifically neurotic traits, in a sample of treatment-seeking alcoholics with comorbid PTSD. The purpose of our current analysis is to extend the characterization of our sample regarding facets of neuroticism and aggression.
The sample was 411 treatment-seeking alcoholics (300 male) undergoing detoxification and inpatient treatment in the NIAAA treatment research program at the NIH Clinical Center. The sample included 79 (19.2%) patients with comorbid PTSD assessed using Structured Clinical Interview for DSM-IV-TR diagnoses. Neuroticism was assessed using NEO Personality Inventory and data from 348 patients were included. Aggression was assessed using Buss-Perry Aggression Questionnaire in a subset of 109 patients.
There was a high prevalence of neuroticism in this sample of patients with PTSD with significant correlation on several facets including: anxiety ($p=0.016$), angry hostility ($p=0.002$), depression ($p<0.001$), self-consciousness ($p=0.003$), and vulnerability ($p=0.003$). Patients with PTSD showed higher verbal aggression ($p=0.016$) and hostility ($p<0.001$) than patients without PTSD. Physical aggression was associated with PTSD only in males ($p=0.053$).
There was a high prevalence of neurotic traits and aggression in this sample of alcoholics with comorbid PTSD, which is consistent with the clinical phenotype of this population. These findings substantiate the heterogeneity of alcoholism and the need for specialized treatment.

0919

CONTRASTING SUBSTANCE USE AND DEMOGRAPHIC CHARACTERISTICS IN TWO GROUPS OF TREATMENT SEEKING ALCOHOLIC WOMEN
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Overview: This study is a preliminary comparison of two groups of treatment seeking women within a common geographic region. One group consists of pregnant women or new mothers (PWNM) seeking treatment in a residential facility directed to their special needs. The second group consists of women in a traditional mixed gender inpatient facility (TW). Although it was anticipated that the samples would differ in certain attributes (e.g., age/education), the overarching objective was to examine substance use patterns in the groups.
Method: Participants [PWNM group (N = 39), TW group (N = 23)] provided written informed consent and completed a packet of questionnaires addressing depression symptoms, alcohol/drug including nicotine use, family histories of substance use and demographic information.
Results: The PWNM group was significantly younger ($M = 24$, $SD = 4.28$) and less educated ($M = 11.7$, $SD = 2.31$) than the TW group ($M = 40.48$, $SD = 13.51$; $M =14.39$, $SD = 1.97$, age and education, respectively); $p's < .001$. The PWNM group reported an earlier age at onset of regular alcohol consumption ($M = 16.73$, $SD = 3.55$) as compared with the TW group ($M = 21.79$, $SD = 7.33$), $t(24.2) = 2.78$, $p = .01$, and, among those with alcohol problems, an earlier age at onset of problematic drinking ($M = 18.44$, $SD = 4.76$ vs. $M = 34$, $SD = 14.88$), $t(14) = 3.62$, $p < .01$. The proportion of those reporting alcohol dependence was similar in the two groups ($p = .22$); 54% PWNM vs. 70% TW. Both groups reported an average of $\sim$ 6 years between age at onset of problematic drinking and the age at accessing current treatment. Importantly, PWNM and TW groups reported similar drinking patterns across the 6 months prior to initiating sobriety; an average of $\sim$ 11 drinks/day. Among drug users in both groups, the preferred drug class was narcotics/analgesics.
Conclusion: This preliminary analysis suggests that the groups are both similar and dissimilar in characteristics likely to impact post-treatment adaptation. For example, despite differences in age of onset variables, the groups were remarkably similar in their current alcohol consumption and drug of choice. On-going analyses examine group differences in FH and depression as well as their association with substance use. Taken together these data reinforce the need for a) diverse longitudinal studies arising from a variety of treatment settings, and b) an explicit consideration of treatment setting when characterizing ''treatment seekers'', per se.

0920

PERSONALITY TRAITS IN THE PREDICTION OF TREATMENT ENGAGEMENT AMONG VETERANS IN ALCOHOL AND DRUG ABUSE PROGRAMS: A MULTI-RATER ANALYSIS
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Objective: Previous studies have examined links between personality disorders and engagement in substance abuse treatment; however, few have examined the utility of personality *traits* in the prediction of these outcomes, and none (to our knowledge) have examined these links using multiple raters. In this ongoing study of veterans in residential alcohol and drug treatment, we examined the predictive validity of self- vs. peer-reports of participants' personalities in the prediction of two treatment outcomes – i.e., participants' perceptions of the treatment environment, and relationship quality with other residents.
Method: The short form of the Schedule for Nonadaptive and Adaptive Personality (SNAP; Clark 1993) inventory, the Community-Oriented Program Environment Scale (Moos, 1974), and Life Stressors and Social Resources (Moos et al., 1988) inventory were administered to participants one month after entry into residential substance abuse treatment, and were used to measure personality traits, perceptions of the treatment environment, and relationship quality with other residents, respectively. Participants also nominated one peer from their program to rate that participants' personality on an observer form of the SNAP.
Results: By and large, peer ratings of participants' personalities did not correspond with participants' self-ratings, with the exception of the positive temperament and aggression scales. Only the personality self-ratings were linked to participants' perceptions of the treatment environment (i.e., higher impulsivity associated with the perception that the program lacks clear rules; higher entitlement and mistrust associated with perceptions that the program is too controlling). However, higher dependency (as rated by peers only) was associated with higher participant ratings of having stressful relations with other residents.
Conclusions: Peer ratings of another resident's personality in treatment may not correspond well with either that individuals' self-ratings or their perceptions of the treatment environment; but may yield unique insights in terms of relationship quality with other residents. Findings from this study will ultimately inform the content of a brief personality assessment feedback intervention for veterans in substance abuse treatment.

0921

PREDICTORS OF SUBSTANCE ABUSE TREATMENT RETENTION AMONG PATIENTS USING CHEMICAL DEPENDENCY SERVICES

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Background: Treatment retention is an important prognostic indicator for patients in alcohol and drug treatment. In this study, we used data from the intake instrument of an innovative Outcomes Monitoring System (OMS) to examine how predisposing (e.g., demographics), enabling (e.g., social support), and need characteristics (i.e. level of severity) measured by the system predicted retention for the full three weeks of initial rehabilitation treatment.
Methods: Data was obtained from EMR records from patients visiting CDRP (Chemical Dependency Recovery Program) or CDS (Chemical Dependency Services) clinics from September, 2009 through February, 2011. Facilities were located in Oakland, CA and Santa Clara, CA. Length of stay in treatment (days) was calculated for each patient and then categorized into whether the patient remained in treatment for the full three weeks of rehabilitation treatment. . Logistic regression analysis was conducted using measures of predisposing, socio-demographic) enabling and need characteristics from the OMS in predicting treatment retention.
Results: The analysis included 1036 observations and 56% of the sample remained in treatment for three or more weeks. The final multivariable logistic regression model indicates that the odds of treatment retention increased significantly if an employer mandated treatment (OR = 2.4, 95% CI: 1.3, 4.6), if there was a referral to treatment made by the legal system/ lawyer/probation officer/court (OR = 1.9, 95% CI: 1.1, 3.3) or an employer (OR = 2.0, 95% CI: 1.1, 3.7), or if the patient had a goal to stop drinking completely (OR = 1.5, 95% CI: 1.2, 1.9). Support from family and friends for the patient to discontinue drinking acted as a confounder in the model (OR = 1.4, 95% CI: 1.0, 1.9).
Discussion: These analyses are consistent with earlier findings in highlighting the importance of mandates to treatment (particularly from employers) and goals to stop drinking. They also demonstrate the potential utility of an Outcomes Monitoring System in that these predictors were identified at the intake appointment and can help identify individuals in need of motivational enhancement techniques (that is, those with no mandates or who do not intend to abstain).

0922

SATISFACTION WITH SOCIAL SUPPORT AND DRINKING MOTIVES IN AN ALCOHOL DEPENDENT SAMPLE

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A number of studies have examined alcohol use as a means of coping, but other facets of drinking motives such as drinking for social enhancement, and conformity have not been fully explored. Social support is often related to drinking motives, whereby many people report drinking more often in social situations, which may be related to: number of social contacts, quality of social support, and drinking to conform to social standards. Little research to date has explored the link between social support and drinking motives, although Sher has conducted studies examining drinking as a function of Greek life affiliation, college dorm life, and attending a ''party school'' as influencing drinking motives. The present study sought to expand this research by examining the connection between satisfaction and current social support as related to the variety of motives people report for drinking alcohol. Participants were 44 men and 42 women between the ages of 17–65 (M = 34.99, SD = 10.12) enrolled in an inpatient substance abuse treatment program for alcohol dependence. At the time of data collection, participants had been in the program for 1–90 days (M = 20.94, SD = 18.29), and had been sober for 2–120 days (M = 45.36, SD = 56.74). Participants completed a battery of self-report measures, including the Social Support Questionnaire (SSQ) and Drinking Motives Questionnaire (DMQ). The DMQ was scored and divided into its respective subscales: Social, Coping, Enhancements and Conformity. Satisfaction with social support was related to social drinking motives (F[1, 23] = 1.47, $p < .001$, $\eta_p^2 = 1.00$) and coping drinking motives (F[1, 23] = 8.25, $p < .001$, $\eta_p^2 = 1.00$). However, satisfaction with social support was not related to enhancement drinking motives (F[1, 23] = 9.43, *ns*) nor conformity drinking motives (F[1, 23] = 23.14, *ns*). Overall, results indicate that satisfaction with social support is related to drinking in social situations, as well as for coping with negative emotions, but not related to enhancement of experiences or conforming to a social group. This implies that treatment efforts geared towards addressing social and coping influences on drinking may be most effective due to the relationship between social satisfaction and drinking. The effect of satisfaction with social support on drinking motives appears more complex than previously thought, warranting additional research into the area as much of previous research has focused on college students.

0923

DRINKING MOTIVES IN HIV PRIMARY CARE PATIENTS SCREENED INTO BRIEF DRINKING-REDUCTION INTERVENTION.

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AIM A large literature exists on drinking motives (DM) as predictors of subsequent drinking in community and college samples. However, despite the importance of increasing motivation to change in clinical settings, little is known about drinking motives in clinical samples. To begin filling this gap in knowledge, we examined the factor structure of a previously used measure of DM (Carpenter & Hasin, 1998; Beseler et al., 2008; 2011) in a clinical sample. METHOD Adult HIV primary care patients (N=253) who drank ≥4 drinks at least once in the prior 30 days completed a drinking motives questionnaire as part of the baseline assessment in a randomized trial of brief intervention to reduce drinking. Using Mplus, exploratory factor analysis was conducted with the DM items to determine their underlying structure, using maximum likelihood estimation and a quartimin rotation. The final factor structure was obtained by determining which factors had eigenvalues >1.0, and through model fit statistics. RESULTS Model fit statistics and eigenvalues indicated that the best solution was a 3-factor model (*CFI*=0.94; *RMSEA*=0.08). Factor 1 (Eigenvalue=5.50) describes drinking for social facilitation. Factor 2 (Eigenvalue=1.98) describes drinking in response to external pressure from others. Factor 3 (Eigenvalue=1.02) largely describes drinking to cope with negative affect. CONCLUSION Drinking motives may play an important role in drinking intervention outcomes. Improving patient motivation to reduce drinking may be facilitated by first understanding the reasons that maintain one's drinking. Future studies should further examine drinking motives as predictor of drinking outcomes in patient samples. Such knowledge may strengthen treatment efficacy and assist in tailoring drinking-reduction strategies.

0924

COMORBID ANXIETY AND DEPRESSIVE DISORDERS ARE ASSOCIATED WITH NEGATIVE CRAVING IN TREATMENT SEEKING ALCOHOLICS

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Background: A tendency to drink in the context of negative emotional situations (interpreted as negative or relief craving) is considered among the clinical predictors of response to acamprosate (Verhuel et al. 1999). Research findings also indicate that craving related to positive and negative situations may have separate underlying mechanisms (Heinz et al 2003). Our previous research demonstrated correlation between intensity of depressive symptoms and intensity of cravings (Boykoff et al 2010; Abulseoud et al. under revision). To investigate the relationship of negative cravings with comorbid anxiety and depressive disorders, we evaluated the presence of these phenotypes in alcohol dependent subjects participating in the prospective study ''A Probe Study of Acamprosate: Genes Associated with Response'' supported by NIAAA P20 Grant ''Mayo Clinic Center for Individualized Treatment of Alcohol Dependence.''
Methods: Participants (N=343; 223 males, mean age=42.0±11.8) were assessed for the presence of alcohol dependence and co-morbid conditions (Psychiatric Research Interview of Substance and Mood Disorders, PRISM) and preferred alcohol use situations (Inventory of Drug Taking Situations, IDTS). T-tests were used to compare mean scores of negative craving subscale of IDTS in alcohol dependent subjects with and without comorbid depressive or anxiety disorders.
Results: All participants met diagnostic criteria for current alcohol dependence (DSM-IV). Frequency of Major Depressive Disorder (MDD) and Substance Induced Depression (SID) were 25.0% and 29.9%, while the frequency of Any Anxiety Disorder (AD) and Substance Induced Anxiety (SIA) were 46.1% and 5.6%, respectively. Negative cravings were associated with the history of MDD (p=0.0004), SID (p<0.0001), and AD (p=0.006) but not SIA (p=0.5690).
Conclusions: We have demonstrated that in treatment-seeking alcoholics negative cravings are associated with a history of comorbid depressive and anxiety disorders. We also found similar frequencies of comorbid MDD and SID in our sample, while comorbid AD was much more common then SIA. The implication of these findings is that presence of comorbid mood and anxiety disorders needs to be considered in selection of appropriate treatment interventions. It is also possible that presence of described disorders may be associated with specific genetic factors, which may also be predictive of treatment response. Both hypotheses will be tested in our ongoing research.

0925

THE STANDARDS OF AUD DIAGNOSIS ACCORDING TO ICD-10 IN COMPARISON TO OTHER SELECTED PSYCHIATRIC DIAGNOSIS IN OUTPATIENT CLINIC IN POLAND

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The goal of the study was to compare diagnostic methods of AUD (F10) in an outpatient clinic in Poland and the following psychiatric diagnosis: paranoid schizophrenia (F20.0), depressive episode (F32.0), personality disorder (F6x), mental retardation (F7x), according to ICD-10 diagnosis. The importance of this study is high for the advanced studies on the international classification revision.
Material and Methods: In this study we analyzed randomly chosen files from the whole group of patients treated in the ''Stawowa'' Outpatient Clinic. The key in this study was the analysis of concordance between diagnosis and clinical description in psychiatric and psychological files compared to scientific diagnostic criteria performed by experienced clinicians. The total number of patients treated in the clinic in 2011 is 6814. The number of patients with certain diagnosis in 2011: F10 – 244 patients, F20 – 728 patients, F 32 – 761 patients, F6x – 429 patients, F7x – 208 patients. During the study a total of 30 patients from each five groups of diagnosis were randomly chosen and analyzed by the accordance of different sources of diagnostic descriptions and diagnostic study criteria ICD-10, based on the content of both psychiatric and psychological documentation and also external data, e.g. hospital papers. The average age of patients in each analyzed group were as followed: F10 – 46 year, F20 – 47 year, F32 – 50 year, F6x – 40 year, F7x – 46 year. The percentage of women in each tested group were: F10 – 20%, F20 – 47%, F32 – 63%, F6x – 47%, F7x – 43%. The results of this study are as follow:
- diagnosis from psychiatric documentations for each diagnostic group: F10 – 53%, F20 – 87%, F32 – 97%, F6x – 13%, F7x – 0%;
- diagnosis from psychological documentations for each diagnostic group: F10 – 10%, F20 – 20%, F32 – 10%, F6x – 50%, F7x – 27%;
- diagnosis from external documentations for each diagnostic group: F10 – 30%, F20 – 67%, F32 – 7%, F6x – 20%, F7x – 27%;
- data insufficient for diagnosis for each diagnostic group: F10 – 27%, F20 – 0%, F32 – 3%, F6x – 30%, F7x – 50%.
Conclusion: These results suggest that diagnosis of AUD (F10) is better documented than F6x or F7x, but worse than F32 and especially F20. Collected data can be use to simplify the diagnostic criteria of the further version of ICD to make them easy – to – use for clinicians.

0926

THE INTERACTION OF IMPULSIVITY AND ABSTRACT REASONING ON RESPONSE TO MOTIVATIONAL INTERVIEWING WITH COLLEGE BINGE DRINKERS

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The purpose of this study was to investigate predictors of response to a motivational interviewing (MI) intervention focused on reducing alcohol use among college binge drinkers. Research suggests impulsivity is related to alcohol use, and that intelligence may be related to treatment response, but the moderating effects of intelligence on the relationship between impulsivity and follow-up drinking has not been examined. Participants included 53 ethnically diverse (45.1% minority) college students (M age=20.02, *SD* = 1.90; Female=58.5%). As part of a larger study examining the nature of binge drinking behavior among college students, participants completed measures of past month quantity and frequency of drinking (TLFB), impulsivity (IMPSS), brief intelligence (WASI vocabulary and matrix reasoning subscales), followed by a MI intervention focused on reducing alcohol use. All participants returned for a follow-up evaluating alcohol use at 1-month post-intervention. The moderating effect of WASI score on the relationship between impulsivity and drinking reductions were examined with multiple linear regressions. Change in the number of drinks per drinking day (DDD) at follow-up was predicted by the WASI score ($B = 0.29$), impulsivity ($B = 8.28$), and the interaction between WASI score and impulsivity ($B = -0.08$; $F(10,30) = 2.29$, $p < .05$). Lower WASI scores combined with higher impulsivity resulted in greater reductions in DDD at follow-up. A non-significant model was found for the verbal subscale regression equation ($F(10,30) = 1.27$, $p = .29$). Change in follow-up number of DDD was predicted by matrix reasoning score ($B = 0.36$), impulsivity ($B = 5.18$), and the interaction between the matrix reasoning and impulsivity ($B = -0.10$; $F(10,30) = 3.00$, $p < .05$). A closer examination of the data indicates that lower matrix reasoning and higher impulsivity resulted in greater reductions in alcohol use. These results suggest college students with high impulsivity and lower abstract reasoning skills (matrix reasoning scores) may be more responsive to a brief MI intervention than their peers. MI appears to provide a context for this subset of students to effectively examine and problem-solve their drinking patterns.

0927

A RANDOMIZED CLINICAL TRIAL COMPARING THE EFFICACY OF TWO ACTIVE BRIEF INTERVENTIONS FOR HEAVY COLLEGE DRINKERS

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Brief interventions for college heavy drinkers have shown promise in reducing alcohol consumption and alcohol-related negative consequences. However, intervention duration, content, and delivery method vary across studies. It is therefore not known whether intervention length influences the efficacy of these interventions. The present study is a randomized clinical trial with college student drinkers in which we evaluated the efficacy of two brief interventions that varied in length and were aimed at reducing alcohol use and alcohol-related consequences. Treatment mediators and moderators were also evaluated. Participants (N = 278) were heavy drinking students randomly assigned to a 10-minute or 50-minute brief intervention, or to an attention-control group. Interventions were provided by clinical graduate students trained in Brief Alcohol Screening and Intervention for College Students (BASICS). The sample was predominantly Caucasian (87%) and female (71%). Mean age was 20.1 (*SD* = 2.4) years. Both the 50-minute p= .01 and 10-minute p= .001 conditions were more efficacious than the control in reduction of alcohol consumption, $F(2, 264) = 9.84$, $p = .001$, $\eta^2 = .07$. However, there were no significant differences between the two active conditions p= .16. Participants in the 50-minute, 10-minute, and control conditions reported consuming on average 12.7 (*SD*=7.3), 11.1 (*SD*=7.4) and 15.2 (*SD*=8.6) drinks per week during 4-week follow up. Participants in the 50-minute intervention reported significantly fewer alcohol-related problems (M = 6.8; *SD*=6.1) at follow up, as compared to the control participants (M = 8.6; *SD*=6.7), $F(2, 264) = 3.08$, $p = .048$, $\eta^2 = .02$. In addition, results supported perceived drinking norms $F(1,267) = 5.4$, $p = .02$, $\beta = .16$, and protective behavioral strategies $F(1,267) = 18.4$, $p = .00$, $\beta = -.33$ as mediators. Hypothesized moderators of interventions efficacy (i.e., gender, readiness to change, and drinking motives) were not supported. The present study prospectively investigated the ''active ingredients'' of intervention efficacy, and thereby contributes uniquely to the brief intervention literature. In addition, preliminary results suggest that both longer and shorter BASICS interventions may achieve comparable efficacy in reduction of alcohol consumption.

0928

REDUCING HEAVY DRINKING AMONG FIRST YEAR UNIVERISTY STUDENTS: A RANDOMIZED TRIAL EVALUATING A PARENT BASED INTERVENTION

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High-risk drinking and the negative consequences associated with heavy alcohol use have been well-documented on college campuses. Relative to the general college student population, first year students have been identified as a high-risk group for heavy drinking. A growing body of research suggests that parent based interventions (PBIs) are effective in reducing heavy drinking in first year college students. The purpose of this study is to compare the effectiveness of PBIs with and without booster brochures vs an assessment only control group with first year students.
Incoming first year students (N=443) ages 18–20 were randomly assigned to one of three groups: 1) PBI alone (PBI; n = 141), 2) PBI plus booster brochures (PBI-B; n = 152), or 3) assessment only control (CNT; n = 149). Participants completed questionnaires on drinking variables at baseline and 4 month follow-up assessments. Parents of students in both intervention groups received a parent handbook the summer prior to fall semester. Parents in the PBI-B group also received three booster brochures throughout the fall semester.
Sixty percent of the students completed the 4 month follow-up. There were no baseline drinking differences between those who completed and those who did not. Repeated measures ANOVAs were conducted to assess changes in weekly drinking, frequency of drinking to intoxication, and peak drinking quantity. Results indicated less growth in frequency of drinking to intoxication and peak drinking quantity relative to students in the PBI group and CNT group.
Results of this study provide support for the use of booster brochures in combination with a parent handbook. Findings add to the growing body of literature suggesting PBIs are a promising strategy for reducing the growth of heavy drinking in first year students.

0929

COMPARISON OF AUTOMATED TECHNOLOGIES TO DELIVER BRIEF ALCOHOL INTERVENTIONS TO UNIVERSITY STUDENTS: A RANDOMIZED CONTROLLED TRIAL

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New technologies have previously been used to deliver alcohol interventions to university students. In this study automated interventions delivered by Interactive Voice Response (IVR) are compared to automated interventions delivered over the Internet (WEB).
A total of 2 825 Swedish university students responded to a web-survey assessing risky alcohol consumption using the Alcohol Use Disorders Identification Test (AUDIT). A total of 1 423 (50%) had a risky alcohol consumption and were randomized to one out of four different intervention conditions: a single IVR or WEB intervention given one week after baseline; a repeated IVR or WEB intervention given one and two weeks after intervention, or to an untreated control group. Each intervention was really short including less than 500 words, giving a brief feedback on the baseline assessment and instructions on how obtain a Blood Alcohol Concentration (BAC) below 0,06 percentage. Follow-up of intervention results were assessed six weeks after the baseline assessment.
At follow-up all intervention groups had significantly reduced their AUDIT scores in comparison to the control group. The reduction in AUDIT scores did not differ between IVR and WEB interventions, and there was no difference between single and repeated interventions.
This study indicates that IVR and WEB interventions are equally effective in delivering brief alcohol interventions to university students, and that there is no additional effect by repeating the intervention.

0930

THE MODERATING EFFECT OF BEHAVIORAL MONITORING ON THE ASSOCIATION BETWEEN URGENCY AND DRINKING OUTCOMES AMONG COLLEGE STUDENTS

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Impulsivity has frequently been associated with alcohol use and associated consequences. Positive and negative urgency, or tendencies to act rashly in response to positive or negative mood, are two dimensions of impulsivity that have been associated with a number of problem behaviors. Recent studies have found that both positive and negative urgency are associated with higher levels of alcohol use and related consequences. However, there has been little research on the relationship between urgency and intervention outcomes. The purpose of this study was to examine the relationship between urgency and drinking outcomes in a randomized clinical trial testing a brief intervention for college students who engage in concurrent smoking and heavy-episodic drinking. A sample of 94 undergraduates, who met screening criteria for binge drinking in the past two weeks and concurrent smoking and drinking at least once a week, were recruited to complete a baseline assessment, which included measures of urgency and alcohol use. A subsample of 65 participants were randomly selected to complete 14 days of daily monitoring via mobile phone, including thrice daily reports of alcohol use, affect, and self-control. During the monitoring period, 32 randomly selected participants received brief interventions after each report. The interventions included feedback, information, and tips about alcohol use. Follow-up data were collected at 1 month. The 29 participants who were not randomized to monitoring served as a minimal assessment control group, completing only the baseline and 1-month follow-up assessments. Results indicate that behavioral monitoring, regardless of intervention exposure, significantly moderated the association between both negative and positive urgency and protective behavioral strategies, alcohol-related problems, and blood alcohol concentration (BAC) during peak drinking occasions. Individuals at the highest levels of positive and negative urgency who participated in daily monitoring used protective strategies more often, reported fewer alcohol related problems, and evinced the greatest reductions in peak BAC in comparison to the minimal assessment control group. There was no effect of monitoring at lower levels of urgency. We hypothesize that monitoring might help to mitigate the negative effects of urgency by raising behavioral awareness. Clinical implications and directions for future research will be discussed.

0931

DOES IT MATTER WHO'S WATCHING? THE INFLUENCE OF MONITORING ON ADOLESCENTS' POST-TREATMENT DRINKING OUTCOMES

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Justice-involved youth demonstrate profound levels of alcohol use and related consequences. However, alcohol treatment development for diverse, high-risk youths is still in its infancy. One factor that appears promising is monitoring. Monitoring has been more broadly related to adolescent risk behavior, but has been less examined for post-treatment drinking outcomes. Thus, in a diverse sample of high-risk youth, we sought to examine the role of two types of monitoring, monitoring by the justice system and monitoring by parents, to determine how these types of evaluations might interact with two different types of brief, individual alcohol use interventions (alcohol education; AE vs. motivational interviewing; MI) to predict 3-month drinking outcomes. As part of a larger study examining adolescent alcohol treatment for justice-involved youth in the southwest, 86% of youth were retained at the 3-month follow-up (N=175, M age=16.1, gender 73.9% male; 57% Hispanic; 24% Caucasian). At the 3-month follow-up, youth demonstrated on overall reduction in drinking (baseline DDD M=7.03, 3-month DDD M=5.13, p<.001). Additionally, youth being monitored by the justice-system evidenced greater reductions in DDD than youth who were not (M=–4.45 vs. M=-.94, respectively; p=.004). But, justice-system monitoring did not moderate the effect of intervention type on 3-month drinking outcomes. In contrast, parent monitoring did not directly influence 3-month drinking outcomes, but did moderate the effect of intervention type on 3-month drinking outcomes [$F(3, 118)=4.97$, $R^2= .09$, $p=.003$; $\beta=.82$, $t=2.27$, $p=.025$]. Specifically, youth who had lower levels of parental monitoring evidenced no difference in outcomes across intervention condition. Contrary to expectations, youth with higher levels of parental monitoring showed greater reductions in the AE vs. the MI condition (M=–4.73 vs. M=–.53, respectively, p=.002). In terms of other potential influential factors, while Hispanic youth evidenced greater alcohol use reductions than Caucasian youth (M=–2.6 vs. M=-.59), this difference was not significant (ns). Further, examined cultural variables (e.g., ethnic identity, acculturation, generational status, years in US) did not moderate intervention effects. Together, these data suggest that closer scrutiny to the influence of both parent and justice-based monitoring is critical to interpreting outcomes following brief interventions with high-risk youth.

0932

EXAMINING THE EFFECTIVENESS OF A SCHOOL-BASED MOTIVATIONAL INTERVIEWING ALCOHOL INTERVENTION WITH MINORITY ADOLESCENTS

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The current study examined data from an NIAAA funded randomized, controlled trial of a school-based motivational interviewing intervention with minority youth (5R01AA013825-02 – Wagner, PI). The goal of this study was to examine the effectiveness of this intervention program in reducing alcohol use among participants. Participants were recruited across 6 high schools in the Miami-Dade Public School system. The sample included 541 adolescents (58% male), aged 14–19 years old (M 15.91, SD 1.02) and was racially/ethnically diverse: Hispanic 68%, African American 13%, White 12% and Other 7%. Participants were randomly assigned to a standard care control condition and a treatment condition which included a motivational interview session reviewing a personalized feedback report. Specifically, we examined differences for participants who responded to treatment (i.e., participants who reported significant ($p < .05$) reductions in drinking across multiple indices - total drinks and drinking days and maximum # of drinks consumed in one occasion; n= 93) at 3 months post intervention vs. participants who did not respond to treatment (n = 45). Although the groups did not differ in gender, ethnicity, age, nativity or baseline levels of alcohol use; there were significant differences in their baseline levels of other drug use. Specifically, participants who did not respond to treatment reported significantly higher cocaine (20%), stimulant (16%) and marijuana (58%) use at baseline than treatment responders (4%, 3%, 39%). Furthermore, at baseline, participants who did not respond to treatment also met criteria for drug abuse (38%) significantly more frequently than those who did respond to treatment (19%). We also found that treatment responders reported significantly less drinking as compared to the standard care control group across multiple domains at 3 months post treatment. Results indicate that this brief intervention appears to be more effective for adolescent drinkers who are not using other drugs or if using other drugs, have not yet experienced a negative consequence from use (no diagnosis). These findings have important implications for treatment in that they provide further information regarding how to triage adolescents into the briefest and most effective level of treatment.

0933

ADOLESCENTS AT RISK FOR EXCESS ALCOHOL CONSUMPTION ARE INFREQUENTLY ASKED OR COUNSELED ABOUT DRINKING ALCOHOL

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Purpose: Alcohol misuse is particularly widespread among adolescents and young adults. Practice guidelines recommend screening and physician advice about alcohol use to help address this common cause of injury and premature death. A recent national survey of adults revealed that, while most saw a physician in the previous year, only a small minority were asked and advised about risky drinking, particularly young adults ages 18–24, those most likely to exceed low-risk drinking guidelines. This study explores the proportions of 10th grade adolescents nationwide who saw a physician, were asked about their drinking, and advised about alcohol-related health risks or to reduce or stop drinking.
Methods: A three-stage stratified sample of school districts, schools within districts, and classes within schools yielded 2,524 students representative of 10th graders in public, private, and parochial schools in the U.S. who completed a self-administered survey of 102 questions taking an average of 45 minutes. Alcohol use, physician contact, and whether respondents received advice about alcohol use were explored.
Results: Of respondents, 83% saw a physician in the past year, 48% were asked at their last visit about drinking alcohol, 39% were given advice about drinking risks, and 15% advised to reduce or stop drinking while, in the past 30 days, 35% drank alcohol, 13% reported being drunk, and 6% drove after drinking. Frequency of drinking or drunkenness were not related to seeing a doctor or being asked about drinking. Drinkers were significantly more often advised about drinking risks (43%) than non-drinkers (36%) as were those who reported being drunk or not (45% vs. 37%). Drinkers were more likely than non-drinkers to be advised by doctors not to drink (22% vs. 12%) as were those who drank to intoxication (24% vs. 12%), but clearly most who drank and were drunk in the past 30 days were not advised about drinking risks or to cut down or stop.
Conclusions: Despite practice guidelines, most U.S. 10th graders are not asked at medical visits about their drinking or advised about drinking risks, or advised to reduce or stop, even those who reported being drunk in the past month. Physicians should routinely ask and advise 10th grade patients about alcohol use because of the immediate health and injury risks and established links between early drinking onset and alcohol dependence and increased risks as adults of injuring oneself and others after drinking.

0934

THE EFFICACY OF BRIEF INDIVIDUAL AND GROUP MOTIVATIONAL INTERVENTIONS FOR MANDATED COLLEGE STUDENTS IN A CAMPUS MENTAL HEALTH SERVICE DELIVERY SETTING

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Research examining the efficacy of brief alcohol interventions for mandated students delivered by trained service providers in the context of naturally existing campus-based health care settings is important for several reasons. Such research can help identify both facilitative factors and potential barriers when translating laboratory findings to practice, and such studies can help us evaluate how we might engage our mandated students in accessible interventions within campus service delivery settings most familiar to them. The aim of this study was to examine further the efficacy of individual and group brief motivational interventions delivered by trained service providers at a counseling center within a large public university in the Northeast to a population of students mandated for alcohol policy violations. Participants were 144 students sanctioned for violations of campus alcohol policy who agreed to participate in the research. These students attended an enrollment meeting, and were randomly assigned to complete either an individual face-to-face BASICS intervention or a group-delivered Alcohol Skills Training Program (ASTP) intervention. Interventionists were psychologists trained to deliver BASICS and ASTP interventions. Significant differences were found between the 6-month outcomes of the BASICS interventions and the ASTP interventions, with BASICS emerging as more effective than ASTP. Specifically, BASICS was significantly more effective than ASTP with regard to reductions in alcohol consumption and negative consequences of alcohol use, and increases in use of protective behavioral strategies at 6-month follow-up. Additionally, BASICS performed significantly better than ASTP in terms of correction of alcohol use norm misperceptions at 6-month follow-up. Results suggest that individual face-to-face brief motivational interventions may be an effective alternative for mandated students. To provide such target population-relevant and responsive screening and brief intervention within naturally-existing and accessible university service delivery environments is a very promising strategy and a feasible and effective solution to the challenge of mandated college student high-risk drinking, with benefits for the individual and the overall quality of campus life. Additional research examining the efficacy of brief motivational interventions for mandated students delivered by trained service providers in campus health care settings is recommended.

0935

RANDOMIZED CONTROLLED TRIAL EVALUATING A WEB-BASED PERSONALIZED NORMATIVE FEEDBACK INTERVENTION FOR REDUCING ALCOHOL-RELATED RISKY SEXUAL BEHAVIOR

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While prior research has shown personalized normative feedback interventions are efficacious at reducing high-risk drinking behavior and are mediated by reductions in normative perceptions, little research has examined personalized normative feedback interventions aiming to reduce alcohol-related risky sexual behavior. The purpose of the present study was to determine if reducing drinking behavior also reduces alcohol-related risky sexual behavior, or whether an intervention specifically targeting alcohol-related risky sexual behavior is necessary. In a randomized controlled trial, 479 heavy-drinking, heterosexual, sexually-active college students were stratified by gender and level of drinking and randomly assigned to receive an alcohol only intervention, a risky sexual behavior only intervention, a combined alcohol and risky sexual behavior intervention, or an attention control group. Retrospective assessments of alcohol use and sexual behavior were conducted at baseline and at three and six months. All assessment and intervention procedures were web-based. Poisson or negative binomial regression was used to analyze data. Results indicated a significant reduction in drinking outcomes for the alcohol only and the combined alcohol and risky sexual behavior interventions relative to control with most intervention effects on drinking outcomes remaining significant at the six-month assessment. The risky sexual behavior only intervention did not impact drinking outcomes. Alcohol-related risky sexual behavior outcomes showed less reduction and more variability relative to alcohol outcomes. Findings further demonstrated a significant reduction in alcohol-related risky sexual behavior outcomes for the risky sexual behavior only and the combined alcohol and risky sexual behavior interventions relative to control with intervention effects only seen at the 3-month assessment. The alcohol only intervention did not impact alcohol-related risky sexual behavior. Finally, results suggested significant evidence of mediation such that reducing normative perceptions was associated with reducing high-risk behaviors. These findings demonstrate that personalized information specific to drinking in sexual situations was needed to reduce alcohol-related risky sexual behavior. Furthermore, this study highlights the potential utility of a very brief intervention that can be delivered via the Internet to reduce high-risk alcohol-related sexual behaviors among college students.

0936

BRIEF ONLINE INTERVENTIONS TARGETING RISK AND PROTECTIVE FACTORS FOR INCREASED AND PROBLEMATIC ALCOHOL USE AMONG AMERICAN COLLEGE STUDENTS STUDYING ABROAD

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Research documents increased and problematic alcohol use during study abroad experiences for American college students. In addition, study abroad students may be a self-selecting subgroup of students who drink at greater rates and experience more consequences than non-study abroad students both prior to and after trips. Despite increasing numbers of students studying abroad each year and a growing concern about this high-risk event among researchers and student affairs personnel, there is limited research available documenting efficacious preventive programs with these students. Previous work suggests perceptions of study abroad peer drinking and host country native adult drinking are risk factors for increased alcohol use while abroad, while components related to positive Sojourner Adjustment (i.e., the process of positive and healthy adjustment among individuals establishing temporary residencies in new cultures) may protect against problematic use. Employing a 2 x 2 longitudinal randomized intervention design with an assessment only control condition, the present study sought to prevent increased and problematic alcohol use by correcting misperceptions of study abroad student and host country native drinking norms and by promoting positive and healthy adjustment into the host culture through brief online personalized feedback interventions. A sample of 343 study abroad students were randomly assigned to one of four conditions including a personalized normative feedback intervention (PNF), a Sojourner Adjustment feedback intervention (SAF), a combined PNF + SAF intervention, and an assessment only control condition. Multilevel regression analyses revealed that, contrary to hypotheses, participants in the SAF intervention condition increased their drinking by a rate of 31% during the first month abroad compared to control. This effect was mediated by perceived abstinence rates, such that increased drinking at first month abroad for SAF participant was explained by participants' decreases in the perceived abstinence rate of their host country. In contrast, SAF and PNF participants reported a 31% and 27% reduction, respectively, in alcohol-related consequences compared to control participants during the last month abroad. This research represents an important first step in designing and implementing efficacious interventions with at-risk study abroad college students using online methodologies with normative information and Sojourner Adjustment content.

0937

SERTRALINE TREATMENT IN SUBTYPES OF ALCOHOL DEPENDENCE: A REPLICATION
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Purpose: There Is Converging Evidence That The Selective Serotonin Reuptake Inhibitor Sertraline May Have Differential Efficacy For Reducing Drinking Between Alcoholic Subtypes. Pettinati Et Al. (2000) Reported That Individuals With ''Lower-Risk/Severity'' Alcohol Dependence Had More Favorable Drinking Outcomes With 14 Weeks Of 200mg/Day Of Sertraline Than Placebo, Whereas Individuals With ''Higher Risk/Severity'' Alcohol Dependence Did Not. The Purpose Of The Present Study Was To Examine The Efficacy Of Sertraline In A Different Sample Of Alcohol Dependent Outpatients Who Also Met Dsm-Iv Criteria For Major Depression.
Methods: This Is A Secondary Analysis Of A Recently Published Trial (Pettinati Et Al. 2010) Of A 14-Week Double-Blind, Placebo-Controlled, Clinical Trial Examining The Efficacy Of Either Naltrexone (100mg/Day) Or Sertraline (200 Mg/Day) Or Their Combination In Depressed Alcoholics Who Also Received Cbt. Examination Of Only The Placebo And Sertraline Groups Allowed For A Replication Of The Pettinati Et Al. (2000) Study's Analysis In A Comorbid Sample. 79 Subjects Were Classified Into ''Lower- Risk/Severity'' ($N = 45$) And ''Higher-Risk/Severity'' ($N = 34$) Alcohol Subgroups Using A *K*-Means Clustering Procedure.
Results: For Both % Days Drinking And % Days Heavy Drinking During The Trial, There Was A Significant Interaction Between Alcohol Subtype And Medication Condition ($F = 7.13$, $P=.01$; $F = 5.01$, $P=.03$, Respectively), Favoring The ''Low Risk/Severity'' Group.
Conclusion: Results From This Study Replicate The Previous Findings Of Pettinati Et Al. (2000) And Provide Further Evidence For A Subgroup Of Alcohol-Dependent Individuals That May Benefit From Treatment With Sertraline (''Lower-Risk/Severity''); As Well As A Subgroup Of Alcohol Dependent Patients Who May Not Benefit (''Higher-Risk/Severity''). This Was True Even Though The two study samples differed in severity of depression and alcohol consumption at study entry, and in racial composition. This increases both confidence in the findings and generality of the results for clinical application. Kranzler et al. (2011) recently reported a similar interaction between late-onset/low-vulnerability alcoholics vs. early-onset/high-vulnerability alcoholics with 200 mg/day of sertraline but only among those homozygous for the long allele of the serotonin transporter gene. Further research is necessary to determine the relationship between genetic variation and SSRI efficacy in these alcoholic subtypes.

0938

COMBINATION PHARMACOTHERAPY SERTRALINE AND NALTREXONE DECREASES SUICIDAL IDEATION SCORES IN CO-MORBID DEPRESSED ALCOHOLICS
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Purpose: Major depressive disorder (MDD) is more common in people who suffer from alcohol dependence (AD) than in the general population (Davis, 2008; Hasin, 2005). Though the risk of suicidality is inherent in depression and research points to AD as a risk for suicide (Vijayakumar, 2011), few studies have looked at the pharmacological treatment of suicidality in depressed alcoholics. People with alcoholism report more suicidal ideation and are at higher risk for attempted suicides (Sher, 2005; Grant, 1999). Research supports the use of antidepressant treatments for suicidality (Baldessarini, 2007; Gibbons, 2005; Gibbons, 2007; Tandt, 2009). Studies of treatments for depressed alcoholics have mainly examined the sole use of antidepressants (Cornelius, 2004). Research has begun to examine the efficacy of combination pharmacotherapy for the treatment of MDD and comorbid AD (Pettinati, et al, 2010) by adding to the antidepressant a medication approved to treat AD. This study aims to analyze the effect of combining sertraline and naltrexone for the treatment of suicidal ideation in depressed alcoholics.
Methods: Data from comorbid AD and MDD patients were pulled from a larger 14-week, double-blind, placebo-controlled clinical trial examining the efficacy of naltrexone alone (100 mg/day), sertraline alone (200 mg/day), or the combination of naltrexone and sertraline. The analysis examined the combination of sertraline and naltrexone (SN) group versus the three other (OT) groups combined. Suicidal ideation was assessed using the Beck Depression Inventory (BDI) item #9. The BDI was assessed at four points during clinical trial.
Results: At baseline, the groups did not differ significantly on suicidality (SN = 0.31; OT = 0.32; t=.12, p=.90). Suicidality was significantly reduced throughout the 14-week clinical trial. By the end of treatment, the SN group had a significantly lower suicidality score than the OT groups (SN=.06; OT=.19; t=2.2, p=.03).
Discussion: Pettinati et al (2010) reported that depressed AD patients tended to not be depressed by the end of treatment after receiving the combination of sertraline and naltrexone. The present study extended these findings to suicidality using the BDI. The data suggested that combining sertraline and naltrexone may be more effective than either medication alone or placebo for the treatment of suicidality in depressed alcoholics.

0939

EFFECTS OF SERTRALINE ON ALCOHOL CRAVING AND CONSUMPTION IN THE LATE LUTEAL PHASE OF NON-TREATMENT SEEKING ALCOHOL DEPENDENT WOMEN
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Background: It has been suggested that the menstrual cycle is able to influence some aspects of alcohol-seeking behavior. For example, a relationship between pre-menstrual syndrome and alcohol consumption has been shown in college women who are relatively early in their drinking careers, before the development of severe alcohol-related problems. It has also been shown that women with alcohol-dependence increase their drinking in the premenstrual phase. Sertraline seems to play a role in the treatment of premenstrual dysphoric disorder with respect to the luteal phase. Together, these data strongly suggest that studying the menstrual cycle in the present study could demonstrate a relationship between alcohol-seeking behavior measures, the menstrual cycle, and sertraline administration.
Aims: We hypothesize that alcohol craving/consumption in menstruating women will be highest during the late luteal phase of the menstrual cycle. Furthermore, we hypothesize that alcohol craving/consumption during the late luteal phase will be reduced when women are receiving sertraline compared to placebo.
Method: A double-blind placebo controlled 2 x 2 design human laboratory pilot study that randomized 58 non-treatment-seeking alcohol dependent persons who were genotyped for their 5'-HTTLPR variant genotype (LL or SS/SL) into one of two counterbalanced arms: participants in the first arm (LL) received either 200mg/day of sertraline or ondansetron 0.5mg/day for 3 weeks followed by an alcohol self-administration experiment (ASAE), then received placebo for 3 weeks followed by a second ASAE. Participants received the second drug for 3 weeks followed by a third ASAE. Participants in the second arm (SS/SL) received the same medications in the same balanced fashion. Weekly measures and ASAEs assessed menstrual cycle phase in women and alcohol craving/consumption.
Results: Considering all women in the study, women receiving the hypothesized matching medication drank less during the week prior to the first ASAE [DDD = 7.9 (4.1)] than women receiving the mismatched medication [DDD = 15.2 (9.3), $t(14.3) = 2.35$, $p = .03$]. Fifteen women met criteria for the sub-analysis. Analysis of craving and consumption during the late luteal phase while taking sertraline compared to placebo will be presented.
Discussion: Implications for pharmacotherapy of drinking by women with sertraline particularly during the late luteal phase will be discussed. Supported by NIAAA Grant R01-AA016079.

0940

USING TEXT MESSAGING AND ASSESSMENT VIA MOBILE PHONE TO IMPROVE ADHERENCE TO NALTREXONE ?AMONG TREATMENT SEEKING HEAVY DRINKERS
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One of only three FDA-approved medications to treat alcohol dependence, naltrexone is a front-line therapy for treatment-seeking heavy drinkers. Unfortunately, previous studies have demonstrated poor adherence among patients receiving naltrexone for alcohol dependence. We are currently examining whether a mobile phone based intervention to improve medication adherence, called AGATE, can improve adherence to naltrexone. AGATE uses text messaging to deliver daily medication reminders and assess self-reported adherence. If after one week good ($\geq$ 80%) adherence is reported, reminder and assessment frequency decreases to every three days. If $\geq$ 80% adherence is not maintained, reminder and assessment frequency reverts to daily. Thus far, thirty treatment-seeking heavy drinkers (5 women) been randomized. Mean age is 38.8 $\pm$ 8.8 years. Sixty-three percent expressed a desire to quit drinking entirely while 37% sought to cut back on their drinking. Mean score on the Short Michigan Alcoholism Screening Test is 7.0 $\pm$ 2.1. All have received a prepaid study cell phone and been prescribed naltrexone 50 mg once per day for eight weeks. All complete daily assessments of side effects, alcohol use, and alcohol craving via mobile phone. Half are randomized to receive AGATE adherence reminders and assessments. Adherence is also measured objectively using the Medication Event Monitoring System (MEMS). Four-week MEMS data are currently available for 21 participants and indicate that adherence very good overall with a mean of 87.2% of scheduled doses taken. Mean adherence is 90.1% in the AGATE group and 85.4% in the non-AGATE group. Thus, early results indicate that AGATE may be a promising intervention to improve adherence to naltrexone among heavy drinkers. Future analyses will examine whether these early results hold with a larger sample size and whether adherence to naltrexone is related to improved drinking outcomes.

0941

PHARMACOGENETICS OF NALTREXONE: BEYOND THE MU OPIOID RECEPTOR

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Naltrexone has received empirical support as a moderately effective treatment for alcohol dependence, with OPRM1 genotype emerging as a predictor of treatment response. However, molecular pharmacology research has shown asymptotic saturation of mu-opioid receptors at relatively low doses of naltrexone, thus placing a ceiling on the clinical utility of OPRM1 pharmacogenetics. Relative to mu receptors, naltrexone's binding affinity for kappa and delta opioid receptors is considerably weaker, thus allowing for potential pharmacogenetic influence of these receptor genes above and beyond OPRM1. The present study consists of a re-analysis of a placebo-controlled laboratory study of naltrexone investigating the pharmacogenetic influences of kappa and delta tag single nucleotide polymorphisms (SNPs) on subjective responses to alcohol and alcohol craving. Non-treatment seeking heavy drinkers (n = 40, 12 women) enrolled in a crossover, double-blind, placebo-controlled, laboratory trial of naltrexone. After taking naltrexone (50 mg/day) or placebo, participants completed an intravenous alcohol challenge session in which they were assessed at baseline and at each of the three target breath alcohol concentrations (BrAC = 0.02, 0.04, and 0.06 g/dl). All analyses controlled for the influence of OPRM1. Results supported pharmacogenetic effects of kappa (OPRK1, rs997917) and delta (OPRD1, rs4654327) opioid receptor SNPs on subjective responses to alcohol and alcohol craving. Specifically, medication × OPRK1 and medication × OPRK1 × BrAC interactions were significant predictors of alcohol induced sedation (*p*s < .05). These interactions were such that, while on naltrexone, C-allele carriers endorsed greater overall sedation and steeper increases in sedation across rising BrAC as compared to placebo. Conversely, T-allele homozygotes showed generally lower sedation across BrAC on naltrexone relative to placebo. Significant medication × OPRD1 interactions were observed in terms of alcohol induced stimulation and alcohol craving (*p*s < 0.05) such that A-allele carriers exhibited greater naltrexone induced blunting of stimulation and craving as compared to G-allele homozygotes. This preliminary study supports the potential utility of kappa and delta opioid receptor polymorphisms as predictors of naltrexone response in the human laboratory. These findings can inform clinical trials of naltrexone, and advance naltrexone pharmacogenetics beyond the A118G SNP of the OPRM1 gene.

0942

META-ANALYSIS OF NALTREXONE AND ACAMPROSATE FOR TREATING ALCOHOL DEPENDENCE: WHEN ARE THESE MEDICATIONS MOST HELPFUL?

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Debates over the efficacy of oral naltrexone and acamprosate to treat alcohol dependence tend to focus on global efficacy (does each medication work better than placebo?) or relative efficacy (is one medication better than the other?) when the underlying reality may be more nuanced. The current meta-analysis examined *when* naltrexone and acamprosate are most helpful by testing: (1) the differential efficacy of each medication given its presumed mechanism of action (maintaining abstinence versus reducing heavy drinking) and (2) the hypothesis that different ways of implementing each medication (required abstinence before treatment, detoxification before treatment, goal of treatment, length of treatment, dosage) moderate its effects. A systematic literature search identified 64 randomized, placebo-controlled, English-language clinical trials completed between 1970 and 2009 focused on acamprosate or naltrexone for the treatment of alcohol dependence. Acamprosate had significantly larger effect sizes than naltrexone on the maintenance of abstinence, and there was a trend for naltrexone to have larger effect sizes than acamprosate on the reduction of heavy drinking and craving. For naltrexone, requiring abstinence before the trial was associated with larger effect sizes for abstinence maintenance and reduced heavy drinking compared to placebo. For acamprosate, detoxification before medication administration was associated with better abstinence outcomes compared to placebo. Although effect sizes were modest, differences emerged for the efficacy of each medication based on targeted outcomes and the manner in which the medication was administered. This meta-analysis highlights the need to draw more fine-grained conclusions on what outcomes and under what circumstances pharmacotherapies for alcohol dependence are most efficacious.

0943

ESENSE 2: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF NALMEFENE, AS-NEEDED USE IN ALCOHOL DEPENDENT PATIENTS

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Current treatments for alcohol dependence, aiming to keep patients abstinent, have shown limited treatment and success rates. Reduction of alcohol consumption is increasingly recognised as a valid and needed option that should be an integrated part of the management of alcohol-dependent patients. The main objective of this study was to evaluate the efficacy over 24 weeks of as-needed use of nalmefene 18mg (base) *versus* placebo in alcohol-dependent patients. Efficacy was assessed using the monthly number of heavy drinking days (HDDs) and the monthly total alcohol consumption (TAC; g/day)
Drinking measures were derived from daily drinking estimates collected with the Timeline Followback method. Safety and additional efficacy data were collected throughout the study.
A total of 718 patients (mean age 44.8±10.7 years, 73% men) were randomised (360 to placebo and 358 to nalmefene). There was a favourable effect of nalmefene on reducing the number of HDDs and TAC already evident at Month 1 ($p<0.05$). At Month 6, there was a statistically significant effect (mixed model repeated measures) of nalmefene compared to placebo in reducing the number of HDDs (−1.7 [95% CI −3.1; −0.4]; p=0.012), and a greater, but not statistically significant effect in reducing the TAC (−5.0 [95% CI −10.6; 0.7]; $p<0.088$). Improvements in Clinical Global Impression, as well as reductions in liver enzymes were greater in the nalmefene group than in the placebo group. Adverse events were more common with nalmefene, whereas the incidence of adverse events leading to withdrawal was at the placebo level.
This 6-month study provides evidence of the efficacy of nalmefene in reducing alcohol consumption. Nalmefene was safe and well tolerated and adherence to the as-needed dosing regimen was considered to be good.

0944

SHIFTING THE PARADIGM: ESENSE 1 — A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF NALMEFENE, AS-NEEDED USE IN ALCOHOL DEPENDENT PATIENTS

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Current treatments for alcohol dependence, aiming to keep patients abstinent, have shown limited treatment and success rates. Reduction of alcohol consumption is increasingly recognised as a valid and needed option that should be an integrated part of the management of alcohol-dependent patients; novel treatments directed at reduced drinking may add to treatment coverage and better health outcomes. The main objective of this study was to evaluate the efficacy of as-needed use of nalmefene 18mg (base) *versus* placebo in reducing the monthly number of heavy drinking days (HDDs) and the monthly total alcohol consumption (TAC; g/day) over 24 weeks in alcohol-dependent patients.
A total of 604 patients (mean age 51.6±9.6 years, 67% men) were randomised to placebo (n=298) or nalmefene (n=306). Monthly drinking measures were derived from daily drinking estimates collected with the Timeline Followback method. Safety and additional efficacy data were collected throughout the study. Data were analysed using a mixed model repeated measures analysis.
At Month 6, there was a statistically significantly superior effect of nalmefene compared to placebo in reducing the number of HDDs (−2.3 [95% CI −3.8; −0.8]; p=0.002) and TAC (−11.0 [95% CI −16.8; −5.1]; $p<0.001$). Improvements in Clinical Global Impression - Global Improvement and Severity of Illness scores and reductions in liver enzymes gamma-glutamyltransferase and alanine aminotransferase from baseline were larger ($p<0.05$) in the nalmefene group compared to placebo at week 24. Adverse events (generally transient; most were *mild* or *moderate*) and withdrawals were more common with nalmefene than placebo. Nalmefene was efficacious in reducing alcohol consumption. Nalmefene was safe and well tolerated and dosing on an as-needed basis was feasible.

0945

LONG-TERM EFFICACY, TOLERABILITY, AND SAFETY OF NALMEFENE AS-NEEDED IN ALCOHOL-DEPENDENCE: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Current treatments for alcohol dependence aim at total abstinence, but have not been very successful in attracting patients, and are only moderately effective. Reduction of alcohol consumption is increasingly recognised as a valid treatment aim; novel treatments directed at reduced drinking may add to treatment coverage and better health outcomes. The primary objectives of this study were to evaluate the safety and tolerability over 52 weeks, and efficacy over 24 weeks of as-needed use of nalmefene 18mg (base) *versus* placebo in alcohol-dependent patients.
A total of 675 patients (mean age [SD] 44.3±[11.4] years, 77% men) were randomised to placebo (n=166) or nalmefene (n=509). Drinking measures were derived from daily drinking estimates collected with the Timeline Followback method. Efficacy was assessed using monthly numbers of heavy drinking days (HDDs) and mean total alcohol consumption (TAC; g/day). Safety and additional efficacy data were collected throughout the study. Data were analysed using a mixed model repeated measures analysis.
The difference between nalmefene and placebo in reducing the number of HDDs and TAC was in favour ($p<0.05$) of nalmefene at the majority of time points throughout the study. At Month 6, there was a greater, but not statistically significant effect of nalmefene compared to placebo in reducing the number of HDDs (−0.9 [95% CI −2.1; 0.4]; p=0.160) and TAC (−3.5 [95% CI −9.2; 2.2]; p<0.232). However, at 1-year, the difference to placebo was in favour ($p<0.05$) of nalmefene: reduction in number of HDDs (−1.6 [95% CI −2.9; −0.3]; p=0.017) and TAC (−6.5 [95% CI −12.5; −0.4]; p<0.036). Improvements in Clinical Global Impression, as well as reductions in liver enzymes were greater in the nalmefene group than in the placebo group throughout the 1-year treatment period. The most frequent adverse events (nausea, insomnia, dizziness, headache, and vomiting) occurred within hours to days after first dose and, while leading to withdrawal in some cases, were generally transient and *mild* or *moderate*.
This 1-year study provides supportive evidence for the efficacy of nalmefene in reducing alcohol consumption. In addition, nalmefene displayed a favourable tolerability and safety profile.

0946

BEHAVIORAL ECONOMIC ANALYSIS OF TOPIRMATE'S EFFECTS ON MOTIVATION FOR ALCOHOL

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Topiramate (TOP) is a glutamate antagonist/GABA agonist anticonvulsant that is efficacious in the treatment of alcohol use disorders (AUDs), but for which the mechanisms of its clinical effects remain unclear. The field of behavioral economics integrates concepts from psychology and economics to understand consumption behavior and BE methods can be applied to understand AUD pharmacotherapy mechanisms. In the current study, we investigated the effects of 200 mg TOP on motivation for alcohol using a behavioral economic alcohol purchase task. This methodology permits efficient multidimensional assessment of motivation for alcohol in terms of estimated consumption, expenditure, and price sensitivity. Participants were 99 non-treatment seeking heavy drinkers who were recruited from the community and randomized to either TOP or placebo (PLA) over a five-week medication mechanism evaluation protocol. The medication was titrated to 200 mg/day over a four-week period and primary analyses compared alcohol demand from baseline to target dose (week four) by medication status. For intensity of demand (i.e., consumption at minimal price), a significant Time x Medication interaction revealed a significant reduction by TOP ($F = 6.977$, $p = .01$; difference: PLA = +2%, TOP = −25%; partial h2 = .07). For Omax (i.e., maximum expenditure on alcohol), a significant Time x Medication interaction revealed a significant reduction by TOP ($F = 9.72$, $p = .002$; difference: PLA = +2%, TOP = −26%; partial h2 = .09). For breakpoint (i.e., price fully suppressing consumption for the first time), a statistical trend was evident for the Time x Medication interaction, reflecting a similar pattern of reduction by TOP ($F = 3.11$, $p = .08$; difference: PLA = −7%, TOP = −26%; partial h2 = .03). Supplementary analyses within the placebo condition revealed nonsignificant effects of time (ps>.40) and significant baseline and week 4 correlations (Intensity: r = .69, Omax: r = .71; Breakpoint: r = .59; ps>.001), further supporting the temporal reliability of the APT. Taken together, these results suggest that TOP mechanisms include reducing the incentive value of alcohol in terms of unconstrained alcohol consumption and maximum monetary allocation, with more modest effects on alcohol price sensitivity. More broadly, these findings support the use of behavioral economics in understanding AUD pharmacotherapy mechanisms. Supported by NIH Grants R01 AA007850 and K23 AA016936.

0947

A COMPARISON OF BACLOFEN AND TOPIRAMATE WITH ACAMPROSATE AS ANTICRAVING AGENTS: A NATURALISTIC FOLLOW-UP IN A TERTIARY CARE DE-ADDICTION UNIT

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Alcohol dependence syndrome (ADS) is a common and disabling mental disorder. Pharmacological management is the mainstay of ADS treatment. Acamprosate is one of the FDA approved anticraving agents available for this condition. Emerging treatment modalities include Topiramate and Baclofen. There have been randomised controlled trials evaluating their efficacy with encouraging results. However there are very few studies on effectiveness in the clinical setting. To study this, we examined the naturalistic follow-up of ADS patients in a tertiary care de-addiction setting to compare the effectiveness of Baclofen and Topiramate vis-a-vis Acamprosate.
All patients with a primary diagnosis of ADS who attended the out-patient services of the De-addiction unit of the National Institute of Mental Health and Neuro Sciences between June-December 2009 and prescribed either Baclofen, Acamprosate or Topiramate as anticraving agents were included in the study (n = 381). After excluding patients with psychosis or bipolar disorder, 317 patients were included in the study. Primary outcome measure examined was maximum period of abstinence during naturalistic one year follow- up. Secondary outcomes included relapse and number of follow-ups. Other characteristics compared were socio-demographic variables, age of onset of ADS, number of co-morbidities, family history of alcoholism, duration of alcohol use and presence of externalizing symptoms. The three groups were compared using the Analysis of Variance and the chi-square tests.
Of the 317 patients, 104 (32.8%) were on Baclofen, 106 (33.4%) on Topiramate and 107 (33.8%) were on Acamprosate. All groups were comparable in the duration of ADS and socio-demographic variables. The age of onset of ADS was lower in the Baclofen and Topiramate groups. Substance dependence comorbidities (Tobacco > Cannabis > Benzodiazepines > Opiate) and externalizing symptoms were significantly greater in the Baclofen group. A significantly high proportion (59.9%) of patients relapsed over the follow up period. There were no differences between the groups with respect to the maximum period of abstinence, number of follow-ups and relapse rates.
These preliminary findings indicate that Baclofen and Topiramate are as effective as Acamprosate in the management of ADS. In addition, Baclofen seems to be useful in early-onset ADS, with externalizing symptoms and multiple substance dependence comorbidities.

0948

EFFECTS OF PRAZOSIN ON DRINKING PARAMETERS IN ALCOHOL DEPENDENCE

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Among the first four Vietnam combat Veterans ever treated for severe PTSD with the CNS active alpha-1 adrenoreceptor antagonist prazosin were two Veterans who met criteria for chronic treatment resistant alcohol dependence. Prazosin was titrated upward to 5 mg b.i.d. and 10 mg at bedtime in 1995. The CNS active beta adrenoreceptor antagonist propranolol 20 mg b.i.d. was added as trauma nightmares remitted, and this regimen has been continued to the present (16 years). Alcohol use was quantified with the AUDIT-C. Based on these Veterans' results (see below) and the likelihood that increased CNS noradrenergic activity lowers the threshold for alcohol misuse relapse, we initiated a randomized controlled trial (RCT) in persons with alcohol dependence but no current PTSD. In this six-week trial, prazosin (or placebo) was titrated over two weeks to 4 mg b.i.d. and 8 mg HS, and maintained constant for the subsequent four weeks.
The two Veterans with severe PTSD and comorbid alcohol dependence have maintained complete sobriety from 1995 to the present on their regimen of prazosin and propranolol. AUDIT-C scores for both were 12 pretreatment and have been consistently zero to the present. In the 19 male completers during the final three weeks of the study, prazosin was superior to placebo for number of drinking days (0.9 ± 0.5 vs. 5.7 ± 1.9, $p < 0.001$) and drinks per week (2.6 ± 1.3 vs. 20.8 ± 6.5, $p < 0.05$). Prazosin was tolerated with no significant difference in blood pressure response between prazosin and placebo.
These data suggest efficacy for prazosin (perhaps further augmented by propranolol) for alcohol dependence both with and without comorbid PTSD and support involvement of noradrenergic activity in alcohol relapse. Larger prazosin RCTs for alcohol dependence with and without PTSD are ongoing.

0949

FINDINGS FROM A PILOT CLINICAL TRIAL OF VARENICLINE FOR THE TREATMENT OF ALCOHOL DEPENDENCE

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Alcohol use, abuse and dependence remains a pressing public health problem. Based on its mechanism of action, varenicline seemed to be a likely candidate for treating alcohol dependence. Alcohol dependent subjects (n = 40) were enrolled in a 13-week double-blind placebo controlled clinical trial. Subject visits were once per week. At each visit, subjects were tested for breath alcohol levels, provided self-report data on alcohol and nicotine use and answered subjective questionnaires on mood, craving and impulsivity. In addition, subjects received once a week medical management (MM) sessions. Changes in alcohol use from baseline to end of study, from baseline to follow-up, and from end of study to follow-up were examined, with varenicline treated subjects showing a significant decline from baseline to follow-up ($p = 0.02$), but no significant effect for baseline to end of study ($p = 0.33$). Depression scores decreased during the trial in both groups, with varenicline-treated subjects showing significantly lower scores than placebo-treated subjects ($p = 0.05$). Similar to the mood findings, alcohol craving decreased during the trial in both groups, with varenicline-treated subjects showing significantly lower scores than placebo-treated subjects ($p = 0.01$). These differences in mood and craving are most evident during the later part of the study (weeks 7–12). Repeated measures negative binomial models comparing baseline and the treatment phase showed a significant group by time interaction for proportion of days smoked ($p=0.04$), and for cigarettes per smoking day ($p=0.03$), with each comparison suggesting a greater reduction for the smokers in the varenicline group. Taken together, these findings support continued investigation of varenicline for treating alcohol use disorders, and comorbid alcohol and nicotine dependence.

11. EPIDEMIOLOGY

a. Alcohol consumption rates, drinking patterns **307–319/950–962**

0950

THE INFLUENCE OF INDIRECT COLLECTIVE TRAUMA ON FIRST RESPONDERS' ALCOHOL USE

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Previous research has suggested an increased risk for hazardous and problematic substance use among first responders involved with responding to a community disaster; however, it is not clear how indirect exposure to a critical incident impacts first responders. This work examined the impact of secondary or indirect trauma on changes in alcohol use among urban firefighters who were not directly involved in the response to a large scale community-level disaster. Firefighters enrolled in larger trial of health outcomes whose interview period coincided with the crash of a commercial airplane were the basis for the current report. Aggregate level data on changes in alcohol consumption for these firefighters were examined pre- and post-incident. There was a significant increase in alcohol use following the critical incident. This increase did not occur immediately; it was observed within several days and peaked about 8 days post-incident. Post-hoc analyses revealed that the increased alcohol consumption persisted for several months finally returning to pre-incident levels by 8 months post-incident. Indirect trauma effects, likely operationalized in part through the "brotherhood" of the firefighters, clearly placed firefighters at risk for negative health outcomes following a disaster. Intervention/prevention efforts aimed at distress reduction among first responders should not solely focus on responders with direct involvement in a disaster.

0951

AN EXAMINATION OF THE CHARACTERISTICS OF DIFFERENT MEASURES OF ALCOHOL RELATED ATTENDANCE IN ADULTS PRESENTING TO EMERGENCY DEPARTMENTS

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There is limited analysis of characteristics for different measures of alcohol misuse in attendees of Emergency Departments (ED). We explored the extent to which different measures identified the same or different alcohol related attenders, and characteristics of attendees that were predictive of alcohol misuse.
A 24-hour national survey of alcohol-related attendances was conducted in 32 randomly selected EDs in England. Researchers administered a questionnaire, which included the Fast Alcohol Screening Test (FAST) and obtained a breath alcohol sample from eligible attendees. 61% (n=1,083) of eligible attendees consented to participate. Four measures were dichotomized as positive or negative for alcohol misuse: Self-reported alcohol-related attendance; FAST score >3; ?80mg/100ml Blood Alcohol Concentration (BAC) and having at least one alcohol binge in the last week (consumption of 6 (women)/8 (men) or more drinks on one or more days). Statistical analysis included chi-squared tests and stepwise backward selection logistic regression models using Stata 11.
46.7% of attendees were positive on one or more of the measures and 9.5% being positive on all four measures. Of those positive, FAST identified 79.8% of those positive, Binge in the last week, 74.9%, Self report, 24.1% and BAC >=80mg/100ml, 20.4% respectively. Being younger, single, not an owner occupier, suffered an assault, mental health problem, physical injury, involved in a violent incident, incident where a weapon was used, being injured and having the last drink in a public house were significantly associated with all measures. Regression analysis identified 19 separate variables were predictive of alcohol related attendance across the measures. No single variable was common in being predictive of alcohol related attendance. Being involved in a incident involving a weapon and attending because of mental health issues were predictive of being FAST positive, intoxicated and binge in the last week. Location of the incident being a public house was predictive of self-reported alcohol related attendance, intoxication and binge in the last week.
There is considerable overlap in the characteristics that are associated with different measures of alcohol related attendance. Logistic regression was predictive of different characteristics for each measure. These findings suggest that multidimensional measures provide the most comprehensive means of identifying of alcohol misuse in ED.

0952

EXTRA-MEDICAL PRESCRIPTION DRUG USE AMONG ADOLESCENTS IN THE EMERGENCY DEPARTMENT: ALCOHOL MISUSE AND OTHER DRUGS

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Extra-medical prescription drug use is a growing problem among adolescent and young adult populations. This study examined factors, including alcohol misuse, associated with past year extra-medical prescription drug use defined as using prescription sedatives, stimulants or opioids to get high, taking them when they were prescribed to someone else or taking more than was prescribed among patients seeking care in an academic Emergency Department (ED). Adolescents and young adults (14–20 years old) presenting for ED care were approached to complete a computerized screening questionnaire regarding demographics, alcohol misuse (AUDIT-C ≥ 3 ages 14–17; ≥ 4 ages 18–20), extra-medical prescription drug use, illicit drug use, and violence over a 12 month period as part of a RCT. Logistic regression was used to predict past year extra-medical prescription drug use. Over the study time period, there were 2156 participants (86% response rate) of which 300 (13.9%) endorsed past year extra-medical prescription drug use. Specifically rates of past year extra-medical use was: 8.7% opioids, 5.4% sedatives, and 8.0% stimulants. Significant overlap existed among classes, with over 40% using more than one class of medications. In the multivariate analysis significant predictors of past year extra-medical prescription drug use included being female (OR 1.34, 95% CI 1.00–1.78), being Caucasian (OR 1.45, 95% CI 1.04–2.02), receiving public assistance (OR 1.45, 95% CI 1.06–1.98) sustaining injury from fighting (OR 2.60, 95% CI 1.78–3.80), alcohol misuse (OR 2.53, 95% CI 1.84–3.47), using marijuana (OR 3.63, 95% CI 2.67–4.94),and using cough or cold medicine to get high (OR 3.80, 95% CI2.78–5.15). Those that were in school were less likely to endorse past year extra-medical prescription drug use (OR 0.67, 95% CI 0.46–0.96). Approximately 1 in 7 adolescents or young adults seeking ED care endorsed extra-medical use of prescription drugs in the past year. While opioids were the most common drug used, significant overlap was found in classes of extra-medical prescription drug use. Given the association of alcohol misuse with extra-medical prescription drug use future alcohol intervention studies should consider addressing extra-medical use of prescription drugs. (Supported by NIAAA #018122)

0953

DISCHARGE RATES FOR ALCOHOL RELATED DIAGNOSES AT A LARGE URBAN HOSPTIAL

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Purpose: There has been a move to institute screening and brief intervention for alcohol use as a standard of care in acute care settings. A critical first step to instituting this policy at the institutional level is to determine the number of discharges with an alcohol-related diagnosis. In this study we examined the discharge rate of alcohol related diagnoses at the primary, secondary and tertiary level to determine the prevalence of alcohol related morbidity in the adult population treated in a large urban medical center.
Methods: this study was a retrospective analysis of a discharge data for 2009 from a large urban hospital in southwest Ohio. Data were analyzed through the calculation of frequencies, distribution and discharge rates International Diagnostic codes 9 classification system. Discharge rates were compared to national rates to determine significant differences between dependent rates.
Results: For 2009 there were 29,665 discharges. The discharge rate for a primary diagnosis of an alcohol use disorder was low at 1.65 per 1000 discharges. When the number of discharges with a secondary or tertiary diagnosis was included in the calculation the rate was 60 per 1000 discharges. When a diagnosis of non dependent alcohol use was included as a diagnosis the discharge rate increased to 150 per 1000 discharges or 15%. The discharge rate for alcohol dependence was even lower at 5 per 1000 discharges.
Conclusion: These findings support the development of screening and brief interventions related to the prevention and early treatment of preventable morbidity related to alcohol use for all patients reporting risky alcohol use on admission to an acute care setting.

0954

CHARACTERISTICS OF ALCOHOL USING AND NON-DRINKING SUBSTANCE USERS SEEN BY AN INPATIENT SUBSTANCE USE DISORDERS CONSULTATION SERVICE

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Purpose: The aim of this study is to characterize patients seen by an inpatient Substance Use Disorders Consultation Service, comparing alcohol using patients to non-drinking substance using patients.
Methods: Participants were patients seen by the Substance Use Disorders Consultation Service (SUDS) at an urban, mid-Atlantic academic medical center. The SUDS provides consultation services for patients admitted with medical problems related to or exacerbated by use of alcohol and other drugs. Between January and June of 2011, there were 564 referrals for SUDS evaluation, representing 477 unique patients. Patients had a mean age of 49.9 years (SD 10.72) were predominantly men (69.5%) and a majority were either uninsured or receiving Medicaid (55.9%). Using data obtained from the SUDS assessment, 2/3 (66.5%) of referrals were identified as using alcohol, with or without concomitant use of other substances. Alcohol users were compared to non-alcohol users using chi-square for categorical variables and Student's t-test for continuous variables.
Results: Men were more likely to be alcohol users when compared to women (69.9% vs. 58.5%, $p = .014$). Alcohol users were significantly older than non-alcohol users (51.8 vs. 46.1 years, $p < .001$). There were no differences in the proportion that were uninsured or on Medicaid or in the proportion of persons who had been previously referred to the SUDS when comparing alcohol users to non-drinking substance users.
Conclusions: Among patients referred for inpatient Substance Use Disorders consultation, alcohol using patients are notably older and more likely to be men. Given the association of these epidemiologic factors with increased morbidity and mortality, results suggest that alcohol using substance users admitted to the hospital may be at increased risk for poorer outcomes not solely explained by substance specific disease pathology. Additional exploration should examine whether and how alcohol use relates to differences in medical comorbidity, length of stay, disposition, and mortality.

0955

PRIOR ALCOHOL TREATMENT MODIFIES THE ASSOCIATION BETWEEN ALCOHOL SCREENING SCORES AND MEAN DAILY DRINKING

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Background: The AUDIT-C is a validated screen for alcohol misuse commonly used for routine alcohol screening. Higher AUDIT-C scores are associated with greater alcohol misuse severity, including more alcohol-related problems. Individuals with prior alcohol treatment report greater alcohol misuse severity at a given AUDIT-C score, compared to those with no history of treatment, but it is unknown whether the increased severity reflects greater alcohol consumption. This study compared mean daily alcohol consumption across AUDIT-C scores among screen-positive individuals with and without prior alcohol treatment.
Methods: This study used National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) data from 2001–2002. Respondents were eligible if they screened positive for alcohol misuse on the NESARC AUDIT-C with scores ≥ 3 (women) or ≥ 4 (men). Mean daily alcohol consumption was based on in-depth assessment of past-year drinking. Prior treatment was defined as any help-seeking related to drinking prior to the past year. Individuals who reported treatment only in the past year were excluded because their reported drinking could reflect the period before or after treatment. Linear regression accounting for NESARC's sampling design was used to estimate mean alcohol consumption across AUDIT-C scores (scores 6–7, 8–9,10–12 collapsed to increase precision) for previously treated and never treated individuals, after testing for effect modification by treatment status.
Results: Among 10,489 eligible individuals who screened positive for alcohol misuse, 6% reported prior alcohol treatment. Prior treatment modified the association between AUDIT-C scores and mean daily drinking ($p<0.01$). Daily consumption increased more steeply as AUDIT-C scores increased in individuals with prior treatment compared to those with no history of treatment: AUDIT-C=3–4, 1.3 (95% CI 1.0–1.6) vs. 1.0 (1.0–1.1) drinks/day; AUDIT-C=5, 2.3 (1.4–3.1) vs. 1.5 (1.4–1.6); AUDIT-C=6–7, 2.5 (1.9–3.1) vs. 1.8 (1.8–1.9); AUDIT-C=8–9, 4.6 (3.7–5.6) vs. 3.7 (3.5–3.9); and AUDIT-C=10–12, 13.9 (12.0–15.8) vs. 10.2 (9.5–11.0).
Conclusion: Alcohol consumption is higher in individuals with prior treatment than in those without, and differences increase with increasing AUDIT-C scores. Thus, the greater severity of symptoms at a given AUDIT-C score in previously treated individuals compared to never treated individuals may reflect higher consumption in the treated individuals for a given AUDIT-C score.

0956

THE EFFECT OF DESIRE FOR ABSTINENCE ON LONGITUDINAL ALCOHOL USE PATTERNS AMONG ALCOHOL DEPENDENT ADULTS

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Aims: To examine the effect of desire for abstinence at baseline on longitudinal drinking outcomes among alcohol dependent adults.
Methods: Data are from a longitudinal study that followed 364 SCID-diagnosed alcohol-dependent individuals over 3 years. At study entry, participants were asked if they wanted to be abstinent. Participants provided sociodemographic characteristics and clinical characteristics such as Alcoholics Anonymous (AA) membership, family history, age of onset, and problem severity. At each wave of data collection (n=7), data on alcohol use was obtained with the Timeline Follow-Back (TLFB) interview to calculate percent of days abstinent (PDA), days since last drink (DLD), and number of heavy drinking days (HDD). Bivariate analyses examined who was most likely to desire abstinence at baseline. To understand how the desires for abstinence at baseline influences alcohol use, a multilevel mixed-effects regression model was constructed to examine change in alcohol use patterns over a 3-year time period.
Results: Bivariate analyses showed that participants who wanted to be abstinent at baseline were more likely to be older in age ($F = 5.41$, $p < .01$), to be male ($\chi^2 = 15.42$, $p < .01$), to have previous experience with AA ($\chi^2 = 45.68$, $p < .01$), and to report less drinking consequences ($F = 7.59$, $p < 01$), compared to those with no desire for abstinence. Controlling for the factors above, across all waves, participants who wanted to be abstinent at baseline had significantly more percent days abstinent (out of 90 days in each wave) (b = 18.3, 95% CI = 11.3, 25.3), more days since last drink (b = 73.5, 95% CI = 8.6, 138.3) and fewer heavy drinking days (b = −7.8, 95% CI = −13.7, −1.9), compared to those reporting no desire for abstinence at baseline
Conclusions: Participants who expressed a desire for abstinence at baseline differed from those reporting no desire for abstinence at baseline along both demographic and clinical variables. Further, when controlling for these differences, participants who expressed a desire for abstinence at baseline showed more lowered alcohol use patterns over time. These results indicate that while treatment for alcohol dependence may be effective, outcomes are in part moderated by client readiness factors such as a desire to be abstinent.
This project was supported by Grants R01 AA014442 and T32 AA007477-21 from the National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health.

0957

THE IMPACT OF PERMISSIVE MINIMUM LEGAL DRINKING AGE LAWS ON ADULT BINGEING AND NON-HEAVY DRINKING BEHAVIOR

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Background: Prior to the implementation of the national minimum legal drinking age (MLDA) of 21 in the United States, many states permitted drinking is early as age 18. It has been shown that exposure to permissive (under 21) MLDA laws is not only associated with elevated drinking among young adults in the short term, but also later in life. For example, individuals who could legally purchase alcohol before the age of 21 are more likely to suffer from alcohol use disorders as older adults. However, it is not known how MLDA exposure affects later moderate drinking behavior. This present study uses the changes in MLDA laws during the '70s and '80s as a natural experiment to investigate the potential impact of MLDA exposure on both heavy and moderate, or non-heavy, drinking.
Methods: Data on MLDA laws were paired with alcohol use data from the 1991-92 National Longitudinal Alcohol Epidemiologic Survey (NLAES) and the 2001-02 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Data from subjects born between 1949 to 1972 were analyzed, yielding 41,878 respondents. Frequency of both heavy-drinking days (5+ drinks) and non-heavy drinking days (fewer than 5 drinks) for the previous year at the time of interview were assessed for each respondent. Logistic regression analyses were performed using frequent bingeing (2+ binges a month) and any non-heavy drinking episodes as the main outcome variables.
Results: Individuals exposed to permissive MLDA laws as young adults were more likely to report frequent bingeing and were less likely to report any moderate drinking; they were at 14% higher odds to binge twice or more a month (p=0.017) but were at 15% lower odds to engage in any non-heavy drinking (p=0.02). However, overall drinking frequency was not affected by permissive MLDA exposure.
Conclusions: While the ability to legally purchase alcohol before the age of 21 does not seem to increase overall drinking frequency, our findings suggest that it is associated with certain types of problematic drinking behaviors that persist well into later adulthood, namely characterized by more frequent binge episodes and less frequent non-heavy drinking.

0958

INDIVIDUAL-LEVEL MEASUREMENT OF ALCOHOL AVAILABILITY AND ALCOHOL-RELATED BEHAVIORS IN URBAN YOUNG MEN

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Although alcohol availability has been found to be associated with drinking and related consequences, the findings are not always consistent. Much of the research on this topic has focused on western and southern regions of the US, which may have different patterns of development, housing, transportation, alcohol beverage control laws, and social norms from other regions such as the Midwest and Northeast. Previously, we found a significant association in multilevel models between alcohol availability and alcohol-related behaviors in models that include all of Erie County, NY. However, we did not find that association in multilevel models of just the urban core (i.e., city of Buffalo and first ring suburbs). The research question addressed in this study assesses whether the use of an individual-level measure of alcohol availability, instead of an aggregated group-level measure, will show a relationship with drinking-related behaviors for young men living in the urban core. The data used for this project are from the Buffalo Longitudinal Study of Young Men, which recruited 625 males (ages 16–19 at wave 1) and followed them for two additional waves of data collection 18 months apart during the 1993–1997. Alcohol outlet data from the NY State Liquor Authority for 1995 were used. A GIS was used to calculate individual-level measures of availability by geocoding the location of the outlets and homes of the subjects. Alcohol availability measures were calculated for each individual by counting the number of outlets within 300 meter and 1000 meter radius. This resulted in four individual-level measures of availability: count of outlets for each distance and the count/miles of road. These measures were correlated with abstention (logistic model), average alcohol consumption, high volume drinking, alcohol-related problems, and number of dependence items. No significant associations between availability and alcohol-related behaviors were found. However, some of the associations approached significance (e.g., p=.08). These results raise issues for future research on alcohol availability. Alcohol availability in the urban core may be an oversaturated system, group and individual measures of availability are so high as to make the variation unimportant in models. This does not meant that alcohol availability is unimportant as a public health topic; just the opposite because there is such a high level of availability. Supported by grant R01 AA016161.

0959

TYPES OF ON-PREMISE ALCOHOL OUTLETS AND ALCOHOL-RELATED BEHAVIORS

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Measures of alcohol availability frequently treat all on-premise alcohol outlets (e.g., bars, restaurants, clubs, etc.) the same regardless of the type of outlet. Thus traditional bars are counted in the same way as restaurants, hotels, or other type of outlets when calculating measures of alcohol availability for neighborhoods. The purpose of this study is to use multilevel models to examine if by segregating on-premise alcohol outlets by type when calculating neighborhood on-premise alcohol availability measures, bar-type outlet availability provides greater explanatory power of individual-level alcohol behaviors compared to the traditional, inclusive measure of all on-premise alcohol outlet density. Alcohol outlet data was obtained for Erie County, NY from the State Liquor Authority. A geographic information system was used to geocode the outlet locations and map those locations at the census-tract level to calculate alcohol availability measures. A general population sample of about 3,700 individuals aged 15–45 years were recruited from Erie County using random-digit dial methods and surveyed on various alcohol and neighborhood measures. Participants' addresses were geocoded to census tracts so that alcohol availability measures could be included in multi-level models examining alcohol consumption (individuals nested within Census Tracts). After controlling for demographic characteristics (gender, race, SES), our results indicate different explanatory relationships for our two alcohol availability measures across the three individual-level alcohol-related behavior measures (average alcohol consumption, heavy drinking frequency, and alcohol-related problems). Neither measure of on-premise alcohol availability provided explanation of the between group differences in average alcohol consumption. The two types of alcohol availability measures yielded very similar results for the explanation of heavy drinking behaviors between Census Tracts. However, the all on-premise alcohol outlet availability measure provided better explanation of the between Tract differences in alcohol related problems. The results suggest that the differentiation of on-premise outlet type does not provide any significant improvements in explanation of alcohol-related behaviors and that the non-bar types of outlets in the inclusive measure of availability are relevant in explaining these behaviors, in particular alcohol-related problems.

0960

HEALTH STATUS AND SOCIO-CONTEXTUAL CORRELATES OF PROBLEM DRINKING

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Previous studies have attempted to identify the individual and contextual factors that contribute to Alcohol Use Disorders (AUD). A limitation of many of these studies has been the difficulty to differentiate between environmental and genetic factors which contribute to findings. The current study utilizes a cotwin control design model in order to control for genetic influences and better address the environmental etiology of AUD. This study utilized data collected for the Vietnam Era Twin Registry to examine twin pairs, each with a history of AUD, who have been discordant on alcohol use the previous 10 years. Results indicated that social functioning, role limitations due to emotional problems, and general mental health were significantly associated with AUD symptoms in the past 10 years. Religiousness/spirituality and the quality of social relationships were shown to not be associated with alcohol use symptoms. These results reveal important associations regarding the environmental influence on AUD using a genetically controlled model.

0961

PLANNING TO BE "SAFE" ASSOCIATED WITH INCREASED RISK DRINKING AT FEMALE ONLY EVENTS

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Bachelorette parties have emerged as a unique ritual in which young women both pursue and encourage each other to participate in heavy alcohol consumption, public drunkenness, and sexualized behavior, representing an embrace of traditionally male behavior (Montemurro & McClure, 2005). The purpose of this study was to examine women's drinking behaviors at bachelorette parties, female-driven venues that present a unique opportunity to explore factors associated with women's event-related risk drinking.

Using a convenience sample of 179 women enrolled or employed at a large public university, an online survey was used to collect data regarding bachelorette party attendance during the previous 12 months. Survey questions asked about the type of party (e.g., bar crawl, in-home), party-related drinking behaviors, and other risk behaviors during the party. Questions also asked about the presence of organized pre-party "safety plans," typical alcohol usage, and general demographic questions.

Preliminary results indicated that travelling from bar to bar during the party was significantly related to the total drinks consumed, i.e., those who reported traveling drank more than those who reported not traveling. Past 12 month incidence of driving after drinking and riding with a driver who had been drinking was significantly correlated with total drinks the day of the party, specifically those who reported driving after drinking or riding with a driver who had been drinking reported consuming more drinks than those who reported no driving after drinking. Additionally, the number of total drinks consumed the day of the party was significantly correlated with age at first drink, frequency of drinking, and largest number of drinks. Most interestingly in terms of application to prevention strategies, 41.5% of the respondents who reported partying in public places indicated the group had a "safety plan" (e.g. designated drivers, making sure no one went off with a male stranger when she was drunk). However, safety plans were significantly correlated with the total number of drinks consumed at the party and the day of the party, with those making safety plans reporting more drinks consumed.

Drinking at bachelorette parties is related to typical alcohol consumption. The use of safety plans could provide an entry point for gender specific interventions. However, the association of these plans with increased consumption suggests a need for further exploration.

0962

DRINKING BEFORE DRIVING AND OTHER RISKY DRIVING BEHAVIORS: AN EVENT-BASED STUDY

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Risky driving, whether driving while impaired, recklessly, or while distracted, is a leading factor in traffic crashes. Drinking and risky driving may be indicators of a common construct of problem behavior; however, most research is based on reports of drivers' usual behavior or past behavior rather than delineating the association of risky driving behaviors within driving occasions. The purpose of this study was to investigate the co-occurrence of risky driving behaviors by asking survey participants to report on the most recent time they drove a car. In an online survey of alcohol use among college students aged 18–24 (82% aged 18–20), 1583 participants (63% female) answered questions about the last time they drove a passenger vehicle, including a checklist of 23 risky driving behaviors that included aggressive (becoming angry, yelling at someone), reckless (running red lights, speeding), and distracting behaviors (cell phone use, adjusting music). Nearly all respondents (93%) reported one or more distracting behaviors during the trip: 78% were adjusting music and 39% used their cell phones to talk or text. 74% reported one or more reckless driving behaviors, most commonly speeding (42%) and accelerating through yellow lights (48%). Drivers who engaged in risky driving behaviors were significantly more likely to engage in distracting behaviors ($r = .46$, $p<.001$). Drinking before driving was reported by 2.3% of men and 2.2% of women. Drivers who drank were significantly less likely than nondrinking drivers to report one or more risky driving behaviors during the trip (50% vs. 75%, $p<.01$) due to a decreased tendency to speed (23% vs. 42%), accelerate through yellow lights (27% vs. 48%), or become angry at another driver, pedestrian, or cyclist (9% vs. 28%). Participants who drank more drinks in the last week engaged in a greater number of risky ($b=.20$) and distracting behaviors ($b=.20$) during the trip ($p<.001$), as did participants who drank more frequently in the last week ($b=.28$ and $b=.29$; $p<.001$). Although heavier drinkers engaged in more risky driving behaviors during their most driving occasion, drinking before that trip was not related to increased risky behavior during the trip. These findings highlight the distinction between global assessments of risk behavior and event-based assessments, and suggest that global associations between drinking habits and driving risk represent a constellation of risk behaviors or personality characteristics.

12. TRAINING/EDUCATION METHODS 320–321/963–964

0963

IMPACT OF TRAINING ON THE EARLY DETECTION/BRIEF INTERVENTION ON DRUG USE AS REGARDS THE BELIEFS AND SELF CONFIDENCE OF HEALTH PROFESSIONALS

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Screening (early detection) of substance use, followed by Brief Intervention (SBI), represents a useful tool for health professionals, since most people who are in early stages of consumption are not detected (and thus receive no guidance) until they have already developed complications from such use. However, despite the evidence of effectiveness of SBI for alcohol/drug use, many health professionals are still resistant to using them. In order to cope with these difficulties, several studies have emphasized the need of training health professionals in SBI. This way changes in beliefs occur and, as a consequence, the professionals' attitudes regarding the assistance to alcohol/drug users. In this sense, the objective of this study was to assess whether health professionals who attended the SUPERA program have changed their beliefs on SBI procedures, as well as if they have changed their confidence level to perform it, upon completion of the course. SUPERA program was structured to train Brazilian health professionals in SBI procedures through distance education.

Methods: 967 health professionals from the public network of health, who had successfully completed the SUPERA course, participated in this study. All participants answered a questionnaire sent via email about their beliefs and attitudes before and after taking the SUPERA course.

Results: 94% of the participants mentioned that, after they had finished SUPERA course, they felt prepared to detect/guide patients with alcohol/drug problems; 75% mentioned that the SUPERA training was able to generate changes in their beliefs and attitudes on alcohol/drugs; 95% mentioned that they now applied the SBI procedures always/almost always; 91% mentioned that the SUPERA had a significant impact on their professional performance.

Conclusions: SUPERA course had a positive impact on the practice of health professionals since most of the participants reported they were prepared to screen/guide patients on their alcohol/drug use, and were applying the SBI as a routine procedure. Moreover, most professionals felt more confident to investigate patient's alcohol/drug use; to detect consumption through the application of questionnaires; to ask personal questions about alcohol and drugs. (Supported by AFIP)

0964

THE ALCOHOL PHARMACOLOGY EDUCATION PARTNERSHIP: EDUCATING HIGH SCHOOL STUDENTS ABOUT ALCOHOL

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The Alcohol Pharmacology Education Partnership (APEP) was developed to help high school students learn about different aspects of alcohol pharmacology while reviewing concepts in biology and chemistry. A series of 4 teaching modules and an instructional curriculum (www.rise.duke.edu/apep) were developed that contained topics of interest to high school students such as "Alcohol, Cell Suicide, and the Adolescent Brain". Previously, a small study showed that using a science-oriented curriculum to teach high school students about alcohol resulted in increased knowledge about alcohol, more negative attitudes toward drinking, and decreased alcohol consumption (Weiss and Moore, 1988). In the current study, we recruited 156 US teachers for professional development and to field-test the APEP modules in their classes. Before the teachers received any training, control data were obtained by testing approximately 7000 students for knowledge of basic biology and chemistry concepts as well as advanced biology and chemistry knowledge involving alcohol. The following year, we provided teacher training workshops through Distance Learning (DL) technology or at the National Science Teachers Association meeting. The teachers then field-tested the modules in their classes, and another 7000 students were tested as described above. Thus, each teacher served as her/his own control. Results indicate that the more APEP modules that the teachers used, the better their students scored on the two knowledge assessment tests. Furthermore, biology students (most of whom had no previous chemistry) in classes using all 4 modules scored better on chemistry questions than chemistry students in the standard curriculum (i.e., using no modules). In addition, teachers who were provided with 6 hours of professional development in a one-day session or via DL had the same increase in knowledge of biology and chemistry, which persisted for at least a year. The results of the current study support our previous findings with the Pharmacology Education Partnership (PEP), which focused on drugs of abuse (Kwiek et al, 2007). While most drug and alcohol-based curricula are taught in health class, we have shown here that incorporating alcohol education into biology and chemistry classes increases knowledge of basic science concepts as well as alcohol pharmacology. Future studies will demonstrate whether such a curriculum will impact teenager's decisions about alcohol use/abuse.

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0965

CONTRIBUTION OF RARE GENETIC VARIANTS TO ALCOHOL LEVEL OF RESPONSE IN THE SAN DIEGO SIBLING COHORT

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Evidence suggests that rare genetic variants may play an important role in complex disease etiology. Genome-wide association studies, however, have limited power to examine the effect of rare variants. For this reason, understanding of the effects of rare variants on complex diseases remains limited. Recently, a number of statistical ''collapsing'' methods have been proposed to examine rare variants from sequence data by testing the aggregate effect of the variants in a gene on disease susceptibility. The goal of the present study is to identify genes in which rare genetic variants contribute to variation in alcohol response using statistical ''collapsing'' methods.

The coding regions and exon-intron boundaries of 240 candidate genes were sequenced in 288 subjects with a familial background of alcohol dependence from the San Diego Sibling cohort. These subjects had been tested for level of response to an alcohol challenge. To assess the association between rare genetic variants and level of response to an alcohol challenge, we used the ''step-up'' statistical approach to combine multiple rare variants in each gene and analyze them as a single group.

Genetic screening of 240 genes in 288 subjects has led to the identification of 4,452 genetic variants (9% of them are rare (MAF<5%)). Out of these variants detected, 30% were non-coding variants, 31% silent variants and 39% missense variants. Using the ''step-up'' statistical method, we found that aggregations of rare variants within *CHRNA3* and *OR13C5* genes were associated with alcohol level of response phenotypes in Latino subjects (p-values<0.05).

Thus, rare variants within *CHRNA3* and *OR13C5* genes contribute to the etiology of level of response to alcohol. These results suggest that rare genetic variants may explain a non-negligible part of the variance of level of response to alcohol.

0966

GENETIC VARIATION IN THE NPY GENE MODERATES STRESS RELATED DRINKING IN COLLEGE STUDENTS OF AFRICAN DESCENT

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Background: Neuropeptide Y (NPY) is abundant in the CNS, has anxiolytic properties and is released in response to stress. Genetic polymorphisms in the NPY gene associated with reduced NPY expression have been correlated with clinical depression and increased emotional reactivity in laboratory settings. We examined whether NPY polymorphisms moderate the association between past-year stressful life events and current drinking in a sample of college students of African ancestry.

Methods: Students recruited at a Historically Black University completed web-based measures of past-year stressful life experiences and daily reports of drinking and heavy drinking over a 30-day period. Participants were genotyped at 4 single nucleotide polymorphisms in the NPY gene (rs16148, rs16147, rs16138 and rs5574). Generalized linear models were used to examine the effects of past-year stressful life experiences, genotype and their interaction on the two drinking measures.

Results: In students who completed 15 or more daily surveys (n=416) there was a significant interaction of past-year stressful events and NPY genotype on the number of drinking days ($p<0.0001$) and heavy drinking days ($p<0.0001$). Students with NPY alleles associated with reduced NPY expression and increased depressive symptoms in prior studies (rs16147 C-allele and rs5574 T-allele) had stronger associations of past-year life stress and increased levels of drinking.

Conclusions: In college students of African descent, the influence of past-year stressful events on current drinking was moderated by NPY gene polymorphisms previously associated with changes in NPY expression.

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0967

META-ANALYSIS OF ASSOCIATION STUDIES EXAMINING ALCOHOL DEHYDROGENASE GENE POLYMORPHISMS AND ALCOHOL DEPENDENCE IN NATIVE AMERICANS

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ADH is responsible for the oxidation of alcohol to acetaldehyde, and thus, directly influences alcohol metabolism. It exists in multiple isozymes that differ in their kinetic properties. These isozymes are encoded by the seven ADH genes (*ADH1A, ADH1B, ADH1C, ADH4, ADH5, ADH6, ADH7*), which are located within a 364 kilobase region on chromosome 4q. A number of linkage and association studies conducted in a number of distinct ethnic groups have suggested a relation between alcohol dependence phenotypes and the alcohol dehydrogenase (ADH) genes. The present study completed a meta-analysis of the associations between DSM-III-R defined alcohol dependence and 18 single nucleotide polymorphisms (SNPs) spanning the seven ADH genes in three Native American samples, a California Indian population (CI), a Southwest American Indian population (SI), and a Plains Indian population (PI), that in total included 1311 participants. The meta-analysis was conducted using the METAL software, which uses study p-values to calculate z-statistics that are then weighted by sample size to calculate an overall Z-score and p-value to determine significance across studies. Significant evidence for an association between alcohol dependence and a polymorphism in the promoter region of ADH4 (rs3762894) that has been shown to produce a more active version of the ADH enzyme was observed ($Z = 2.70$, $p = 0.0069$). A trend towards an association between the *ADH1B*2* allele (rs1229984) allele and alcohol dependence was also identified ($Z = 1.820$, $p = 0.0687$). The minor alleles of each SNP were associated with a reduced risk for alcohol dependence. These results provide strong evidence for the involvement of these polymorphisms in the etiology of alcohol dependence among Native Americans. Nonetheless, associations between both SNPs and alcohol dependence have been observed in other ethnic groups suggesting that these relations are not specific to Native American populations.

0968

AUSTRALIAN ALCOHOL GENOME-WIDE ASSOCIATION STUDY FINDINGS AFTER 1000 GENOME IMPUTATION

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We update results from the Australian Alcohol (OZ-ALC) GWAS study, in the light of SNP imputation using data from the 1000 Human Genomes Project. The OZ-ALC study uses a family-based design, with families ascertained for their informativeness for heaviness of drinking (HoD), and includes in excess of 6300 individuals with HoD data and GWAS genotyping on Illumina SNP platforms. Data were analyzed using MERLIN, taking into account the probabilistic nature of imputed SNP genotypes. The most strongly associated SNP met genomewide significance, p=6.2E-9, but accounted for only 0.77% of the variance in HoD, and approximately 0.3% of the variance in alcohol dependence or abuse/dependence factor score measures. This SNP, though intergenic, was in high LD (r2=0.94, D'=1) with intronic SNPs in the Transmembrane Protein 108 (TMEM108) gene, a gene of unknown function that we had previously identified as likely associated with heaviness of alcohol consumption. No other genes had associated SNPs that met genomewide significance. These findings provide further evidence that for human alcohol phenotypes, gene discovery using traditional human genetic approaches is likely to be challenging, and of limited payoff.

0969

ASSOCIATION OF SGIP1 TO ALCOHOL USE DISORDERS IN A NATIVE AMERICAN POPULATION

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A genome-wide association study for alcohol dependence was carried out in a small (N=327) Plains Indian cohort. This previously unreported GWAS yielded no associations at the genome-wide significant level. However four SNPs that lie within the SH3-domain GRB2-like (endophilin) interacting protein 1 gene (SGIP1) were shown to be significantly associated with elevated theta (3–8Hz) resting EEG power. These SNPs are represented on two closely related low frequency haplotypes that span almost the whole of SGIP1. EEG variability has long been regarded as an intermediate phenotype for alcoholism. We therefore analyzed the SGIP1 gene for an association with alcohol use disorders (AUD).
Participants were recruited from a Plains Indian tribe living in rural Oklahoma. A total of 225 individuals had a diagnosis of lifetime DSM-III R AUD: 101 women, mean (SD) age = 41.8 (12.1) yrs; 124 men, mean (SD) age = 41.0 (11.4) yrs). There were 156 non-alcoholics (112 women, mean (SD) age = 44.5 (16.3) yrs; 44 men, mean (SD) age = 39.6 (18.5) yrs. Individuals with AUD had been diagnosed with either alcohol dependence (N = 222) or alcohol abuse (N = 3).
The four SNPs that showed significant GWAS association to theta EEG power (rs6588207, rs10889635, rs66881460, rs10789215), along with 3 SNPs that were sub-threshold in the GWAS but present on two related haplotypes (rs2146904, rs536410, rs2483704), were genotyped by 5'-exonuclease assay.
Six of the SNPs showed significant association with AUD (p-values 0.028–0.001, uncorrected for multiple testing, with the remaining SNP (rs10789215) showing a trend association (p=0.076). Although these are uncorrected p values it should be noted that these SNPs are in linkage disequilibrium and therefore not independent. The alleles associated with increased theta power were underrepresented in individuals with AUD, consistent with an earlier report of lowered theta power in alcoholics from this dataset.
Our results show that SNPs at a gene originally identified by GWAS for an EEG phenotype also show association with AUD. In addition to identifying SGIP1 as a candidate gene for an alcohol related trait, these findings also validate theta EEG power as an intermediate phenotype for alcoholism and demonstrate how the use of intermediate phenotypes reduces the size of study population required for genpome-wide significance n complex traits.

0970

GWAS OF ALCOHOL CONSUMPTION AND PROBLEMS IN THE FINNTWIN12

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To date, several GWAS on alcohol dependence have been published without producing robust, replicable genetic association signals. One such problematic aspect of conducting genetic analyses on alcohol problems is the imprecise and heterogeneous nature of the phenotype. Results from our previously published twin analyses indicate that different aspects of alcohol consumption and problems are genetically heterogeneous. In the present study, we examine the genetic architecture of five measures of alcohol consumption and problems within the Finntwin12, a large population based twin study. We used the resulting genetic factor structure to create genetic factor scores for each individual. We then conducted a genome wide association study in the same twin sample utilizing the information gained from the twin analyses; in addition to analyzing our primary phenotype of interest, DSM4 Alcohol Dependence symptoms, we also analyzed two genetic factor scores that emerged from the multivariate twin analyses. The first genetic factor accounts for the genetic variation shared across five measures of alcohol consumption and problems (drinking frequency, drinking quantity, intoxication frequency, maximum drinks/24 hr period, and DSM4 Alcohol Dependence symptoms) and the second genetic factor exclusively loads onto DSM4 Alcohol Dependence symptoms. GWAS data was available on 1,069 individuals (406 MZs; 614 DZs) who were genotyped on the Illumina 670K Custom Array. Regression analyses were carried out in Plink using a quantitative family based method that accounted for the twin structure of the sample. GWA analyses indicated no individual single nucleotide polymorphism (SNP) that met criteria for the genome wide significance threshold, however many SNPs were approaching this threshold, including SNPs located within genes DOK7, UPK1B, FXYD6 and TSHZ2. Additionally, we ran gene-based analyses that produced a number of top gene results including AMPD2, FGF5, and HSPA2. Each of these potential genetic risk factors for alcohol consumption and/or problems needs to be replicated in an independent sample with comparable phenotypic measures.

0971

A FAMILY HISTORY OF SUBSTANCE DEPENDENCE OBSCURES THE GROUP DIFFERENCES IN BRAIN FUNCTION ASSOCIATED WITH HIV-1 AND ART

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Recently, the NIMH called for additional research on the topic of viral and host factors contributing to HIV-Associated Neurocognitive Disorders (HAND) and their response to treatment. This investigation responds to that call by examining a host factor–a family history of substance dependence–often ignored in cognitive and neuroimaging studies of HIV/AIDS patients. We categorized 146 HIV-1 seropositive patients receiving antiretroviral treatment (ART) and 92 seronegative volunteers by the presence (n= 78 pts, 58 control) versus absence (n=68 pts, 34 control) of alcohol, cocaine, or heroin dependence affecting their biological parents. Seropositive patients were further classified by the estimated ability (see McArthur et al 2010) of their individual ART regimens to penetrate the CNS. The indicator of brain function was a 3–7 Hz electroencephalographic oscillatory response (theta ERO) evoked by target stimuli presented during a simple selective attention task. The analysis revealed that the presence of a family history of substance dependence blunted the reduction in frontal theta ERO power accompanying the presence of HIV-1 as well as the improvement in frontal theta ERO power accompanying treatment with ART agents with greater versus lesser CNS penetrance. Secondary analyses employing sLORETA source localization techniques revealed that the source of the theta ERO response evoked by the target stimulus was reduced similarly by the presence of either HIV-1 or a family history of substance dependence. We conclude that a family history of substance dependence complicates and obscures the subtle neurocognitive changes which now accompany HIV/AIDS and ART. Studies of new therapuetic agents for HAND must therefore consider this complication and either exclude or control it.

0972

VARIATION IN *GRM7* IS ASSOCIATED WITH ALCOHOL CONSUMPTION IN A FAMILY BASED ANALYSIS

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The glutamate metabotropic receptor 7 gene (*GRM7*) has been identified in a mouse model as a strong candidate for involvement in voluntary alcohol consumption (Vadasz 2007). To date, most human studies of *GRM7* have been Genome-Wide Association Studies (GWAS) that have found nominal associations between single nucleotide polymorphisms (SNPs) and copy number variants in *GRM7* and substance abuse, specifically nicotine dependence (Uhl 2010) and alcohol abuse (Joslyn 2010; Li 2011).
The current report investigated two SNPs (rs3749380 and rs1485175) in *GRM7* in families from the Colorado Center on Antisocial Drug Dependence (Stallings 2005), an ongoing study between the Universities of Colorado Boulder and Denver. We focused on a measure of alcohol consumption, since this study was conducted to follow-up on the mouse model, where *Grm7* was identified as a strong candidate gene for two-bottle choice voluntary alcohol consumption. Subjects were selected from a combined clinical and community-based sample of adolescents and adults with available genotypic and phenotypic data. The analysis was limited to 2,137 self reported Caucasians, ages ranging from 10 to 80 years (mean age 32). Data were collected in two waves and for the purposes of this study were preferentially used from the more recent wave. The phenotypic data available from each wave are slightly different but were harmonized across the two waves to create a lifetime measure of highest number of drinks consumed in one day. In order to standardize the data, subjects were split into two groups depending on the source of the data, referring to a later or earlier wave. For each wave the phenotypic measure for the clinical subjects were age- and sex-corrected based on the distribution of the community sample (i.e. z scores of clinical subjects were expressed as deviations from the mean of the community subjects). A family based association test for the phenotype was performed using FBAT (Rabinowitz and Laird 2000). The results showed a significant association only between rs3749380 in exon 1 of *GRM7* and alcohol consumption (nominal p=0.037). These results suggest that variation in *GRM7* may be involved in alcohol consumption, which is likely to contribute to future alcohol problems, and may provide a new target for pharmacogenetic therapies.
This work supported by AA017889, DA011015 and DA017637.

0973

HERITABILITY OF AGE AT FIRST DRINK IN INDIVIDUALS WITH AND WITHOUT A FAMILY HISTORY OF ALCOHOL PROBLEMS

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Previous research has demonstrated genetic overlap in the development of alcohol dependence and the timing of alcohol use initiation, as well as increased risk for alcohol problems with a declining age at first drink (AFD; Agrawal et al., 2009; Sartor et al., 2009). While the link between early AFD and alcohol use disorders is well investigated, researchers have not yet explored whether genetic contributions to drinking debut differ depending on people's family history of alcohol problems. The current study employed a sample of 5,868 monozygotic (MZ) and dizygotic (DZ) male and female Australian twins (2,695 complete pairs and 478 singletons) to assess whether the heritability of AFD differed between individuals with and without a parental history of alcohol problems. Twin pairs were classified as family history positive (FH+) if at least one twin reported that their mother or father drank excessively and/or their drinking caused them to have problems with their health, family, job, police, or other problems. Twin pairs were classified as family history negative (FH-) if neither twin reported that either of their parents drank excessively or had any problems. A series of univariate twin models were fit to the data to assess the contribution of genetic, shared environmental, and unique environmental factors to AFD in the overall sample. Sex differences were also assessed. A series of model comparisons, in which parameters were selectively constrained across family history groups, were performed to determine if genetic and environmental contributions to drinking differed. Including a scalar parameter to account for variance differences in AFD across sex resulted in a significant improvement in model fit ($\Delta\chi^2_{(1)} = 6.67$, $p < .01$). In addition, initial model comparisons indicated that constraining estimates for genetic, shared family environmental, and unique environmental parameters across family history groups resulted in a significant deterioration in model fit ($\Delta\chi^2_{(3)} = 23.80$, $p < .001$). However, significant changes in model fit were no longer observed when variance differences between family history groups were taken into account ($\Delta\chi^2_{(3)} = 6.84$, $p = .08$). While AFD was not found to be more heritable in FH+ than FH- individuals, FH+ respondents exhibited greater variance in drinking initiation. Results highlight the importance of accounting for group differences in variability across drinking phenotypes. Supported by NIAAA grants AA007535 and AA013526.

0974

ANALYSIS OF GENETICS OF ANTISOCIAL BAHAVIOR: EFFECT OF PHENOTYPE MEASURES ON FAMILIALITY AND MAOA ASSOCIATION

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The goal of our study is to identify genetic variants associated with behavioral traits that are in turn associated with risk for alcohol use disorder (AUD). The subjects are participants in the Michigan Longitudinal Study, which has been tracking children of alcoholic parents and SES-matched control families for > 25 years. Starting with the enrollment age of 3–5 years, children were assessed at 3-year intervals for a variety of traits including externalizing and internalizing behaviors, temperament, and comorbid symptomatology.

We hypothesized that by selecting those behavioral traits that run in families we can identify a set of the potentially most powerful behavioral phenotypes for genetic studies. Due to the longitudinal nature of this dataset we could test familiality of each of the traits across several time points. Among moderate, but highly significant, heritable traits was a measure of Antisocial Behavior (ASB) ($p < 0.05$). ASB was measured using two developmentally appropriate but slightly different questionnaire forms: (A) The adolescent form of the instrument at ages 12–14 yrs ($h^2 = 26\%$, $p = .04$), 15–17 yrs ($h^2 = 57\%$, $p < .005$), 18–20 yrs ($h^2 = 35\%$, $p = .005$); and (B) the Adult form of the instrument at ages 18–20 yrs ($h^2 = 52\%$, $p < .005$). Some studies have found associations between antisocial and conduct behavior measures and genetic variation in the MAOA promoter as well as interaction with childhood maltreatment, others have found a direct association of MAOA genotype and ASB irrespective of childhood maltreatment, others have failed to replicate either.

We tested the association of the MAOA promoter variant and ASB in a set of 248 unrelated male children of alcoholic parents and SES-matched control families. We found a small main effect of MAOA on ASB (p-value = 0.01) in the age group of 18 to 20 year olds measured using the adult form of the questionnaire, but not with the ASB adolescent form. We are currently addressing questions of the interaction of the MAOA genetic effect and several maltreatment variables. Our preliminary results demonstrate that when testing genetic association, small differences in phenotypic measures across time can affect the association findings.

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0975

EPIGENETIC CHANGES IN ALCOHOL-DEPENDENT INDIVIDUALS: INFLUENCE OF WITHDRAWAL CHARACTERISTICS?

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Objective: Evidence mainly from laboratory studies indicates that ethanol ingestion may cause changes in methylation of CpG promoter regions of candidate genes. These changes may result in subsequent alteration of protein expression. However, evidence for these epigenetic modifications in alcohol-dependent patients and their relationship to clinical phenotypes is scarce. The aim of this initial study is to investigate CpG island methylation changes of GABRA2 and their relationship to clinical phenotypes like withdrawal, tolerance or delirium.
Methods: 47 alcohol-dependent individuals (DSM IV) and 20 controls were characterized according to their methylation rate in 29 GABRA2 promoter CpG sites using quantitative PCR (Polymerase Chain Reaction). Clinical phenotypes like withdrawal, tolerance and delirium tremens were obtained by a semi-structured interview (SSAGA).
Results: Alcohol-dependent subjects had a significantly lower CpG methylation rate compared to controls ($p < 0.001$). Among patients those with tolerance, alcohol withdrawal and delirium, a significantly lower rate of CpG methylation was detected too.
Conclusion: This initial study in alcohol-dependent individuals confirms epigenetic changes as a consequence of alcohol intake which may be related to physiological characteristics of alcohol dependence. Subsequent studies are required to investigate if alcohol intake-related GABRA2 promoter CpG methylation causes changes in mRNA or protein expression.

0976

INTERACTION BETWEEN THE DRD4 VNTR POLYMORPHISM AND PERCEIVED PEER DRINKING NORMS IN ADOLESCENT DRINKING

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Emerging research indicates that the effects of alcohol-conducive social environments on the risk for alcohol use and related-problems differ as a function of the dopamine receptor D4 (DRD4) variable number of tandem repeats (VNTR) genotype. Compared to non-carriers, carriers of the 7-repeat allele of the DRD4 VNTR show greater levels of alcohol consumption and dependence symptoms when exposed to drinking-facilitating social contexts (such as being in the company of heavy drinkers). Another important aspect of the social environment is perceived peer drinking norms. Perception about peers' drinking behavior (descriptive norms) and perception about peers' approval of drinking (injunctive norms) are associated with drinking behavior among adolescents. This study tested whether effects of perceived peer drinking norms would differ as a function of the DRD4 VNTR genotype.

Path analyses using maximum likelihood estimation with robust standard errors estimator were conducted using two-wave prospective data obtained from 176 adolescents (14 to 18 years, 56% female, 44% Black, 21% White, 35% multi-racial or other races). Prior drinking behavior, sex, puberty status, parental education (a proxy of social-economic status), and self-reported race were controlled for in the analyses. A significant interaction between injunctive norms and the DRD4 VNTR genotype was found in the past-month frequencies of drinking and getting drunk. That is, compared with non-carriers, adolescents carrying the 7-repeat allele were more likely to drink alcohol and get drunk when they perceived that their peers approved of drinking. No significant interaction between descriptive norms and the DRD4 VNTR genotype was observed. To test potential population stratification effects, separate analyses were conducted with Black adolescents ($n = 76$); results were the same in Black adolescents.

These findings corroborate prior research on the differential vulnerability to social influences as a function of the DRD4 VNTR genotype, and suggest that perceptions about peers' approval of drinking may play a more important role in adolescents with a risky gene than do perceptions about peers' drinking behavior. Future studies are needed to identify mechanisms by which social environments activate the genetic predisposition to affect adolescents' drinking behaviors. [supported by Chancellor's Initiative funds at Syracuse University]

0977

CATECHOL-O-METHYLTRANSFERASE (COMT) VAL158MET POLYMORPHISM, CHILDHOOD TRAUMA, AND RISK FOR POSTTRAUMATIC STRESS DISORDER AMONG TREATMENT-SEEKING ALCOHOLICS

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The prevalence of childhood trauma among alcoholics is high, as is co-morbidity with posttraumatic stress disorder (PTSD). However, not all alcoholics exposed to childhood trauma develop PTSD. Recent evidence suggests that the COMT Val158Met polymorphism is associated with risk for PTSD, and that traumatic load may moderate this association. In this study, we investigated the roles of childhood trauma and variation at the COMT Val158Met locus in determining risk for PTSD among treatment-seeking alcoholics. The sample included 191 subjects (129 males, 62 females) admitted for inpatient treatment in the NIAAA research program at the NIH Clinical Center; 47 of the 191 subjects (24.6%) were diagnosed with co-morbid PTSD using the Structured Clinical Interview for DSM-IV-TR Diagnoses (SCID). Data on childhood trauma exposure were collected retrospectively using the Childhood Trauma Questionnaire (CTQ). Multiple logistic regression analysis was used to assess risk for PTSD, and included demographic variables such as age, gender, and race, in addition to COMT genotype and the number of childhood trauma types experienced (ranging from 0 to 5) as measured by the CTQ .Results indicated significant effects of gender, the number of childhood trauma types experienced (i.e., traumatic load), and COMT genotype, as well as an interaction effect of traumatic load and genotype. Males were less likely to have co-morbid PTSD (OR = 0.29, 95% CI = 0.12, 0.67) compared to females. The interaction of traumatic load and COMT genotype revealed that the number of childhood trauma types experienced significantly increased risk for PTSD among Val/Met (OR = 2.84, 95% CI = 1.65, 4.89; n = 96) and Met/Met (OR = 4.42, 95% CI = 1.62, 12.09; n = 39) subjects, but not among Val/Val subjects (OR = 1.3, 95% CI = 0.88, 1.88; n = 56). Our results are consistent with previous reports that demonstrate a role for COMT Val158Met genotype and traumatic load in the development of PTSD. Among treatment-seeking alcoholics, those individuals carrying either one or two copies of the Met allele show a stronger association between childhood traumatic load and risk for PTSD. These data add to existing evidence of the complex interaction of genetics and environment in the etiology of PTSD.

0978

EFFECTS OF *ALDH2*2* ON ALCOHOL CONSUMPTION AND PROBLEMS OVER FOUR YEARS OF COLLEGE

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The purpose of this study was to prospectively examine the effect of the *ALDH2*2* allele on drinking-related outcomes during college. We built upon prior research by studying trajectories over four time points, which allowed for latent variable modeling, and by examining trajectories for multiple drinking outcomes: past 90 day drinking frequency, average quantity, and heavy (binge) drinking episodes, and past year drinking-related problems. Our sample consisted of 433 Chinese- and Korean-American undergraduates attending a public university in California who were recruited for participation during their freshman year in college and followed annually for four years (mean age 18.2 - 21.4 years); we included the 416 lifetime drinkers in these analyses. Latent growth models indicated gender and ethnicity were associated with initial levels of alcohol consumption and problems in freshman year, but neither were related to rates of change in alcohol involvement over the college years. *ALDH2*2* was not associated with initial levels of alcohol involvement, but was associated with the growth of alcohol-related problems over the course of college, with individuals who possessed *ALDH2*2* showing a slower rate of increase in problems compared with individuals who did not have *ALDH2*2*. Contrary to our prediction, *ALDH2*2* was not directly associated with trajectories of alcohol consumption, but was found to moderate the relationship between drinking frequency and alcohol-related problems, such that drinking frequency was less strongly associated with problems among individuals with at least one ALDH2*2 allele, particularly in the third year when average rates of alcohol consumption and problems peaked. Possessing a second *ALDH2*2* allele did not significantly alter this relationship. This study represents one of the first longitudinal studies to model the effects of *ALDH2*2* on the development of alcohol consumption and problems throughout the course of college. Our results offer insight into the potential mechanism for how *ALDH2*2* protects against the development of alcohol problems during young adulthood. This research was supported by California Tobacco-Related Disease Research Program grant 10RT-0142 & 12RT-0004 and National Institutes of Health grants K02 DA017652, K02 AA00269, K08 AA14265, R01 AA11257, and R01 AA18179.

0979

INTERACTION OF SEROTONIGENETIC PHARMACOTHERAPIES BASED ON 5-HTTLPR AND D4 ALLELES ON DRINKING IN NON-TREATMENT SEEKING ALCOHOL DEPENDENT WOMEN

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Background: Gene x gene interactions are increasingly important in research of personality traits and endophenotypes. 5-HT plays a central role in the rewarding and addictive properties of alcohol by activating the DA mesolimbic system. There are also direct synaptic contacts between 5-HT terminals and DA cells in the midbrain and 5-HT may help regulate DA function. It is thought that reduced 5-HT neurotransmission in alcoholics with the L/L 5-HTTLPR genotype results in changes in DA function. Ss with SS/SL were hypothesized to respond better to sertraline than ondansetron or placebo. Ss with LL were hypothesized to respond better ondansetron than sertraline or placebo.
Aim: This analysis examines the influence of the DRD4 exon III 7-repeat allele and the 5-HTTLPR polymorphisms and their interaction on alcohol use in women. As far as we are aware, no study has ever examined this gene x gene interaction in an alcohol dependent population receiving medication.
Method: A double-blind placebo controlled 2 x 2 design human laboratory pilot study that randomized 58 non-treatment-seeking alcohol dependent persons genotyped for their 5'-HTTLPR variant genotype (LL or SS/SL) into one of two counterbalanced arms: participants in the first arm (LL) received either 200mg/day of sertraline or ondansetron 0.5mg/day for 3 weeks followed by an alcohol self-administration experiment (ASAE), then received placebo for 3 weeks followed by a second ASAE. Participants received the second drug for 3 weeks followed by a third ASAE. Participants in the second arm (SS/SL) received the same medications in the same balanced fashion.
Results: All Ss have been scheduled for the first ASAE. Women receiving the hypothesized matching medication drank less during the week prior to the first ASAE [DDD = 7.9 (4.1)] than women receiving the mismatched medication [DDD = 15.2 (9.3), t(14.3) = 2.35, p = .03]. Furthermore, this effect appeared to be more pronounced in those women without the DRD4 repeat allele [t(4.3) = 2.80 compared to t = 2.35].
Discussion: Treatment matching based on genotyping could be of significant value in an era of personalized medicine. Such genotyping could save a significant amount of money, reduce treatment failures and therefore lives. Supported by NIAAA Grant R01-AA016079

0980

EYE GAZE ANALYSIS IN BIPOLAR DISORDER WITH AND WITHOUT A HISTORY OF SUBSTANCE ABUSE OR DEPENDENCE

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An individual's face communicates valuable information regarding emotion, direction of attention and a person's identity during social situations. It is not known how important social cues i.e., facial affect, effect the temporal processing of faces in bipolar disorder (BPD). Because there is a high rate of co-morbid substance use disorders in BPD, understanding how substance use may influence facial processing in the presence of BPD could provide important information in the development and prevalence of dual diagnoses. Event related potential (ERP) studies investigating processing of emotional faces in bipolar disorder (BPD) are rare but can provide a window into understanding some of these issues. The aim of the study was to investigate early encoding differences and later higher order processing of emotional faces in BPD and how substance abuse history may impact this processing utilizing the N170, a face-specific ERP component, and the P300, which is thought to reflect stimulus evaluation and resource allocation, elicited in response to emotional faces. Nineteen individuals diagnosed with BPD completed an eye gaze task during electroencephalogram (EEG) and ERP acquisition. Eight of the participants had a history of substance abuse or dependence (SA) and ten had no history of SA. Participants identified whether a target face was looking at them or away from them. The target faces varied in eye gaze direction, head orientation (direct, averted) and emotion (fearful, neutral). Preliminary data analyses reveal that BPD participants with a history of SA showed reduced N170 and P300 components in response to facial stimuli compared to BPD participants without a SA history. This supports abnormalities in early structural facial processing and allocation of cognitive resources when processing emotional and neutral faces, especially in the presence of SA history.

0981

KNOCK-OUT OF *KCNJ9*, A WITHDRAWAL-RELATED GENE, ALTERS A SUBSET OF FEAR CONDITIONED BEHAVIOR

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Kcnj9, which codes for a G-protein coupled inwardly rectifying potassium channel subunit (GIRK3), is a high quality quantitative trait gene (QTG) candidate for physiological dependence and associated withdrawal in mice. Inbred strain panel and congenic analyses demonstrate that lower *Kcnj9* expression is significantly correlated with less severe ethanol withdrawal, and GIRK3 knockout (GIRK3-KO) mice exhibit significantly less severe withdrawal from ethanol and other sedative drugs than wildtype (WT) littermates. Using GIRK3-KO and WT genetic models, ongoing studies are assessing the potential role of GIRK3 expression on additional ethanol related behaviors using ethanol withdrawn and appropriate control animals. The present studies assess the potential role of GIRK3 in fear-based learning and memory. GIRK3-KO and WT littermates (both on an inbred DBA/2J background) were trained using two fear conditioning paradigms (trace fear conditioning [TFC] and delay conditioning [DFC]) and tested for context- and cue-related behavioral responses. The learned association in DFC relies primarily on plasticity in the amygdala, while TFC recruits other brain regions, including the dorsal hippocampus and prelimbic cortex, allowing us to examine multiple pathways for learning and memory. When trained using DFC, both GIRK3-KO and WT animals showed increased freezing in response to the training context and the tone used during training. However, following TFC training, KO animals showed significantly reduced freezing in response to the training tone compared to WT, while both groups responded equally to the training context.

Our results implicate GIRK3 in fear-based learning. Reduced response to the trained cue in TFC but not in DFC in GIRK3-KO compared to WT littermates implicates GIRK3 in the pathways recruited by TFC. However, as is the case with traditional KO models, differences from WT mice may also be influenced by potential developmental compensation. Region-specific shRNA-mediated GIRK3 knock-down will be used in future experiments to address this issue.

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0982

ETHANOL WITHDRAWAL ASSOCIATED C-FOS EXPRESSION IN GIRK3 KNOCKOUT MICE

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Our goal is to dissect the neural and molecular substrates by which quantitative trait loci (QTLs) and the underlying quantitative trait genes (QTGs) influence ethanol physiological dependence and associated withdrawal. We previously identified QTLs on distal chromosome 1 with large effects on ethanol withdrawal convulsions in mice using chronic and acute administration models (Buck et al. 1997, 2002) using several mapping populations derived from inbred strains which demonstrate severe ethanol withdrawal (DBA/2J, D2) and mild ethanol withdrawal (C57BL/6J, B6). A congenic strain (D2.B6-*D1Mit206*) was created that possesses this QTL interval from the C57BL/6J (B6) strain superimposed on a genetic background that is >98% from the DBA/2J (D2) strain (i.e., using donor and background strains with mild and severe ethanol withdrawal, respectively). Because of near elimination of genetic ''noise'' from loci elsewhere in the genome, comparisons of congenic and background strain mice are useful in determining neural circuitry affected by QTL status. Here, c-Fos expression is used as a high-resolution marker of neuronal activation in the congenic and background strains using ethanol withdrawn and control (saline) animals. Our results reveal less ethanol withdrawal associated neuronal activation in regions of the medial prefrontal cortex, amygdala, ventral striatum, and substantia nigra pars reticulata. Fine-mapping of this QTL to a 0.44Mb interval (syntenic with human Chr 1q23.2–23.3) and detailed molecular analyses of genes within this interval identify *Kcnj9* as a probable QTG to underlie this QTLs influence on withdrawal from ethanol and other sedative drugs (Kozell et al. 2009). This gene encodes GIRK3, a subunit member of a family of G-protein-dependent inwardly-rectifying K+ channels. Currently, we are assessing c-Fos expression in GIRK3-KO and wildtype littermates (both inbred DBA/2J genetic background) using ethanol withdrawn and control (saline) animals. Additionally, ongoing double fluorescent labeling studies are examining c-Fos and Forkhead Box Protein 2 (FoxP2, which is a molecular marker of the intercalated cells of the amygdala) expression in order to assess the potential role for the intercalated cells of the amygdala in ethanol withdrawal. [Supported by the VA, T32AA007468, R01DA005228, P60AA010760]

0983

MPDZ EXPRESSION IS REDUCED AND ETHANOL WITHDRAWAL SEVERITY INCREASED BY *MPDZ* RNA INTERFERENCE IN THE SUBSTANTIA NIGRA PARS RETICULATA

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Using robust behavioral models, positional cloning, sequence and expression analyses, we identified *Mpdz* as a quantitative trait gene for ethanol physiological dependence and associated withdrawal in mice (Shirley et al. *Nat Neurosci* 7:699, 2004). This gene encodes the multi-PDZ domain protein (MPDZ/MUPP1) and is widely expressed in the brain. These data suggested that lower MPDZ expression may be associated with more severe ethanol withdrawal. Analyses using a congenic mouse strain (possessing this QTL from C57BL/6J [B6] donor strain superimposed on a genetic background that is >98% DBA/2J [D2] strain) demonstrate significantly less severe ethanol withdrawal than background strain mice, significantly less withdrawal associated neuronal activation within the substanita nigra pars reticulata (SNr), and focused lesions of the caudolateral SNr (clSNr) significantly reduce ethanol withdrawal severity (Chen et al *J Neurosci* 28:9840, 2008 and *Behav Brain Res* 218:152 2011). These findings suggest that MPDZ actions on ethanol withdrawal may involve its expression in the clSNr. The present studies directly test this hypothesis. Adult male DBA/2J mice were stereotaxically infused for lentivirus-mediated delivery of MPDZ shRNA or a scrambled control into the clSNr (10^8 TU/ml, 1 μl per side). Four weeks later mice were assessed for severity of acute ethanol withdrawal. Each mouse was tested twice for baseline (pre-ethanol) handling induced convulsions (HICs), then received a single hypnotic dose of ethanol (4.0 g/kg, i.p.) and scored hourly for HICs between 2 and 12 hours post injection. Four days later, mice were tested for pentylenetetrazole (PTZ) enhanced HICs using a dose (30 mg/kg, i.p.) that increases HIC intensity, but does not induce other types of convulsions (e.g., tonic hindlimb extensor). Finally, we assessed *Mpdz* expression using laser capture microdissection of the clSNr and quantitative PCR. Based upon results for animals with confirmed bilateral infusions of the clSNr we conclude that MPDZ shRNA animals had significantly less MPDZ mRNA within the clSNr and significantly more severe ethanol withdrawal compared to control animals, but no difference in baseline HICs or PTZ enhanced HICs. We conclude that endogenous MPDZ in the clSNr plays a crucial role in ethanol physiological dependence and associated withdrawal. [Supported by the VA, T32 AA007468, RO1 AA011114 and P60 AA010760]

0984

BK CHANNEL BETA1 SUBUNIT MODULATES BEHAVIORAL ADAPTATIONS TO CHRONIC ETHANOL EXPOSURE

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Alcohol abuse disorders have devastating health and societal consequences. Development of more efficient alcoholism treatments requires a better understanding of the molecular mechanisms mediating the intoxicating and motivational effects of ethanol. One of the well-established molecular targets of ethanol is the large conductance calcium-activated potassium (BK) channel. BK channels are highly expressed in the brain and play a key role in several aspects of neuronal physiology. Ethanol is a potent activator of BK channel gating, but *in vivo* evidence for a causal relationship between BK channel potentiation and ethanol's behavioral effects is scarce. Interestingly, association of the auxiliary beta1 subunit with the pore-forming alpha subunit precludes ethanol-induced potentiation of BK currents *in vitro*. In the present study, we investigated how deficiency in BK beta1 subunit affects ethanol intoxication, tolerance, dependence and drinking in mice. We found that sensitivity to ethanol-induced ataxia, sedation and hypothermia was similar between BK beta1 wild-type, heterozygous and knockout male mice. Acute functional tolerance to ataxia was also equivalent across genotypes. Mice were exposed to three cycles of intermittent ethanol vapor, and a time-course of handling-induced convulsions was conducted to evaluate dependence. Knockout and heterozygous mice experienced an earlier and more intense physical withdrawal syndrome than wild-type counterparts. Ethanol-induced ataxia, sedation, and hypothermia were measured approximately 26 h into withdrawal to assess the development of tolerance, and tolerance to sedation and hypothermia was reduced in knockout mice. Finally, an independent cohort of mice was subjected to continuous or intermittent (every other day) two-bottle choice (water/ethanol) drinking. Deletion of BK beta1 subunit did not affect ethanol self-administration under either schedule of access. These findings suggest that the beta1 subunit may be recruited upon chronic intoxication to dampen ethanol-induced potentiation of BK currents, thereby minimizing behavioral responses to ethanol. Absence of the beta1 subunit in knockout mice may, on the other hand, promote counter-adaptive changes downstream of BK channel overstimulation by ethanol and exacerbate withdrawal. Voluntary ethanol drinking in non-dependent mice was not sensitive to BK beta1 deficiency, but intake in dependent mice still needs to be investigated.

0985

GENETIC DELETION OF ADENYLYL CYCLASES 1 AND 8 ATTENUATES THE LOCOMOTOR STIMULATING EFFECTS OF ETHANOL

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AC1 and AC8 generate cAMP from ATP and are the only AC isoforms primarily stimulated by calcium-calmodulin activation. They are localized synaptically, in proximity to NMDA receptors, and are known regulators of behavioral and neuronal plasticity. Their localization also suggests their involvement in NMDA-dependent events, such as ethanol action. Previous data from our lab demonstrates that mice lacking the calcium-stimulated adenylyl cyclases 1 and 8 (AC1 and AC8, DKO) exhibit prolonged ethanol-induced sedation compared to wild-type controls (WT) following acute ethanol treatment. This behavioral impairment is accompanied by reduced phosphorylation of presynaptic vesicle-release proteins by protein kinase A in both the hippocampus and cortex compared to ethanol-treated WT mice. Although a role for AC1 and 8 in the sedating effects of ethanol has been examined, their ability to regulate the stimulating effects of ethanol is still unclear. Therefore, using mice lacking AC1 and AC8 (DKO), we evaluated the ability for AC1 and AC8 to mediate ethanol-induced alterations in locomotor activity at stimulating concentrations of ethanol. WT and DKO mice were treated with 1.0 or 2.0 g/kg ethanol (i.p.) and monitored for locomotor activation for 10 min in novel chambers equipped with activity monitors. In WT mice, both doses of ethanol increased distance traveled compared to saline controls. Conversely, DKO mice demonstrated no increase in locomotor activation at 1.0 g/kg compared to saline controls, with significantly reduced locomotor activity at both 1.0 and 2.0 g/kg compared to ethanol-treated WT mice. These data suggest that AC1 and 8 are critical mediators of the acute, stimulating effects of ethanol.

0986

PKM ZETA IN MOUSE MODELS OF ETHANOL CONSUMPTION AND REWARD

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Protein kinase M zeta (PKMζ), protein kinase C zeta (PKCζ) and protein kinase C iota (PKCι) comprise the atypical subfamily of PKCs. PKMζ and PKCζ are transcribed from different transcriptional start sites within the *Prkcz* gene. PKMζ is constitutively active and is expressed in the brain, whereas PKCζ is found mainly in peripheral tissues. Previous studies show that high ethanol consuming mouse strains have greater abundance of *Prkcz* transcripts in the brain compared with strains that consume relatively little ethanol (Mulligan, M. K. et al., 2006, *Proc Natl Acad Sci U S A*). Additionally, a single bout of ethanol consumption increases *Prkcz* transcript levels in C57BL/6 mouse brain (Mulligan, M. K. et al., 2011, *Alcohol Clin Exp Res*). Our goal was to investigate the effect of ethanol on PKMζ expression, and the contribution of PKMζ to ethanol consumption. We found that an overnight incubation of PC12 cells with pharmacological concentrations of ethanol increased the abundance of PKMζ transcripts but had no effect on PKCι transcripts ($F_{isoform}$ (2,24)=5.251, P=0.013). In hybrid C57BL/6 X 129 wild-type mice that had been consuming ethanol intermittently for 6 weeks, there was an increase in PKMζ protein levels in the nucleus accumbens (P=0.03) but not in the dorsal striatum (P=0.68). These data show that ethanol can increase PKMζ transcript and protein. We also generated *Prkcz* $^{-/-}$ mice and evaluated their ethanol intake under procedures that produce high and moderate levels of consumption. *Prkcz* $^{-/-}$ mice consumed more ethanol than wild-type mice in a 4-h limited access protocol three days (M,W,F) per week for 3 weeks ($F_{interaction}$ (9, 374)=2.472, P=0.01). However, *Prkcz* $^{-/-}$ and wild type mice consumed similar amounts of ethanol in a 24-hour two-bottle choice paradigm ($F_{genotype}$ (4,84)=0.009, P=0.93) and a 4-day limited access drink-in-the-dark procedure ($F_{genotype}$ (1,117)=1.908 P =0.18). *Prkcz* $^{-/-}$ mice also did not differ from wild-type mice in ethanol conditioned place preference (2 g/kg, P=0.85) or in the duration of the ethanol-induced loss of the righting reflex (3.6 g/kg, P=0.80). Our results indicate that ethanol can specifically induce PKMζ expression, and suggests that PKMζ may be part of a signaling pathway that suppresses chronic binge ethanol consumption.

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0987

MUTANT MICE LACKING THE RIIβ SUBUNIT OF PKA EXHIBIT ALTERED DARPP-32 ACTIVITY IN THE STIATUM AND NUCLEUS ACCUMBENS

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Protein kinase A (PKA) modulates neurobiological responses to ethanol. For example, mutant mice lacking the regulatory RIIβ subunit of PKA (RIIβ-/- mice) exhibit increased ethanol consumption, increased ethanol-induced locomotor sensitization, and reduced sensitivity the sedative effects of ethanol relative to wild-type RIIβ+/+ mice. An important target of PKA activity in dopaminergic neurons is dopamine- and cAMP-regulated phosphoprotein of 32 kDA (DARPP-32). Because DARPP-32 has been shown to modulate neurobiological response to ethanol, we assessed DARPP-32 activity in RIIβ-/- and RIIβ+/+ mice following saline or repeated ethanol injections (in a regimen shown to induced enhanced locomotor sensitization in RIIβ-/- mice). Sixteen RII$\beta^{+/+}$ mice and fifteen RII$\beta^{-/-}$ mice were assigned to either ethanol or saline groups. Mice were given 5 intraperitoneal (i.p.) injections of 20% (w/v) ethanol or 0.9% saline, one injection per day (each injection was separated by 2–4 days). Approximately 24 hrs after the last injection, mice were perfused and the brains were process for immunohistochemistry. We assessed total DARPP-32 and phosphorylation of DARPP-32 at threonine-34 (pThr34) and threonine-75 (pThr75). Immunoreactivity (IR) was measured within the core and shell of the NAc as well as the dorsolateral, dorsomedial, ventrolateral, and ventromedial striatum using densitometry. Relative to RII$\beta^{+/+}$ control mice, RIIβ-/- mice showed significantly greater pThr34 IR in each of the regions examined, regardless of history of ethanol exposure. Further, a significant ethanol-induced reduction of pThr34 IR was observed in the dorsal striatum, but this effect did not interact with genotype. RIIβ-/- mice also showed significantly greater pThr75 IR relative to RII$\beta^{+/+}$ mice in all brain regions examined, and a history of ethanol injections attenuated pThr75 IR selectively in regions within the NAc. Interestingly, there was a significant ethanol history and genotype interaction in the NAc core and dorsomedial striatum, with RIIβ-/- mice showing significantly greater ethanol-induced attenuation of pThr75 IR. In general, RIIβ-/- mice showed attenuated total DARPP-32 when compared to RIIβ+/+ mice, perhaps reflecting compensation for elevated pThr34 and pThr75. Together, these results suggest that altered neurobiological responses to ethanol by RIIβ-/- mice may be modulated by abnormal pThr34 and pThr75 activity in the striatum and NAc

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0988

VIRAL VECTOR MEDIATED OVEREXPRESSION OF CYTOCHROME P450 SIDE CHAIN CLEAVAGE IN THE VTA PRODUCES LONG-TERM REDUCTIONS ON ETHANOL SELF-ADMINISTRATION

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Neuroactive steroids are endogenous neuromodulators synthesized in the brain, adrenal glands, and gonads. Systemic administration of endogenous and synthetic neuroactive steroids can alter ethanol self-administration in rodents. We have hypothesized that neuroactive steroids alter ethanol self-administration by modulating mesolimbic circuitry. In the current study, a previously characterized adeno-associated serotype 2 viral vector (AAV2) expressing the mitochondrial cytochrome P450 side chain cleavage (P450scc) enzyme was used to produce long-term increases in P450scc expression. P450scc converts cholesterol to pregnenolone, which is the rate-limiting enzymatic reaction in neurosteroidogenesis. Overexpression of P450scc should allow us to investigate how sustained increases in steroidogenesis, isolated to specific brain regions, affect ethanol self-administration. The P450scc expressing vector (AAV2-P450scc) or control green fluorescent protein (GFP) expressing vector (AAV2-GFP) were injected bilaterally into the ventral tegmental area (VTA, 2μL/hemisphere) or nucleus accumbens (NAc, 3μL/hemisphere) of alcohol preferring (P) rats (n=7–8/group) previously trained to self-administer ethanol. Following viral vector injection the animals were given 1 week to recover from surgery before operant self-administration sessions resumed. P450scc overexpression in the VTA reduced ethanol responding by 25% compared to controls (2-way ANOVA, p<0.01) over the 3 week test period. The reduction in responding following injection was due in part to a persistent reduction in responses (28%, 2-way ANOVA w/Bonferoni post-test, p<0.001) during the first 5 minutes of operant sessions over 3 weeks of testing. In contrast, P450scc overexpression in NAc did not significantly alter long-term ethanol self-administration. General locomotor activity was not altered by vector administration in VTA or NAc. P450scc overexpression did not increase allopregnanolone-like immunoreactivity in NAc; however, vector delivery in the VTA produced a 34% increase in allopregnanolone positive cells in the VTA, which did not reach statistical significance. These results provide evidence that P450scc overexpression, and presumably increased steroidogenesis, in the VTA reduces ethanol reinforcement. Investigating how neuroactive steroids modulate ethanol reinforcement may lead to the development of new therapeutic strategies for treating alcoholism.

0989

MIDBRAIN AND FOREBRAIN CRF-R1 INVOLVEMENT IN EXCESSIVE ALCOHOL DRINKING: PHARMACOLOGICAL AND MOLECULAR GENETIC APPROACHES

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Extrahypothalamic CRF1 receptors (CRF-R1) are thought to mediate anxiety-related aspects in the transition to alcoholism (i.e. binge drinking alternating with withdrawal). Escalated consumption is largely modulated by brain sites important to reward and affect such as the ventral tegmental area (VTA) and the dorsal raphé nucleus (DRN). Efferent projections from different sources in the midbrain to the prefrontal cortex may be differentially inhibited by action of CRF-R1. However, it is also unknown what role forebrain CRF-R1 may wield on alcohol consumption. The current studies investigated the roles of CRF-R1 within this network using both pharmacological and molecular genetic approaches. Adult, male C57BL/6J mice were given 24-hour access to 20% ethanol or water on an intermittent schedule (3 days per week). Mice were surgically implanted with cannulae targeting the VTA or DRN. On test days, 2-, 4-, and 24-hour fluid consumption were measured after a microinfusion of a CRF-R1 antagonist (aCSF vehicle, 0.3 ug CP-154,526, and 0.6 ug CP-154,526). Microinfusion of the CRF-R1 antagonist into the VTA dose-dependently suppressed ethanol drinking, and had a mild effect on water drinking. Intra-DRN microinfusion suppressed ethanol drinking at the highest dose. To investigate blockade of CRF-R1 through an inducible genetic deletion, mice were generated to have a functional knock-out (KO) of forebrain-specific CRF-R1. Deleted *crh1* transcript is controlled by a tetracycline-controlled transactivator protein through removal of doxycycline from the diet, and the deletion is specific to the forebrain due to a cre-lox system. Male and female littermates are tested since 75% expected progeny are functionally wild-type (WT) and 25% expected progeny are CRF-R1 KO. Ongoing studies explore the CRF-R1 KO phenotype in several alcohol drinking protocols, including drinking-in-the-dark, continuous access, and intermittent access. Males and females are tested with doxycycline in the diet and without. After testing baseline alcohol drinking and alcohol preference, mice will be challenged both systemically and intra-VTA and intra-DRN with a CRF-R1 antagonist. These experiments may reveal differential roles of CRF-R1 in midbrain sites and forebrain sites, or an important communication between the two, as possible systems that mediate excessive drinking.

0990

CHARACTERIZATION OF ALCOHOL DRINKING IN GHSR1A KNOCKDOWN MICE

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Recent studies suggest the orexigenic peptide ghrelin and its associated receptor, growth hormone secretagogue receptor 1a (Ghsr1a), play an important role in aspects of alcohol consumption and reward. The specific mechanisms, including the neuroanatomical regions of interest that mediate the effects of ghrelin in the context of alcohol abuse remain unclear. To elucidate the role of ghrelin and Ghsr1a in alcohol consumption and reward, we are using a Ghsr1a knockdown mouse model. Ghsr1a knockdown mutants were generated by insertion of a transcriptional blocking cassette into the promoter region of the mouse Ghsr1a gene. *In-situ* hybridization indicated that Ghrsr1a expression is ablated everywhere in the brain except within the centrally projecting Edinger-Westphal nucleus (EWcp), where expression is reduced, but not eliminated. Adult male and female Ghsr1a null-mutant mice backcrossed onto a C57BL6/J background drank similar amounts of alcohol relative to their wildtype (WT) littermates in the 2-bottle choice procedure. Similarly, experiments with the drinking-in-the-dark model of excessive alcohol drinking indicated no baseline differences between Ghsr1a knockdown animals and WT littermates in alcohol drinking or food intake. In addition, administration of the Ghsr1a antagonist [D-Lys^3]-GHRP-6 (400 nm/animal i.p.) caused reductions in both alcohol- and food-consumption in both WT and knockdown animals. Our results in the Ghsr1a knockdown mutants differ from the significant reduction in alcohol intake in the standard (global) knockouts of Ghsr1a observed by other researchers. Our preliminary interpretation is that the remaining expression of Ghsr1a in EWcp is sufficient for the regulation alcohol intake in the knockdown mutants. Elucidating the mechanisms underlying differences between Ghsr1a mouse models might provide important clues to understanding neural substrates involved in regulation of excessive alcohol intake.

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0991

REDUCING UNC-13, A PRESYNAPTIC ETHANOL BINDING PROTEIN, IN DROSOPHILA MELANOGASTER INCREASES ETHANOL SELF ADMINSISTRATION

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An important source for new therapeutics to fight alcohol abuse and addiction will come from the analysis of the proteins that will bind to ethanol, resulting in changes in neutral activity. Most of the known ethanol receptors are post-synaptic, yet ethanol can dramatically alter presynaptic activity by affecting synaptic vesicle release. It is our goal to functionally and biochemically characterize the Unc-13 presynaptic protein as an ethanol binding protein. Through photolabeling experiments, we have found a high affinity alcohol binding site in the C1 domain of munc-13.1. The binding of diacylglycerol (DAG) to this C1 domain lowers the barrier for vesicle fusion and promotes release of neurotransmitters(1). Hence, a high affinity ethanol binding site within this domain may have significant consequences in neural activity and behavior. To assess these consequences, we have begun examining the behavioral effects of reducing unc-13 levels in *Drosophila melanogaster*. The Drosophila dunc-13 molecule has a highly conserved C1 domain. The dunc13 protein also has a conserved function and is essential for neurotransmission(2). The *dunc13*^{f07072}mutation is a loss-of-function lethal mutation in *dunc-13*. Heterozygotes for this amoprhic allele have approximately ½ the wild type amount of *dunc-13* mRNAs within their nervous system and hence represent a genetically sensitized state with reduced dunc-13 levels. These heterozygotes display a significant increase in ethanol self administration using CAFÉ assay, a two-bottle choice paradigm for Drosophila. Moreover these flies are significantly more resistant to the sedative effects of ethanol vapor in a loss-of-righting assay. Together these data suggest an important role for the unc13 ethanol binding protein in regulating ethanol related behaviors in Drosophila.

1. Andrews-Zwilling, Y. S., Kawabe, H., Reim, K., Varoqueaux, F., and Brose, N. (2006) *J Biol Chem* 281, 19720-19731
2. Aravamudan, B., Fergestad, T., Davis, W. S., Rodesch, C. K., and Broadie, K. (1999) *Nat Neurosci* 2, 965-971

0992

AGE AND ETHANOL CONCENTRATION-DEPENDENT EFFECTS OF ACUTE BINGE DRINKING IN THE HIV-1 TRANSGENIC RAT

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Binge drinking is a common form of alcohol abuse. Alcoholic beverages vary significantly in their ethanol (EtOH) concentration [alcohol by volume (ABV)]. We previously showed EtOH concentration-dependent activation of the supraoptic nucleus in the hypothalamus. In the HIV-infected population, incidence of alcohol abuse is close to 50%. We also found age-dependent expression of HIV-1 viral proteins in the HIV-1 transgenic (HIV-1Tg) rat. Thus, we hypothesized that there are age- and EtOH concentration-dependent effects of binge drinking in the HIV-1-infected population. Blood EtOH concentration (BEC) was measured in F344 rats after gavage (i.g.) administration of water, 20%, or 52% EtOH. We also compared the expression of the HIV-1 viral protein, Tat, in the brain, spleen, and liver of adult and adolescent HIV-1Tg rats following i.g. administration of water, 20%, or 52% EtOH for 3 d (4.8 g/kg per d). HIV-1 Tat expression was determined using absolute quantitative real-time RT-PCR. In a parallel study, we assessed age-dependent motor function deficits in the HIV-1Tg rats one day after exposure to 20% EtOH using Open Field test. BEC was significantly higher in the 52% EtOH-treated group compared to the 20% EtOH group at 90 min post treatment. In the adult animals, HIV-1 Tat expression (copies per μg of total RNA) was significantly increased in the brain, liver, and spleen of the 52% EtOH group, but not the 20% EtOH group. However, in the adolescent animals, HIV-1 Tat expression was increased in the brain and liver of the 52% EtOH group, but not in the spleen. A significant reduction in locomotor activity occurred in EtOH-treated adult HIV-1Tg rats compared to control, although no difference was observed in the adolescent HIV-1Tg animals. Our data indicate that binge alcohol drinking can have age- and EtOH concentration-dependent effects in the presence of HIV-1 infection.

0993

A ROLE FOR THE MITOCHONDRIAL RESPIRATORY CHAIN IN GENETIC VULNERABILITY TO ETHANOL PHYSIOLOGICAL DEPENDENCE AND ASSOCIATED WITHDRAWAL

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The brain is particularly vulnerable to oxidative stress, which is thought to contribute to a variety of psychiatric diseases including alcohol dependence and associated withdrawal. Previously, we fine-mapped a quantitative trait locus (QTL) on chromosome 1 with large effects on ethanol withdrawal in mice using acute and chronic administration models (*Genes Brain Behav* 7:560, 2008). Systematic molecular analyses identified a small number of QTL candidate genes with non-synonymous coding sequence variation between the two progenitor strains (C57BL/6J [B6] and DBA/2J [D2]) and/or expression differences in the brain between B6.D2 congenic animals and background strain mice for the 1.1 Mb QTL interval (*Genes Brain Behav* 7:599, 2008). Two of these code for integral subunits of mitochondrial respiratory chain (MRC) complexes I and II, and a third is involved in the mitochondrial heme biosynthesis on which MRC function is dependent. Using blue native gel electrophoresis (BN-PAGE) and measuring complex I and IV specific enzymatic activities, we assess the abundance and activity of specific MRC complexes in their native conformation and supramolecular organization in order to evaluate whether strain differences exist in brain MRC components and/or become apparent in ethanol withdrawn animals. Using mitochondria prepared from whole brain, we find qualitative and quantitative differences between B6 and D2 in higher order MRC organization and activity, primarily for supercomplexes containing complex I (CI-SCs). In naïve animals, CI-SCs are more abundant and show higher associated complex I activity in D2 than B6. Using ethanol withdrawn and appropriate controls animals, qualitative and quantitative differences in the content of CI-SCs and associated complex I activity are preserved in ethanol withdrawn animals. Further, in supercomplexes that also contain complex IV, complex IV enzymatic activity is greater in D2 than B6. We are currently assessing the extent to which a B6.D2 strain congenic for just the 1.1 Mb QTL interval resembles the donor and background strains in MRC organization and function. Finally, ongoing analyses suggest that *in vivo* administration of an antioxidant agent may attenuate ethanol withdrawal behavior. Together, our results indicate a role for the MRC in genetic susceptibility to ethanol withdrawal and suggest a mechanism by which this QTL influences this phenotype. [Supported by I01-BX000222, AA017342, AA007468 and AA010760]

0994

FINE MAPPING AND CANDIDATE GENE ANALYSES OF A LOCUS ON MOUSE CHROMOSOME 19 INVOLVED IN ETHANOL PHYSIOLOGICAL DEPENDENCE AND ASSOCIATED WITHDRAWAL

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Physiological dependence and associated withdrawal episodes are thought to constitute a motivational force perpetuating alcohol use and abuse. Although no animal model duplicates alcoholism, models for specific factors, like the withdrawal syndrome, are useful to identify potential determinants of liability in humans. We previously detected a quantitative trait loci (QTL) on distal chromosome 19 with a large effect on predisposition to ethanol physical dependence and associated withdrawal in mice. Here, we provide the first confirmation of this QTL in a congenic strain. Furthermore, using novel interval-specific congenic strains, we narrow its position to a maximal 2.8 Mb interval (syntenic with human chromosome 10q25.1). This 2.8 Mb QTL interval contains only six genes (4 protein coding genes, 1 ribosomal RNA and 1 lincRNA). Our novel congenic animal models will be invaluable for determining whether this interval harbors a gene(s) involved in additional alcohol responses for which suggestive QTLs are detected on distal chromosome 19, including ethanol preference and ethanol induced locomotor activation. The possibility that this QTL may play an important role in diverse responses to ethanol makes it an important target. Moreover, at least one human study has identified markers on chromosome 10 that are significantly associated with response to ethanol in individuals with an alcoholic parent and are therefore at increased risk for alcoholism. Thus, the fine mapping of this QTL and analyses of the genes within the QTL interval may inform developing models for genetic determinants of alcohol dependence in humans. Supported by the VA, AA010760 and AA011114.

2. MOLECULAR / CELL BIOLOGY C.N.S

a. Gene expression **31–48/995–1012**

0995

ETHANOL-INDUCED DIFFERENTIAL GENE EXPRESSION OF 5-HT_{1A} AND YIF1B IN HIPPOCAMPAL PYRAMIDAL AND GRANULE CELLS IN CYNOMOLGUS MACAQUES

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Heavy drinking is known to produce neuroadaptive changes that can facilitate the transition to compulsive consumption of alcohol, one of the hallmarks of addiction. The hippocampus is particularly vulnerable to ethanol-induced neuroplasticity and the 5-HT_{1A} receptor plays an important modulatory role in this region. We have shown previously that chronic ethanol self-administration is associated with 43% greater hippocampal 5-HT_{1A} receptor density. We hypothesized that increased 5-HT_{1A} receptor density may be paralleled by concomitant alterations in 5-HT_{1A} gene expression as well as changes in Yif1B, a trafficking protein crucial for 5-HT_{1A} dendritic targeting. To this end, RNA was isolated from hippocampal CA1 pyramidal neurons and dentate gyrus granule cells from male cynomolgus macaques. Drinkers voluntarily self-administered ethanol during daily 22 hour sessions in their home cage for at least 12 months (n=9) while their control counterparts remained ethanol naïve (n=8). At necropsy, brains were blocked, flash-frozen and processed for laser capture microdissection (LCM). Eight hundred to 1,200 CA1 pyramidal neurons and the entire dentate gyrus granule cell layer from four sections per brain were microdissected from each subject. Isolated RNA from each sample was reverse transcribed and processed for qPCR. qPCR values for 5-HT_{1A} and Yif1B were normalized to three endogenous control genes that were stable across all subjects. No significant between group differences in 5-HT_{1A} receptor gene expression were observed in either the dentate gyrus or CA1 of the hippocampus ($p \geq 0.3$). In contrast, a preliminary analysis uncovered a trend for greater gene expression of the 5-HT_{1A} receptor trafficking protein, Yif1B, in both dentate gyrus granule cells ($p=0.06$) and CA1 pyramidal neurons ($p=0.07$) in ethanol drinkers. These data suggest that the greater hippocampal 5-HT_{1A} receptor density observed in chronic drinkers is not due to an increase in receptor gene expression but perhaps an increase in the trafficking of the receptor to specific dendritic sites.

0996

ACUTE EFFECTS OF ALCOHOL ON CIRCADIAN GENES IN THE RAT BRAIN

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Background: Sleep cycles are regulated by circadian genes. The peak and nadir of the circadian gene Period 1(mPer1) expression is observed during wakefulness and sleep, respectively. Sleep disorders, especially insomnia, are among the most common problems in alcoholics and are present both during active drinking and withdrawal. It is not known whether alcohol (EtOH) modulates the expression of mPer1 to affect sleep. We hypothesized that acute EtOH treatment in the rats will affect the expression of mPer1in specific brain regions which are known to regulate sleep and EtOH addiction.
Methods: Male Sprague-Dawley rats were used. The animals were divided into two groups; control and experimental. The controls were administered water (100 mL/Kg) whereas, the experimental rats were administered EtOH (3g/Kg) at the onset of active (light-off) period. 2 hours after treatment, the rats were euthanized and the following brain regions were rapidly dissected out: basal forebrain, cortex, nucleus accumbens, and suprachiasmatic nucleus. Subsequently, RNA was isolated and reverse transcribed to prepare cDNA which was used to quantify the expression of mPer1, using specific primers, by real time PCR.
Results: Our preliminary results suggest that the expression of mPer1 gene was increased in the nucleus accumbens (brain region implicated in EtOH addiction and sleep regulation) following EtOH treatment (N=6) as compared to the water-treated controls (N=3). We are in the process of examining mPer1 expression in other brain regions.
Conclusion: Our initial results suggest that EtOH induced alteration in mPer1, in brain regions important for EtOH addiction and sleep, may be the cause of sleep disruptions including insomnia observed in alcoholics.

0997

GLUTAMATERGIC GENE EXPRESSION IN POSTMORTEM HIPPOCAMPUS FROM ALCOHOLICS AND COCAINE ADDICTS

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Background: Chronic exposure to heavy alcohol or drug use is known to result in widespread neuronal adaptations. The aim of this study was to detect changes in expression of genes encoding glutamate receptors and transporters that might be specific to alcohol or drug exposure or might reflect shared pathways in addiction. We focused on the hippocampus, a brain region that is a constituent of the memory/conditioning neuronal circuitry of addiction that is considered to be important in reinforcement behaviors in animals and craving and relapse in humans. We have performed a similar analysis of GABAergic pathway genes in the same samples (Enoch et al., PLoS ONE, 2012).
Methods: Using RNA-Seq we quantified mRNA transcripts in postmortem total hippocampus from 8 alcoholics, 8 cocaine addicts and 8 controls, all male. An analysis of the 28 genes expressed in the hippocampus that encode glutamate ionotropic (AMPA, kainate, NMDA) and metabotropic receptor subunits, together with glutamate transporters was undertaken.
Results: The alcoholics showed FDR corrected ($p < 0.05$) up-regulation of six genes relative to controls and cocaine addicts: *GRIA4* (encoding the AMPA subunit GluA4); *GRIK3* (kainate receptor subunit GluR7); *GRIN2D* (NMDA receptor subunit GluN2D); and *GRM1*, *GRM3* and *GRM4* (metabotropic receptor subunits mGluR1, mGluR3 and mGluR4 respectively). Both alcoholics and cocaine addicts showed up-regulation of *GRIN2B* ($p = 0.008$) that encodes the NMDA receptor subunit GluN2B but the effect was greater in cocaine addicts. The only finding unique to cocaine addicts was down-regulation of *GRIN3A* that encodes the NMDA receptor subunit GluN3A. Finally, *SLC1A3* that encodes the glial high affinity glutamate transporter EAAT1 (GLAST) was down-regulated in the alcoholics.
Conclusions: Our study has shown that, at least in the hippocampus, the effect of chronic, heavy alcohol use is largely to up-regulate genes encoding subunits in all four groups of glutamate receptors whereas the effect of chronic cocaine exposure appears to be more limited. It is possible that NMDA GluN2B may be implicated in a common pathway to addiction. In contrast, our earlier study showed that there were specific and common effects of both chronic alcohol and cocaine exposure on multiple GABAergic genes and this was predominantly down-regulation of expression. These opposing effects might be expected since glutamate and GABA are respectively the major excitatory and inhibitory neurotransmitters.

0998

MICRORNA EXPRESSION PROFILING COMBINED WITH GLOBAL PROTEOMICS FOR A MOLECULAR CHARACTERIZATION OF CHRONIC INTERMITTENT ETHANOL DRINKING.

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"Omic" approaches unveil information on altered pattern of gene/protein expression following excessive alcohol exposure and suggest interactions that regulate the wide range of adaptations in brain function. However, genes and their encoded proteins do not necessarily follow a parallel trend in expression levels. Indeed, the expression of both of these molecules can be finely orchestrated by microRNAs, which may underlie many of the widespread genomic changes produced by alcohol consumption. The interpretation of transcriptomic and proteomic data are rich with biological information, but no single approach can fully decode the complexities of crucial neurobiological events associated with complex traits such as alcohol dependence. Nevertheless, an appropriate combination of such diverse tools can lead to integrative analyses that would provide insights not accessible through one single dataset. We have investigated the changes in miRNA as well as protein expression levels in cerebral cortices (CTX) and midbrains (MB) from C57BL/6J mice subjected to a Chronic Intermittent Ethanol – Two Bottle Choice (CIE-2BC) paradigm. Mice were given 5d of 2h limited access 15% ethanol (EtOH) and water to measure EtOH drinking and preference for the EtOH solution following air (control) or EtOH vapor chamber exposure. Mice were then allowed a 2-week period of abstinence and then the air/EtOH vapor exposure and 5d of 2 bottle choice testing were repeated for a 2nd bout. Repeated exposure to bouts of EtOH vapor was associated with subsequent increases in EtOH drinking under 2BC conditions. A third group of mice (naïve) had no access to EtOH bottles and was never exposed to vapor. CTX and MB were dissected, and total RNA and proteins were isolated. Total RNA was processed with EXIQON miRCURY LNA™ microRNA arrays (6^{th} generation) to assess miRNA expression levels in 21 CTX and 21 MB samples (7 CIE-2BC -exposed mice, 7 matched controls, plus 7 EtOH naïve mice). These arrays include 1,223 human, 1,055 mouse, and 680 rat probes as referenced by miRBase v.16, in addition to a number of proprietary probes. Plus, two-dimensional differential in –gel electrophoresis (2D-DIGE) was used to assess protein expression levels in protein samples from the same mice.
These complementary technologies allow high-throughput analysis which may improve our understanding of the molecular events associated with alcohol dependence and eventually help to define new molecular sites for drug treatment.

0999

ADOLESCENT ALCOHOL EXPOSURE (AIE) ALTERS THE CENTRAL BRAIN CIRCUITS KNOWN TO REGULATE THE STRESS RESPONSE

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Alcohol exposure during adolescence (AIE) is thought to exert long-term effects on the adult brain. Here we tested the hypothesis that the brain regions that are affected include the rat hypothalamic-pituitary-adrenal (HPA) axis. Specifically, we examined the consequences of AIE [postnatal days (PND) 28-42] on the HPA axis-related brain circuitry of adult male and female animals challenged with an intragastric (ig) injection of alcohol (4.5 g/kg) in adulthood (PND 61-71), as compared to control animals with no adolescent alcohol experience. Using *in situ* hybridization and immunohistochemistry, we measured signals for corticotropin releasing factor (CRF) and vasopressin (VP) in the paraventricular nucleus (PVN) of the hypothalamus, as well as *c-fos* and phenylethanolamine N-methyltransferase (PNMT) in the adrenergic brain stem regions (C1 and C2). Blood alcohol levels of AIE animals were 212.8 ± 5.7 mg % for males and 196.3 ± 4.4 mg % for females on PND 40. While acute ig alcohol administration significantly increased PVN CRF mRNA levels in control male rats at PND 61-62, induction of CRF gene expression was significantly blunted in AIE males. In contrast, alcohol-induced increases in PVN VP mRNA levels were significantly blunted in adult AIE female rats compared to their controls, while CRF gene expression was unaffected. Brain stem data indicated that male animals exposed to acute alcohol displayed a significant increase in the number of PNMT-ir cells/section in the C2 area while females showed a significant increase in the number of PNMT-ir cells/section in the C1 area. Collectively, these results suggest that exposure to alcohol vapor during adolescence has long-term effects on the ability of the PVN to mount a response to an acute alcohol administration in adulthood in both genders (albeit on different nuclei of the HPA axis), possibly mediated by medullary catecholamine input to the PVN. Supported by NIH NIAAA 5U01AA019973.

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GENE EXPRESSION PROFILING IN THE NUCLEUS ACCUMBENS OF INBRED ALCOHOL-PROFERRING, –NONPROFERRING, AND RECIPROCAL CONGENIC RATS BY RNA-SEQ

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The alcohol-preferring (P) and alcohol-nonpreferring (NP) rat lines were developed for high and low alcohol consumption through bidirectional selection. Selective breeding followed by quantitative trait locus (QTL) analysis has identified specific regions of chromosome 4 which are partly responsible for disparate alcohol drinking behavior. The strategy of making reciprocal congenic animals (P.NP and NP.P) and then using RNA-seq analysis to determine which genes are altered in expression and variable in sequence provides a powerful approach toward identifying gene(s) in the QTL contribute to the phenotype. RNA from the nucleus accumbens was isolated from iP, iNP, P.NP, and NP.P rats, strand-specific RNA-seq libraries were prepared and sequenced using the Illumina GAIIx sequencer. Expression levels were normalized using the quantile normalization method and three comparisons were performed, iP vs iNP (inbred comparison), P.NP vs iP, and NP.P vs iNP (congenic vs background comparisons). There were 381 differentially expressed genes ($P < 0.05$) between the iP and iNP rats. We also observed a significant number of genes that may be *trans*-regulated (P.NP vs iP and NP.P vs iNP) by genetic loci in the Chr. 4 QTL region. Analyzing the sequence variations from the transcribed regions between the P and NP rats and comparing them to the reciprocal congenic rats, the boundaries of the QTL region were determined. Genes shown to have genetic and expression differences are potential causative candidates for producing the difference in alcohol preference and consumption between the iP and iNP rats.

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ALCOHOL INTOXICATIONS DURING ADOLESCENCE INCREASE MOTIVATION FOR ALCOHOL IN ADULT RATS AND ALTER GENE EXPRESSION IN THE NUCLEUS ACCUMBENS AND AMYGDALA

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Adolescent binge drinking constitutes a major vulnerability factor to develop alcoholism. However, mechanisms underlying this susceptibility remain unknown. We analyzed, in adults SD rats, consequences of intermittent ethanol (EtOH) intoxications (IEI) during adolescence on later vulnerability to alcohol abuse by assessing motivation to self-administer EtOH and gene expression in the nucleus accumbens (Nac) and amygdala (AMYG). The adolescent period window (adolescence, puberty and adulthood) and the frequency of EtOH exposure were analyzed. Every 2 days, adolescent rats received an EtOH injection (3.0g/kg) for 2 consecutive days across 14 days. At adulthood, we measured their motivation to drink EtOH in the operant self-administration task and EtOH's rewarding and aversive properties in conditioned place preference (CPP) and conditioned taste aversion (CTA) paradigms. Finally, we analyzed gene expression in the Nac and AMYG of adult rats using an array of neurotransmission-specific genes. We found that adolescent IEI provoked a two-fold increase in the number of lever presses and a higher breakpoint for EtOH in the self-administration paradigm associated with a loss of EtOH-induced CPP and CTA. Importantly, these alterations were specific for alcohol as we observed no modification in sucrose self-administration or amphetamine-induced CPP. Adult IEI rats also display increase in their basal level of anxiety-like behaviour and voluntary ethanol intake in different two-bottle choice paradigms. Furthermore, adolescent IEI induced persistent alterations in gene expression in the Nac and AMYG under basal condition (i.e. Gabrg2, Grm2, Htr1a, Htr3a, Slc6a4, Crh) and after an EtOH challenge (Penk, Htr2c). Altogether, our data demonstrate that IEI during adolescence robustly increase motivation to drink EtOH alcohol and reduce both its rewarding and aversive EtOH's properties. As observed in humans, our data confirm that early adolescence is a window of vulnerability regarding the long term effect of binge-like EtOH exposure on later liability to alcohol abuse and anxiety-like behaviour. This long term vulnerability to EtOH alcohol abuse is associated with enduring alterations of specific genes in the Nac and AMYG that have been shown to play a critical role in alcoholism.

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AMYGDALA GENES AND ESCALATION OF ALCOHOL INTAKE IN MICE

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Alcoholism is characterized by compulsive alcohol intake and affects over 140 million people worldwide. In order to develop novel treatment strategies for this devastating disorder, it is important to identify neurogenetic mechanisms that contribute to alcoholism. C57BL/6J mice show a rapid escalation of alcohol intake that depends upon mechanisms in the amygdala. Here, we show the staged occurrence in C57BL/6J mice of two distinct behavioral characteristics of human alcoholism, i.e. inflexible and indifferent drinking. After two weeks of alcohol experience, adulteration of the alcohol solution with an aversive quinine concentration failed to reduce alcohol intake, indicative of inflexible alcohol intake. After eight weeks of alcohol consumption, the mice also became indifferent to quinine. That is, they consumed an aversive, quinine-containing alcohol solution, despite simultaneous availability of an unadulterated alcohol solution. To identify molecular pathways in the amygdala involved in the development of alcoholism, we used microarrays to profile gene expression changes during escalation of alcohol intake in mice. Amygdala samples were taken after 1, 2 or 4 weeks of daily alcohol intake in the limited access choice paradigm and RNA was isolated and processed for hybridization to microarrays. The microarray data confirmed involvement of the amygdala in escalation of alcohol intake in that the majority of the gene expression changes occurred after 1 week of alcohol experience, i.e. during the transition from low to high alcohol intake. In addition, this experiment revealed expression changes for genes that have been previously associated with alcoholism, including AMPA and GABAA receptor subunits, but also for interesting novel genes, including the adapter protein 14-3-3ζ. We used RNA interference to bring down the levels of this protein. Local knockdown of 14-3-3ζ in the amygdala resulted in augmented levels of alcohol intake in mice. In addition, knockdown of amygdala 14-3-3ζ promoted the development of inflexible alcohol drinking, as apparent from insensitivity to adulteration of alcohol using quinine. Taken together, this study underlines the involvement of the amygdala in escalation of alcohol intake and identifies amygdala 14-3-3ζ as a novel key modulator that is engaged during the descent of alcohol intake into alcoholism-like behavior.

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REGULATION OF STEM CELL DIFFERENTIATION BY ETHANOL AND RETINOIC ACID

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Alcoholism affects almost 20 million people in the United States alone, and can lead to numerous health problems including cardiovascular disease, liver damage, and cancer. Additionally ethanol consumption is particularly damaging to developing embryonic precursor cells and can lead to developmental defects including fetal alcohol syndrome. However, the exact mechanism by which ethanol regulates stem cell differentiation is unclear. In other cell types it has been shown that chronic alcohol consumption is associated with decreases in the absorption and storage of vitamin A, and its metabolic derivative, all-trans retinoic acid (RA). As the ligand for the retinoic acid receptor (RAR/RXR) heterodimer, RA plays a major role in regulating cell proliferation, differentiation and apoptosis in stem cells. We hypothesize that in embryonic stem cells, ethanol promotes differentiation by regulating RA levels. Mouse embryonic stem cells treated with ethanol, its metabolite acetaldehyde, or RA, followed by quantitative real-time PCR analysis were used to determine whether these treatments altered stem cell marker expression. We found that ethanol, acetaldehyde, and RA promote expression of the early differentiation marker Hoxa1 gene and the late differentiation marker Collagen IV, while inhibiting the expression of stem cell markers including Nanog, Oct4, and Rex1. Interestingly, we found that ethanol and acetaldehyde promote expression of genes associated with vitamin A metabolism, including Crbpl, Stra6, and Cyp26a1. Using chromatin-immunoprecipitation we found that ethanol promotes the histone activation marks acetylated H3K27 and dimethylated H3K4 at the retinoic response elements in the Hoxa1 and Cyp26a1 promoters, suggesting that epigenetic modification is a mechanism by which ethanol and its metabolite acetaldehyde promote the metabolism of vitamin A and subsequent embryonic stem cell differentiation.

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CHARACTERIZING THE INFLAMMATORY RESPONSE IN THE CENTRAL NERVOUS SYSTEM DURING ALCOHOL WITHDRAWAL

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Alcohol exposure alters the CNS inflammatory environment. We suspect that individual cell types within the CNS tissue differentially contribute to this inflammation. Study of the dynamics of this behavior in the neuronal, endothelial and microglial compartments would give us a more complete understanding of how these cells interact to form a tissue level response and how it evolves. This may have implications of the treatment of alcohol withdrawal and related neurodegeneration.

Five different treatments will be tested spanning a 7 day time period during alcohol withdrawal. This time span will capture the behavior of both the innate and adaptive immune responses during the course of alcohol withdrawal. In vivo samples will be collected from 3 biological replicates for each treatment. We will use a high-throughput, low-variability qRT-PCR platform to simultaneously measure the expression of 87 genes related to various aspects of innate and adaptive immune response.

Initial results show that following a chronic alcohol exposure, withdrawal resulted in statistically significant increases in the mRNA expression of the innate immune cytokines Ccl2, TNF-α, iNos, Tnfrsf1a, and Cd74. This was present in both the CeA and DVC and was most prominent at 48h. Confocal IHC of samples taken 48h into withdrawal showed the presence of TNF-α staining surrounding cells expressing the neural marker NeuN absent in control samples. Similarly, withdrawal demonstrated an co-labeling of RECA-1 positive endothelial cells with the adhesion molecule ICAM-1, demonstrating the presence of activated endothelial cells during withdrawal. Again findings were consistent in both brain regions.

The initial results demonstrate a temporal induction in the gene expression of Ccl2, TNF-α, iNos, Tnfrsf1a and CD74 during alcohol withdrawal in both the CeA and DVC. IHC dual labeling showed an increase in neural expression of TNF-α and endothelial expression of ICAM-1 48h into withdrawal, confirming the inflammatory response at the protein level. These findings suggest that an abrupt cessation of alcohol intake leads to an exacerbation of the inflammatory response seen during chronic alcohol exposure. Moving forward, gene expression measurements will be taken from specific cell groups and provide insight into the cellular contributions to the overall inflammatory response observed during alcohol withdrawal. This may implicate new targets for treatment for alcohol withdrawal.

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CHRONIC ETHANOL UPREGULATES TOLL-LIKE RECEPTORS INCREASING NEUROINFLAMMATION AND NEURODEGENERATION MIMICKING HUMAN ALCOHOLIC PATHOLOGY

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Toll-like receptors (TLRs) are involved in innate immunity, in development and regulation of neuroinflammation and neurodegeneration. We found that human postmortem alcoholic brain has significant increases in the number of TLR2, TLR3 and TLR4 positive immunoreactive cells, compared to human moderate drinking control brain. Using a model of alcoholic binge drinking (5 g/kg, i.g., daily for 10 days) in C57BL/6 mice, we discovered increased gene expression and immunohistochemistry of TLR2, TLR3 and TLR4.
To evaluate the impact of increased TLRs on neuroinflammation and neurodegeneration, ethanol and polyinosine-polycytidylic acid (poly I:C), a synthetic dsRNA TLR3 agonist, were used to activate innate immune signaling. Ethanol treatment increased mRNA and protein levels of TNFa, MCP-1 and IL-6 in brain, determined by real-time PCR and ELISA. Ethanol significantly increased protein synthesis of NADPH oxidase (NOX) $gp91^{phox}$ and production of $O_2^{\cdot}$ and O_2^{-} -derived oxidants. Further, ethanol treated mice showed increased markers of cell death, Fluoro-Jade B staining, and activated caspase-3 immunohistochemistry in several brain regions including cortex and hippocampus. These markers of cell death were colocalized with Neu-N, a neuronal marker, consistent with ethanol induced neurodegeneration. Human postmortem alcoholic brain also showed increased NOX $gp91^{phox}$ and Fluoro-Jade B marker of cell death. Pretreatment with ethanol significantly potentiated poly I:C (250 μg/kg, i.p. plus D-galactosamine 20 mg/kg, i. p.) induced TNFα (345%), MCP-1(190%), IL-6 (167%), compared with lone poly I:C treatment. Ethanol administration significantly increased poly I:C-induced $gp91^{phox}$ mRNA and protein, ROS, microglial activation and neurodegeneration as shown by caspase-3 activation and Fluoro-Jade B staining. To test the hypothesis that chronic ethanol activates TLR-microglial cells increasing NOX and ROS we studied inhibitors. Chronic ethanol increased caspase-3 and microglial activation were reduced by naltrexone, minocycline and DPI, respectively. These studies indicate that human alcoholics have increased levels of TLRs, NOX, and cell death similar to mice chronically treated with ethanol.

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CHRONIC ETOH INCREASES CYTOKINES, TLR4, AND HMGB1 IN RATS.

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A number of factors have been implicated in initiating and sustaining alcohol abuse and alcoholism, but more recently dysegulation of the neuroimmune system has come to light as playing a significant role in a maladaptive process induced by chronic ethanol. In the current study we examined changes in cytokines (CCL2, IL1-β, and TNFα), Toll-like receptors (TLR-2, 4), receptor for advanced glycation end product (RAGE) as well as downstream effectors of the TLRs and RAGE receptors (MyD88 and NF-κB) following 15 days of 7% (vol/vol) EtOH provided in a liquid diet. Additionally, we measured changes in high-mobility group box 1 (HMGB1). HMGB1 is a key regulator of the innate immune response that works in a feed forward mechanism to activate RAGE, TLR2, and TLR4 upon release from cells. CCL2, IL1-β, and TNFα showed significant increases in mRNA expression over controls (n=8-12/group; t=4.53, p=0.0004; t=3.43, p=0.0027; t=5.14, p<0.0001, respectively). Fifteen days of chronic EtOH caused a significant increase in TLR4 mRNA expression (n=12–14/group; t=2.67, p=0.014) with no increase in either RAGE or TLR2 or the downstream signaling partners MyD88 or NF-κB. Further, HMGB1 mRNA expression was significantly elevated in response to chronic EtOH (n=9/group; t=3.62, p=0.0023). These results further implicate HMGB1 in the elevated levels of cytokines observed following chronic EtOH administration.

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DANGER SIGNAL HMGB1 MEDIATES ETHANOL-INDUCED NEUROINFLAMMATION THROUGH ACTIVATION OF TLR4-RAGE

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Activation of TLR4-RAGE signaling leads to the induction of NF-KappaB-dependent gene expression. High-mobility group box 1 (HMGB1) is a nuclear protein released as part of cellular danger signals that are recognized by TLR4 and RAGE receptors as an endogenous agonist. Previous studies have found that ethanol activates NF-KappaB transcription of proinflammatory genes in vivo and in organotypic hippocampal-enorhinal cortex (HEC) brain slice cultures. The present study tests the hypothesis that ethanol induces proinflammatory genes through activation of danger signaling, e.g. HMGB1 stimulation of TLR-RAGE receptor activation of NF-KappaB transcription. Ethanol treatment of HEC slices induced HMGB1 mRNA and immunohistochemistry (+IR) in slices as well as increasing HMGB1 in the culture medium (ELISA), suggesting ethanol induces and releases HMGB1. Postmortem human alcoholic brain was found to have increased HMGB1+IR. Addition of exogenous HMGB1 to HEC slices induced proinflammatory genes similar to ethanol. TLR4 receptor antagonist Lps-Rs or siRNA knockdown of TLR4 or RAGE blocked both ethanol and HMGB1 induction of proinflammatory cytokine genes. These findings are consistent with ethanol inducing and releasing HMGB1 leading to induction of proinflammatory genes. Furthermore, ethanol treatment induces integrin alpha 1 and 6 as well as beta 1 and 3, components of HMGB1 receptor responses. These results indicate that danger signal HMGB1 is induced and released by ethanol and activates TLR4-RAGE induction of proinflammatory genes. (supported by NIAAA)

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CLOCKΔ19 AND NPAS2 MUTANTS EXHIBIT INCREASED ETHANOL PREFERENCE AND CONSUMPTION

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Several studies have suggested a role for molecular components of the circadian clock as key players in drug reward and drug-associated responses. The circadian clock consists of transcriptional-translational feedback loops that control cycles of physiology and behavior with a duration of approximately twenty-four hours. Circadian genes are widely expressed throughout the brain, with high levels of expression in brain reward regions. Our lab has identified a key role for the circadian locomotor output cycles kaput (*Clock*) gene, a transcription factor that drives the positive loop of the circadian clock, in the regulation of drug reward. Mice bearing a dominant negative mutation in the *Clock* gene (CLOCKΔ19 mice) exhibit increased cocaine sensitivity and preference. To extend these studies, we assessed whether CLOCK and NPAS2, homologous transcription factors, have a role in alcohol intake. We measured ethanol preference and consumption in two lines of mice, ClockΔ19 and NPAS2 mutant mice (and their wild-type littermates), using the continuous access two bottle choice paradigm (n=10-11/genotype). Escalating ethanol concentrations were offered versus water for two days each, starting with 3% ethanol (v/v in tap water) and continuing with 3% increases up to 21% ethanol. To determine the effect of genotype and ethanol concentration offered, a two-way ANOVA was performed for ethanol preference and consumption data. Both ClockΔ19 and NPAS2 mutant mice exhibited increased ethanol preference and consumption as compared to their wild-type littermates (ClockΔ19 preference $p< 0.05$, consumption $p< 0.05$; NPAS2 preference $p<0.001$, consumption $p<0.001$). Further, both ClockΔ19 and NPAS2 mutant mice exhibited increased significantly higher ethanol preference and consumption at higher ethanol concentrations (as revealed by Bonferroni post-hoc analysis). Total fluid consumption did not differ between mutant and wild-type mice. Studies generally show that very few genetically modified mice exhibit increased alcohol intake. In addition to ClockΔ19 mutants and NPAS2 mutants, mice with a null mutation in the circadian gene *Per2* also exhibit increased alcohol intake. *Per2* expression is regulated by the transcription factors CLOCK and NPAS2. These results suggest an important role for circadian genes in alcohol intake. Current studies include identification of novel target genes of these transcription factors. Supported by grants from NIDA (F32 AA020452, T32 DA7290, R01 DA023988).

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RELATIONSHIP BETWEEN OPRM1 GENOTYPE AND THE EFFECTS OF ALCOHOL AND NALTREXONE IN RHESUS MONKEYS SELF-ADMINISTERING ALCOHOL

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Evidence suggests that the A118G single nucleotide polymorphism (SNP) in the mu opioid receptor gene (OPRM1) may contribute to variation in responsiveness to naltrexone pharmacotherapy and, possibly, sensitivity to various abuse-related effects of alcohol in humans. We investigated the contribution of an orthologous C77G SNP in the rhesus monkey OPRM1 to the reinforcing effects of alcohol and sensitivity to naltrexone in monkeys trained to self-administer alcohol. We selected monkeys a priori on the basis of OPRM1 genotype (C/C, C/G, G/G) and trained them to self-administer alcohol under a fixed-ratio schedule and limited access conditions. Alcohol intake by monkeys varied with genotype such that animals with the G/G genotype drank consistently more alcohol than those animals with the C/C genotype, across a range of alcohol concentrations. Naltrexone attenuated alcohol drinking in a dose- and genotype-dependent manner. NTX was approximately 10-fold more potent at reducing self-administration in animals harboring the G/G genotype. These observations cannot be explained by pharmacokinetic differences, as no genotype-dependent differences in alcohol or naltrexone metabolism were evident. Moreover, no differences in baseline observable behavior amongst the animals contributed to the disparities in self-administration. Rather, in competition binding assays with [3H]naloxone, the monkey C77G SNP modified mu opioid receptor sensitivity to the endogenous opioid beta-endorphin in a manner similar to the human A118G SNP. These data suggest that genetic variation in OPRM1 in monkeys can contribute significantly to individual differences in sensitivity to the reinforcing effects of alcohol and responsiveness to naltrexone treatment. Moreover, they raise the possibility that the mechanism underlying this variability may be related to individual differences in sensitivity to endogenous opioids. Supported by: AA016828 (DP), AA019688 (EV), DA025697 (GM), RR00168 (DP, EV, GM).

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THE ''ANTI-BINGE'' EFFECTS OF PKCE INHIBITOR INVOLVES GROUP I MGLURS AND PI3K IN THE NUCLEUS ACCUMBENS

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Binge alcohol drinking elevates PKCε activity within the nucleus accumbens (NAC) shell, and neuropharmacological studies indicated a role for NAC PKCε in regulating binge alcohol drinking under Drinking-in-the-Dark (DID) procedures. Moreover, the ''anti-binge'' effect of inhibiting PKCε requires intact Homer2, a scaffolding protein likely involved in linking PKCε to Group I metabotropic glutamate receptors (mGluRs). The present study sought to extend these earlier data by testing the hypothesis that signaling from Group I mGluRs to PKCε within the NAC is a molecular pathway regulating binge alcohol intake. Furthermore, as mGluR5-mediated activation of PKCε depends upon intact PI3K signaling, and intra-NAC blockade of PI3K using both selective and non-selective antagonists also reduces binge alcohol intake under DID procedures, we tested the hypothesis that signaling from PI3K to PKCε within the NAC regulates binge alcohol drinking. For these studies, groups of C57BL/6J mice were trained to drink 20% alcohol from a 50 ml bottle under DID procedures (2 hrs, bottle presentation at 3 hrs into the circadian dark) for at least 4 days prior to microinjection with the peptide inhibitor of PKC epsilon TAT-eV1-2, or vehicle, followed 20 min later by microinjection of the mGluR5 antagonist MTEP (3 μg), the mGluR1 antagonist JNJ16259685 (15 pg), or the selective PI3K antagonist LY294002 (0.17 ng). Intra-NAC blockade of mGluR1, mGluR5, PI3K and PKCε alone all reduced binge alcohol drinking, with the most robust effect (50%) observed upon infusion of the PKCε inhibitor alone. Co-infusion of mGluR1, mGluR5 and PI3K antagonists all partially reversed the effect of the PKC inhibitor, but did not produce effects that were statistically different than any antagonist infused alone. These data demonstrate for the first time that intra-NAC blockade of mGluR1 using a highly potent antagonist is sufficient to reduce binge alcohol intake and that signaling from both mGluR1 and mGluR5 through PKCε is involved in the maintenance of binge alcohol drinking. Moreover, these data extend earlier neuropharmacological data by demonstrating that signaling from PI3K to PKCε within the NAC proper is a pathway regulating binge alcohol intake. Funding: NIAAA grants AA016650 (KKS) and AA013588 (ROM), as well as funds provided by the State of California for medical research on alcohol and substance abuse through University of California, San Francisco (UCSF) (ROM).

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LOWER GABA-ASSOCIATED GENE EXPRESSION IN THE ACCUMBENS SHELL OF ALCOHOL-PREFERRING P RATS ACROSS PERI-ADOLESCENCE VS. THE EARLY ADULT WISTAR RAT

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Adolescence is a period of neurodevelopment often characterized by overexpression and subsequent pruning of synaptic interconnections. This maturation process moves from ''lower'' limbic structures to ''higher'' cortical structures across peri-adolescence. In adulthood, the alcohol-preferring (P) rat has higher GABAergic terminal densities in the nucleus accumbens (NAcb) than its alcohol-nonpreferring (NP) counterpart. The present study examined whether differences in GABA-associated genes in the NAcb shell (NAcbSh) could be detected between the male P rat, across adolescence and early adulthood, and the early adult male Wistar (W) rat. P rats served as an animal model of alcoholism, whereas W rats served as an animal model of moderate ethanol intake. Postnatal days (PNDs) 28 and 45 were taken as early and late adolescence, respectively; whereas PND 75 was taken as early adulthood. Brains (n = 4-5 for each age and line) were extracted on the respective PND, flash-frozen and stored at -80 deg C. Later the NAcbSh was micropunched from brain slices. TaqMan® Low-Density Arrays (TLDAs) were used to assess mRNA levels of 32 GABA-associated genes in the NAcbSh. The primary finding was that P rats have lower levels of GABA-associated gene expression in the NAcbSh than W rats. The following GABA-associated genes had significantly ($p<0.05$, a priori 2-tailed Dunnett's t-test following significant higher-order effects) lower expression in the PND 28 P vs PND 75 W rat: GABA-A alpha2, beta1, beta2, beta3, gamma1 receptor subunits; diazepam binding inhibitor (DBI); a GABA-A receptor clustering protein; GABA-transaminase (GABA-T), which facilitates GABA degradation to glutamate; L-glutamic acid decarboxylase (GAD65), which facilitates the synthesis of GABA; as well as the GABA transporters SLC6A1 and SLC32A1. Fewer significant differences were observed at PNDs 45 and 75, although expression levels remained lower in P vs. PND 75 W rats. These findings provide further support for the hypothesis that altered GABAergic activity in the NAcb may facilitate the development and expression of alcohol abuse/dependence. Funded in part by NIH/NIAAA AA013522.

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CHANGES IN MRNA EXPRESSION OF DRD1A AND SLC18A2 DUE TO VOLUNTARY DRINKING, BUT NOT RUNNING, IN MICE

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Prior research has revealed a relation between natural reward seeking behavior and drugs of abuse at the behavioral and neurobiological levels (Nestler, 2005). Our laboratory recently reported that in C57Bl/6J mice, preference for alcohol decreases when there is an exercise wheel present (Ehringer et al. 2009). Given that the release of dopamine in the nucleus accumbens is a crucial step in signaling reward that has been implicated in both alcohol and exercise behaviors (Di Chiara and Imperato, 1985, Dishman et al. 2006), we measured mRNA expression of five genes important in regulating this pathway, tyrosine hydroxylase (*Th*), dopamine receptors D1 (*Drd1a*) and D2 (*Drd2*), dopamine active transporter (*Slc6a3*) and vesicular monoamine transporter (*Slc18a2*). We hypothesize that changes in gene expression will be influenced by different environmental stimuli (alcohol, exercise, both, or neither). Adult female C57Bl/6J mice were housed individually in one of four cage conditions: empty with water, empty with alcohol and water, running wheel with water, or running wheel with alcohol and water. After 16 days, mice were sacrificed and the cortex, striatum, and midbrain were collected. Total RNA was extracted, reverse transcribed, and TaqMan® probes for were used for real-time quantitative PCR with an endogenous control (*Gapdh*). Results indicate that striatal expression of *Drd1a* is decreased ($p=0.05$) while midbrain expression of *Slc18a2* is increased ($p=0.02$) in response to alcohol consumption, regardless of exercise. No changes were observed for other genes, and no interactions were observed between alcohol and exercise. While both *Drd1a* and *Slc18a2* have been implicated previously, no studies have shown expression changes as a result of voluntary alcohol consumption. Results from this research should provide improved understanding of the neurobiology of alcohol use and exercise, and suggests further studies are needed to identify candidate genes involved in mediating interactions between rewarding behaviors. This may lead to improvements in the prevention and treatment of alcohol disorders in humans. Supported by R01 AA017889, T32 DA017637.

3. PHARMACOLOGY C.N.S.
a. Neuropeptides 49–65/1013–1029

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ALCOHOL ALTERS INSULIN-LIKE GROWTH FACTOR-1 IGF-1 AND IGF-1/ESTRADIOL INDUCED TRANSFORMING GROWTH FACTOR ß1 RELEASE FROM HYPOTHALAMIC ASTROCYTES

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Hypothalamic glial-neuronal communications are important for the activation of luteinizing hormone releasing hormone (LHRH) secretion at the time of puberty. Growth factors such as insulin-like growth factor-1 (IGF-1) and transforming growth factor ß1 (TGFß1) produced in hypothalamic astrocytes and are known to facilitate LHRH release. IGF-1 acts within the median eminence to stimulate LHRH release directly from neuronal terminals and TGFß1 facilitates this by causing retraction of tanycyte processes to better allow for entry of the peptide into hypophyseal portal blood. Similarly, both IGF-1 and estradiol (E_2) also effect the remodeling of tanycyte end feet that surround LHRH nerve terminals. Because the relationship between these three factors regarding remodeling in the hypothalamus is not known, we used pure populations of rat hypothalamic astrocytes grown in culture to assess the potential for IGF-1 and E_2 to stimulate TGFß1, and then analyzed the effects of alcohol (ALC) on both basal and stimulated TGFß1 secretion. Upon reaching confluence, astrocytes were placed in serum-free medium for 8 hours then removed and exposed to medium only, medium containing IGF-1 (100 ng/ml) or IGF-1 (100 ng/ml)+E_2 (5 nM), or medium from each of these groups in the absence or presence of 50 mM ALC. After 18 hours, media were collected and assayed for TGFß1. Results showed that the astrocytes markedly released basal TGFß1 ($p<0.001$) when compared to that released from astrocyte-free media. This basal release of TGFß1 was blocked by exposure to ALC ($p<0.05$). IGF-1 alone increased TGFß1 release ($p<0.05$) over basal, an action potentiated by E_2. Furthermore, ALC blocked the stimulation of TGFß1 caused by IGF-1, as well as its potentiated release induced by the presence of E_2. These data demonstrate a role for IGF-1 and E_2 regarding TGFß1 secretion from hypothalamic astrocytes. We suggest that these three factors work together to facilitate LHRH release and that IGF-1 plays a duel role in this regard. It is known that IGF-1 in the presence of E_2 stimulates LHRH secretion from nerve terminals and also causes retraction of the tanycyte end feet from the portal vasculature. We now suggest that this latter action is mediated by TGFß1 following its release induced by IGF-1. Furthermore, the fact that ALC blocks the IGF-1/E_2 release of TGFß1 from hypothalamic astrocytes further demonstrates the inhibitory actions of ALC on hypothalamic LHRH release. Supported by NIH-AA07216.

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ANGIOTENSIN (1-7)-MEDIATED NITRIC OXIDE PRODUCTION IMPAIRS VASOPRESSIN RESPONSE TO HEMORRHAGE DURING ACUTE ALCOHOL INTOXICATION

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Acute alcohol intoxication (AAI) impairs hemodynamic counter-regulation and blunts the arginine vasopressin (AVP) response to hemorrhagic shock (HS). We have demonstrated that AAI disrupts signaling mechanisms controlling AVP release through up-regulation of paraventricular (PVN) nitric oxide (NO) and attenuated angiotensin (ANG) II response to HS. We hypothesized that AAI may also enhance ANG Converting Enzyme (ACE) 2 activity promoting the conversion of ANG II to the NO-stimulating peptide ANG (1-7) further contributing to AAI-induced suppression of AVP release. To examine if ANG (1-7) stimulates NO production in the PVN as well as to examine the ability of A-779 to block the Mas receptor, normotensive male Sprague-Dawley rats (250–300g) were administered intracerebroventricular (ICV) injections of either vehicle (sterile water), ANG (1–7) (10pmol/μL) or the Mas receptor antagonist, A-779 (10pmol/μL) + ANG (1-7). ICV administration of ANG (1-7) significantly increased NO content in the PVN compared to vehicle-treated animals (25±3 μmol/mg tissue vs. 11± 3 μmol/mg tissue). This increase in central NO content was associated with a decrease in MABP (~8% decrease from baseline) 30-60 minutes post-administration of ICV ANG (1-7). Central pretreatment with the A-779 prevented the ANG (1-7)-mediated increase in PVN NO content and produced no changes in MABP, confirming A-779-mediatedinhibition of the Mas receptor. To test the prediction that the alcohol-induced increase in central NO was the result of accentuated ANG (1-7) stimulation of the Mas receptor, conscious animals received a primed (2.5g/kg + 0.3g/kg/h) 15h intragastric infusion of alcohol or dextrose (DEX). An ICV injection of A-779 was administered prior to a to fixed-pressure (40 mmHg) HS. AAI increased PVN ACE2 activity (41%) and ANG (1-7) content (137%) compared to DEX+HS. AAI increased NOS activity (30%) and NO levels (40%) in the PVN compared to DEX controls. Administration of A-779 decreased NOS activity (66%), NO levels (27%; p=NS) and partially restored circulating AVP levels (20%) in AAI-treated animals. These results suggest that increased hypothalamic Mas receptor activation by Ang 1-7 partially contributes to the alcohol-mediated NO-dependent inhibition of AVP release during HS. DOD PR-054196, NIAAA-AA7577, APS Porter Fellowship.

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RECEPTOR-SPECIFIC EFFECTS OF BINGE-LIKE ETHANOL DRINKING ON NPY MODULATION OF SYNAPTIC TRANSMISSION IN THE EXTENDED AMYGDALA

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Endogenous anti-stress systems, including neuropeptide Y (NPY) signaling, protect against the deleterious effects of alcohol by acting in key brain regions involved in the regulation of emotional and drinking behaviors, including the bed nucleus of the stria terminalis (BNST) in the extended amygdala. We hypothesized that repeated cycles of binge alcohol drinking and withdrawal cause persistent adaptations in the NPY system in the BNST that contribute to negative behavioral consequences, such as increased alcohol drinking. Because the anti-drinking effects of NPY are thought to occur via activation of the NPY Y1 receptor (Y1R), while activation of the NPY Y2 receptor (Y2R) leads to increased ethanol intake, the pro-drinking effects of chronic alcohol exposure may be due to dysregulation of NPY signaling via alterations of Y1R and/or Y2R. We recently showed that NPY reduces GABAergic transmission in the dorsolateral BNST (dlBNST) via activation of presynaptic Y2R. Therefore, the goals of the current study were to 1) determine the role of Y1R in NPY modulation of inhibition of the dlBNST, 2) examine the receptor-specific effects of binge-like ethanol drinking on NPY signaling, and 3) establish a direct relationship between NPY in the BNST and alcohol drinking in male C57BL/6J mice. When we examined the role of Y1R in NPY's modulation of inhibition in the dlBNST, we found that Y1R activation locally and presynaptically increases GABA release. We also found that mice exposed to three cycles, but not one cycle, of binge-like ethanol drinking had reduced Y2R-mediated NPY modulation of inhibitory transmission in the dlBNST. In addition, both Y1R and Y2R protein expression were increased in the dlBNST after three cycles of drinking. Our results suggest that Y1R and Y2R functionally oppose one another in the BNST, possibly via direct interaction at presynaptic terminals of NPY neurons, and that three cycles of binge drinking and withdrawal may lead to increased alcohol drinking via alterations in the expression of NPY and its receptors, as well as functional dysregulation of Y2R-mediated NPY signaling in the dlBNST. Ongoing experiments are examining the signaling pathway(s) by which Y1R presynaptically decreases GABA release and the effects of binge-like ethanol drinking on Y1R-mediated modulation of inhibition in the dlBNST. We are also currently examining the effects of local pharmacological manipulation of Y1R and Y2R in the BNST on binge-like ethanol drinking.

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THE EFFECT OF NEUROKININ-1 RECEPTOR ANTAGONIST ON NEURONAL ACTIVATION OF STRESS CIRCUITRY DURING FOOTSHOCK-INDUCED REINSTATEMENT OF ALCOHOL SEEKING

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The neurokinin-1 receptor (NK1R) serves as the primary target of the neuroactive peptide substance P (SP). The SP/NK1R system has been shown by our lab and others to be involved in alcohol related behaviors. Specifically, we have shown that mice with a genetic deletion of the NK1R consume less alcohol than controls, and this effect is mimicked by administration of NK1R antagonists to wild type mice. In the studies presented here we used L822429, an NK1R antagonist that has high affinity for the rat NK1R and has anxiolytic properties when administered systemically. In previous studies, we have found that this compound dose-dependently blocks the expression of footshock stress-induced reinstatement in rats, while leaving primary reinforcement and cue-induced reinstatement unaffected. In these experiments, L822429 or vehicle pretreatment was given prior to footshock-induced reinstatement testing, and brain tissue was collected for immunohistochemical analysis. In vehicle treated animals, Fos immunoreactivity was increased in many regions of the brain stress circuitry including the amygdala, nucleus accumbens, dorsal raphe nucleus, prefrontal cortex and bed nucleus of the stria terminalis. L822429 suppressed the stress-induced increase in c-fos in a subset of these regions, particularly the dorsal raphe nucleus and nucleus accumbens shell, suggesting that these regions regulate the behavioral effect of NK1R antagonism. Future experiments will use intracranial injections of L822429 during stress-induced reinstatement to further confirm the specific site of action of NK1R antagonists on this behavior.

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A LOW DOSE OF THE MELANOCORTIN AGONIST MTII SYNERGISTICALLY AUGMENTS NALTREXONE-INDUCED ATTENUATION OF BINGE-LIKE ETHANOL DRINKING IN C57BL/6J MICE

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The central polypeptide precursor proopiomelanocortin (POMC) gives rise to beta-endorphin, an endogenous opioid peptide, and the melanocortin (MC) peptides including alpha-melanocyte stimulating hormone. Opioid receptor antagonists, such as naltrexone (NAL), have been demonstrated to reduce ethanol consumption in rodents, and a growing body of evidence indicates that MC receptor agonists blunt ethanol intake. Interestingly, central opioid and MC pathways have been demonstrated to interact in their modulation of nociception and feeding behavior. Since opioids and MC peptides modulate ethanol consumption, the goal of the present work was to determine if these peptides, when presented in combination, interact additively or synergistically in the modulation of binge-like ethanol drinking in C57BL/6J mice. We used drinking in the dark procedures, an established model of binge-like ethanol drinking, to first established dose-response effects of intraperitoneally (i.p.) injected NAL or the MC agonist MTII (0, 0.3, 3.0, and 10 mg/kg for each drug) on binge-like drinking. Based on these data, we established the ED_{20} and ED_{30} for each drug, and then combined the low (ED_{20}) and high (ED_{30}) dose of each drug with the dose-response range of the other drug. Results showed that MTII was 3.4-fold more potent than NAL in blunting binge-like ethanol drinking (based on ED_{50} values). MTII was also more effective, as the 10 mg/kg dose of MTII produced a 72% reduction of binge-like ethanol drinking while this same dose of NAL reduced drinking by only 49%. When administered in combination, the low ED_{20} (but not the ED_{30}) dose of MTII (0.26 mg/kg) shifted the NAL dose-response curve to the left by a factor of 7 (i.e., NAL was 7-fold more potent when administered in combination with MTII relative to when it was administered alone). Subsequent isobolographic analyses of these data showed that MTII synergistically augmented the ability of NAL to blunt binge-like ethanol drinking. NAL shifted the MTII dose effect curve to the left, but this effect was additive. The present results show that a low dose of MTII synergistically potentiates the ability of NAL to blunt binge-like ethanol drinking. These observations suggest that MC receptor agonists may improve the therapeutic effectiveness of NAL in the treatment of alcohol abuse disorders when these drugs are given in combination. (Supported by NIH grants AA013573 and AA015148, and the Department of Defense grant W81XWH-09-1-0293).

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THE C-TERMINAL FRAGMENT OF THE CORTICOTROPHIN RELEASING FACTOR BINDING PROTEIN (CRF-BP) POSITIVELY MODULATES CRF-RECEPTOR 2 ACTIVATION

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A stress response is believed to involve the corticotropin releasing factor (CRF) system. Deregulation of the CRF system at any point can lead to a variety of psychiatric disorders, such as anxiety, depression, post-traumatic stress disorder, and alcohol use disorder. The precise role of corticotrophin releasing factor binding protein (CRF-BP) in the brain is still the subject of intense investigation. In the periphery, it is believed CRF-BP, due to the higher affinity with its endogenous ligand, plays a buffer role by reducing the amount of free CRF. In the CNS however, the interaction of CRF-BP with CRF-receptor 2 (CRF-R2) results in increased of receptor responsiveness to CRF. CRF-BP is susceptible to autocatalytic proteolysis yielding a larger N-terminal fragment of 27-kilodalton, CRF-BP(27kD), which retains the binding site for CRF and a smaller, 9.6-kilodalton C-terminal fragment, CRF-BP(10kD) with no apparent physiological or pathological role. Loss of the CRF-BP gene in mice has been associated with increased anxiety-like behavior.

Using a novel cellular-based assay, we have shown here, that CRF-BP(10kD) is responsible for enhancing CRF-induced CRF-R2 signaling. Additionally, CRFBP -/- mice exhibited an increase in anxiety-like behavior as compared to their CRFBP +/+ littermates in the open field and elevated plus maze tests.

Our findings support the hypothesis that CRF-BP in a target for addiction and specifically CRF-BP(10kD) may act as endogenous allosteric modulator of CRF-R2 signaling. Our long term goal is to identify small molecules and novel ligands that target this CRF-BP(10kD) interaction with CRF-R2 to develop pharmacotherapies used for stress and to treat alcohol use disorders (AUDs).

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ALCOHOL EFFECTS ON SERUM OXYTOCIN LEVEL IN ALCOHOLICS

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Oxytocin (OXT), a 9-amino acid peptide produced by the posterior pituitary gland and other brain areas, plays a key role in facilitating social behaviors, including maternal behavior and pair-bonding. Oxytocin also possesses anxiolytic, stress reducing and anticraving effects, which suggests that OXT could play a role in the neurobiology of alcohol dependence. Acute alcohol is a potent inhibitor of OXT release and chronic alcohol exposure has neurotoxic effects on OXT neurons and induces behavioral deficits suggestive of a central OXT deficiency. However, there are few studies that administer OXT to animals or alcohol dependent humans to determine its effect on drinking. We recently conducted a experiment to measure OXT in actively drinking alcohol dependent humans. OXT was measured using a multiplexed, competitive format immune-assay (Millipore, Billerica, MA) for the detection of neuropeptides in serum using a Bioplex analyzer (BioRad, Hercules, CA). Non-treatment seeking alcohol dependent subjects recruited for a laboratory alcohol self-administration study (n=34) had elevated plasma OXT (420± 29 pg/ml) compared to non-alcoholic, social drinker controls (211± 12 pg/ml). Our data confirm the increased OXT levels previously observed by Marchesi et al (1997). Nine of the alcohol dependent subjects subsequently participated in an alcohol self-administration experiment. Baseline (recently drinking, but not intoxicated) OTX levels (352±57 pg/ml) were elevated compared to the non-alcoholic controls. Six weeks later, pre-drinking OXT levels were still increased at 523±68 pg/ml (n=7). These subjects then consumed one or more alcohol drinks in an alcohol self-administration experiment and blood OXT levels were repeated 1 hour later. Post-drinking blood OXT levels were decreased during intoxication (238± 47 pg/ml), although the pre-post difference was not significant, probably due to different amounts of alcohol consumed. The data are consistent with an increase in peripheral oxytocin levels in actively drinking alcoholics. Alcohol intoxication still reduces oxytocin levels in these individuals, although the levels remain elevated compared to non-alcoholics. The increased peripheral oxytocin levels are surprising, given the behavioral deficits, increased anxiety and stress seen in alcohol dependence that are more indicative of a central deficiency of OXT. The discrepancy may be due to differences in central and peripheral oxytocin regulation.

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IDENTIFICATION OF NOVEL PEPTIDES THAT ALTER ETHANOL MODULATION OF BK CHANNEL FUNCTION

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The BK channel is an evolutionarily-conserved target of ethanol. Genetic manipulation of the BK channel affects behavioral sensitivity to ethanol in a numerous of model systems. Several studies suggest that the BK channel is a viable therapeutic target for alcohol intoxication and addiction. To achieve this end, we have developed a screen identifying peptides that alter BK channel function. Using a monovalent phagemid display technique, we screened 30 million 9 amino acid sequences for those that bind to the BKα channel. Twenty-seven unique peptides remained after panning for sequences that bind to the human BKα channel but not the rat SK2 channel or human glycine α1 receptor. Sequences bearing clusters of positively charged amino acids were enriched 100-300 fold. Three motifs were enriched 3000–6000 fold. To rapidly screen for functional effects of select peptides, we made use of the nematode, *C. elegans*. Peptides were tested for their abilities to alter locomotion, an ethanol- and BK-channel dependent behavior in *C. elegans*. Locomotion is suppressed by enhancing BK channel activity, and acute exposure to pharmacologically-relevant concentrations of ethanol enhances BK channel function. A peptide, pskan4, was identified that had no effect on locomotion when administered alone but enhanced ethanol suppression of locomotion ($p<0.0001$). The effect of this peptide was abolished in BK knockouts. These data suggest that pskan4 enhances the ethanol-dependent increase in BK channel activity, but does not alter activity in the absence of ethanol. Another peptide, pskan1, had BK channel- but not ethanol-dependent effects on locomotion. While these two peptides had motifs enriched 4000–6000 fold, a peptide without a highly enriched motif caused only non-specific behavioral effects. Further, a similar 9 amino acid peptide not selected in the panning procedure did not have significant effects on locomotion indicating that the screening technique was specific for the desired target. Overall, these findings show that we have developed and successfully employed a screen for identifying and characterizing novel peptides that alter BK channel-dependent behavior in the presence of pharmacologically-relevant concentrations of ethanol. Future electrophysiological testing will characterize the abilities of peptides to alter BK channel function in the presence or absence of ethanol. This screening technique can be applied to identify peptide modulators of other ion channels.

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EXCESSIVE ETHANOL CONSUMPTION DISRUPTS BDNF-MEDIATED CONTROL OF ETHANOL DRINKING BEHAVIORS – A ROLE FOR THE P75-NTR RECEPTOR

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Previously, we reported that the expression of brain-derived neurotrophic factor (BDNF) in the dorsal striatum (DS) of rodents is induced in response to moderate intake of ethanol[1,2]. We further showed that the BDNF-mediated pathway in the DS, and specifically in the dorsolateral striatum (DLS), is part of a homeostatic pathway that gates ethanol-related behaviors[1-3]. Specifically, we showed that the activation of the BDNF receptor TrkB in the DLS of rats attenuated, whereas siRNA-mediated knockdown of BDNF expression increased operant self-administration of ethanol[3]. The level of corticostriatal BDNF is reduced in mice exhibiting excessive ethanol drinking behavior[4]. We therefore hypothesized that high levels of ethanol intake results in the breakdown of the protective actions of BDNF. To test this possibility, rats with a history of excessive ethanol intake (20% v/v, 2-bottle choice) were trained to self-administer 20% ethanol in an operant self-administration paradigm, and BDNF's actions in the DLS were assessed. We found that under these conditions, knockdown of BDNF levels or activation of the BDNF pathway in the DLS do not alter ethanol operant self-administration, suggesting that the transition from moderate to excessive ethanol drinking results in a breakdown of the BDNF pathway. Activation of the other BDNF receptor, p75-NTR, produces responses that are opposite to those of TrkB[5]. We therefore hypothesized that a history of excessive drinking alters p75-NTR expression and/or neuronal localization. We found that the synaptic localization of p75-NTR is increased in the DLS of rats with a history of excessive ethanol drinking following 24 hrs of withdrawal, suggesting that p75-NTR reduces normal BDNF signaling during excessive ethanol intake. Together, our data suggest that the p75-mediated disruption of the BDNF pathway in the DLS contributes to the development of excessive drinking behavior.

1. McGough, J Neurosci 2004; 2. Logrip, FASEB J 2008; 3. Jeanblanc, J Neurosci 2009; 4. Logrip, J Neurochem 2009; 5. Teng, Dev Neurobiol 2010

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DRINKING 20% ETHANOL ON AN INTERMITTENT ACCESS SCHEDULE INDUCES CHANGES IN BEHAVIOR AND NEUROPEPTIDE EXPRESSION IN LONG-EVANS RATS

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The intermittent-access 20% ethanol drinking paradigm developed by Wise (1973) and recently implemented in Bartlett's laboratory (2008) results in relatively high levels of ethanol intake in outbred rats. While the effects of manipulations on drinking have been described with this model, the impact of the drinking itself on behavior and neuropeptide expression remains to be determined. In the present study, adult male Long-Evans rats separated into ethanol- and water-drinking groups (n=8/group) were first examined using behavioral tests and then, after seven weeks of drinking, were sacrificed for analysis with quantitative real-time PCR. The ethanol-drinking rats were trained using the intermittent-access paradigm, with access to a bottle of 20% ethanol provided for three 24-hr sessions per week. Water and chow were available *ad libitum*, and a second bottle of water was provided when the ethanol was removed. The water-drinking group was kept ethanol-naïve, with two bottles of water made available. Alcohol intake reached highly stable levels by the fifth exposure, averaging 3.5±0.8 g/kg/24 hr and ranging from 1.3 to 8.0 g/kg/24 hr. Since the rats consumed a significant amount of their daily ethanol (24%, 0.8±0.2 g/kg) during the first 30 min, the behavioral tests and peptide analyses were performed after 30 min of ethanol. Compared to the water-drinking rats, the ethanol-drinking rats exhibited significantly less anxiety on an elevated plus maze, spending 49±5% vs. 31±7% of their time on the open arm ($p<0.05$), and they tended to show more novelty-seeking in a hole-board apparatus, approaching the first hole sooner (1±1 sec vs. 21±13 sec, $p=0.13$). In an open field, they showed no difference in ambulatory distance (4154±531 cm vs. 4408±383 cm) or time (133±18 sec vs. 136±12 sec), suggesting no decrement in motor ability, but they did move more slowly (45±1 cm/sec vs. 50±1 cm/sec, $p<0.05$). Along with these changes, the ethanol-drinking Long-Evans rats showed increased expression of both orexin (+55%, $p<0.05$) and melanin-concentrating hormone (+71%, $p<0.05$) in the perifornical lateral hypothalamus, similar to that reported with acute ethanol administration in Sprague-Dawley rats. Therefore, with this drinking paradigm, outbred rats will consume enough ethanol to significantly alter their behavior. With these neuropeptides found to stimulate ethanol intake when injected, their increased expression may be responsible, in part, for the elevated ethanol intake.

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AMPA RECEPTORS IN THE CENTRAL AMYGDALA REGULATE OPERANT RESPONDING FOR ETHANOL IN C57BL/6J MICE

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Rationale: Chronic exposure to ethanol (EtOH) leads to glutamatergic neuroadaptations that underlie multiple facets of alcohol addiction such as learning and memory and behavioral deficits. Specifically, altered function of the α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor may be one mechanism by which EtOH modulates brain plasticity; however, the role of AMPA receptors in EtOH self-administration remains to be fully characterized.
Objective: To address this goal, we first quantified levels of GluR1 phosphorylation (pGluR1) as an index of AMPA receptor activation. Next, we used pharmacological strategies to evaluate potential mechanistic regulation of EtOH self-administration by AMPA receptors.
Methods: C57BL/6J mice self-administered EtOH either in their home cage or in an operant conditioning chamber. The latter group was trained on a fixed-ratio 4 (FR4) schedule of reinforcement to lever press for the delivery of EtOH. In Experiment 1, both groups of mice self-administered EtOH for 30 days before intracardial perfusion. Tissue was analyzed for pGluR1 immunohistochemistry. In Experiment 2, operant self-administering mice were injected with the AMPA positive modulator, CX 546 (0–30 mg/kg, i.p.), prior to a test session. In Experiment 3, operant self-administering mice were surgically implanted with a guide cannula into the central nucleus of the amygdala (CeA). After recovery, the AMPA receptor antagonist, NBQX (3μg/side), was microinjected prior to a test session.
Results: Both models of EtOH self-administration significantly upregulated pGluR1 immunoreactivity in the CeA. Positive modulation of the AMPA receptor significantly increased active lever responding for EtOH while inhibition of the AMPA receptor in the CeA selectively inhibited operant responding for EtOH.
Conclusions: EtOH self-administration leads to increased GluR1 activation/phosphorylation within the CeA. Furthermore, AMPA receptor activity is functionally involved in regulating the reinforcing properties of EtOH – this effect appears to be specifically due to involvement of AMPA receptors within the CeA. Support contributed by: AA014983, AA016629, AA011605

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DIFFERENTIAL INVOLVEMENT OF UROCORTIN-1 ACROSS SEVERAL ETHANOL DRINKING PARADIGMS IN MICE

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Prior work from our laboratory showed that ethanol (EtOH) drinking resulted in robust activation of neurons within the rodent centrally-projecting Edinger-Westphal nucleus that contained the CRF-related neuropeptide Urocortin-1 (Ucn1), and that genetic deletion of Ucn1 dampened EtOH-induced reward. The current studies investigated the experimental variables underlying Ucn1's involvement in EtOH intake. Earlier studies showed that genetic deletion of Ucn1 in mice on a C57BL/6J background dampened EtOH intake in a continuous access ''two-bottle choice'' (2BC) EtOH drinking procedure using 3–10% EtOH, but not in a limited access ''drinking-in-the-dark'' (DID) binge model in which mice had access to a single bottle containing 20% EtOH. Because these two procedures differ in several aspects (EtOH concentration, concurrent water availability, length of EtOH access), we performed a series of experiments in Ucn1 genetic knockout (KO) and wild-type (WT) littermate mice in order to determine the relative importance of each variable in mediating Ucn1's effects on EtOH intake. Experiment A implemented a continuous access 2BC procedure similar to that used previously, except that concentrations of EtOH were increased to 10–40%. Experiment B implemented a limited access DID procedure similar to that used previously (2–4hr access to EtOH, beginning three hrs into the dark cycle), except that access to EtOH was accompanied by concurrent access to a second bottle containing water (2BC-DID). Experiment A revealed that genetic deletion of Ucn1 dampened EtOH intake and EtOH preference at concentrations of 20% and 40%, indicating that the previously-observed lack of effect of Ucn1 KO on EtOH intake in the DID protocol cannot be attributed to the high concentration of EtOH used in that procedure (20%). Experiment B found that genetic deletion of Ucn1 had no effect on EtOH intake (and sex-specific effects on EtOH preference), indicating that the previously-observed lack of effect of Ucn1 KO on EtOH intake in the DID protocol also cannot be attributed to the absence of water availability during EtOH access. In conclusion, these experiments indicate that Ucn1 involvement in EtOH intake depends on the length of EtOH access (or the extent of EtOH history), rather than EtOH concentration or concurrent water availability. These findings lend further support for the importance of Ucn1 in development of alcohol use disorders resulting from prolonged alcohol self-administration.

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CROSS-TALK BETWEEN THE CANNABINOID CB1 RECEPTOR AND OREXIN A RECEPTOR IN THE VTA, BUT NOT THE PVT, MEDIATES CUE-INDUCED RELAPSE TO ALCOHOL

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Cannabinoid and hypocretin/orexin signaling are widely recognized as crucial players in drug addiction and reward. Very recently, it has been demonstrated that cross-talk exists between the CB1 cannabinoid receptor and the orexin A/hypocretin 1 receptor in the diencephalon. The functional significance of this interaction with regard to addictive behavior, however, remains to be investigated. Here, we hypothesized that alcohol cue-reactivity may be mediated by input from orexin- and cannabinoid-containing neurons toward the ventral tegmental area (VTA) and the paraventricular nucleus of the thalamus (PVT). To elucidate this question, we studied how intra-VTA and intra-PVT microinjections of CB1 cannabinoid receptor- and orexin A (or hypocretin 1) receptor antagonists, alone or in combination at sub-threshold doses, modify cue-induced reinstatement of alcohol-seeking behavior. For these experiments, male Wistar rats were initially trained to self-administer alcohol (10%) in an environment, with discriminative stimuli linked to ethanol availability. Following extinction, the effects of intra-VTA or intra-PVT microinjections of the hypocretin 1 receptor antagonist SB 334867 (0.05 μg/side, i.c.) and the CB1 cannabinoid receptor antagonist AM-251 (1 μg/side, i.c.), administered alone or in combination, were examined on conditioned reinstatement induced by ethanol-related stimuli. While intra-VTA and intra-PVT administration of both antagonists alone did not produce any effect on cue-induced reinstatement, combined intra-VTA administration of these sub-threshold doses of SB 334867 and AM-251 significantly reduced alcohol seeking-behavior. Furthermore, intra-PVT infusions of higher doses of SB 334867 (1 and 5 μg, i.c) and AM-251 (3 μg, i.c.) did not alter conditioned reinstatement. These results suggest that interactions between the CB1 receptor- and the orexin/hypocretin type 1 receptor signaling systems within the VTA, but not the PVT, participate in mediating cue-induced alcohol seeking behavior.

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EFFECTS OF AN OPIOID AGONIST (U50,488H) AND ANTAGONIST (NALTREXONE) ON THE SEEKING AND INTAKE OF SUCROSE AND ETHANOL IN SELECTED AND NONSELECTED RATS

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Naltrexone (NTX) is clinically efficacious at attenuating alcohol intake in non-abstinent alcoholics and, to a lesser extent, craving, independent of intake. While generally regarded as a nonselective opioid antagonist, NTX has been shown to have concentration dependent selectivity with lower doses (< 1.0 mg/kg) selective for the mu receptor and doses exceeding 1.0 mg/kg capable of binding to kappa receptors. While the mu system has been implicated in mediating the reinforcing effects of EtOH, the role of the kappa system is less clear. Recent evidence suggests that kappa activation may mediate EtOH aversion. Thus, the present study sought to evaluate the effects of the kappa agonist U50,488H (U50) in a paradigm that procedurally separates the motivation to seek vs. consume a reinforcer to assess whether U50 differentially affects these behaviors in both selected (alcohol-preferring P rats) and nonselected (Long Evans) rats, and whether these effects are specific to EtOH. The effects of a low (mu specific) and high (nonspecific) dose range of NTX were also assessed. Rats were trained to complete a single response requirement that resulted in access to either 2% sucrose or 10% EtOH for a 20-min drinking session. In three separate experiments, rats were injected (using a balanced design) with either saline or 1 of 3 doses of drug: U50 (IP; 2.5, 5.0, or 10.0mg/kg), low NTX (SC; 0.1, 0.3, or 1.0 mg/kg) or high NTX (SC; 1.0, 3.0, or 10.0 mg/kg) on both consummatory and appetitive treatment days. Following either a 15 (U50) or 30 minute (NTX) pretreatment, rats were placed into an operant chamber and intake (consummatory) or lever responses (appetitive) and response latencies were recorded. The results showed that overall, U50 and NTX attenuated intake and responding for sucrose and EtOH. Independent of reinforcer, LE rats were more sensitive to U50's effects on intake while P rats were more sensitive to the effects on seeking. P rats were more sensitive overall to lower doses of NTX than LE rats and lower doses of NTX were more selective in attenuating EtOH responding vs. sucrose. Higher doses of NTX suppressed intake and responding across both lines and reinforcers. These results demonstrate that craving and intake may be differentially regulated by the kappa and mu opioid receptor systems as a function of "family history" and suggest that different mechanisms of the same (opioid) system may differentially affect craving and intake. Supported by T32-AA007462.

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CHRONIC ALCOHOL INCREASES CENTRAL AMYGDALA DYNORPHIN AND INDUCES ESCALATED SELF-ADMINISTRATION THAT IS RESCUED BY KAPPA-OPIOID RECEPTOR BLOCKADE

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Research has shown that alcohol dependence-induced neuroadaptations in central extended amygdala (cEA) kappa-opioid receptors (KOR) and dynorphins (DYN; endogenous peptide for the KOR) systems promote excessive operant alcohol self-administration and increase negative affective-like states. Indeed, KOR antagonism in the nucleus accumbens shell (a component of the cEA) attenuates dependence-induced excessive alcohol self-administration. The primary hypothesis of the current study was that site-specific infusion of a KOR antagonist (nor-binaltorphimine; nor-BNI) in the central amygdala (CeA; also part of the cEA) would ameliorate dependence–induced excessive alcohol self-administration. A secondary goal included the evaluation of intra-CeA infusions of a CTOP/naltrindole cocktail (selective for mu-/delta-opioid receptors; MOR/DOR, respectively) and nalmefene (a MOR/DOR antagonist with partial KOR agonist properties that just completed Phase III clinical trials) to reduce alcohol self-administration in dependent and non-dependent cohorts. The final goal was to characterize DYN A-like immunoreactivity in the CeA of air- and vapor-exposed rats. Male Wistar rats were trained to self-administer 10% alcohol (w/v) and implanted with cannula guides targeting the CeA. Once recovered, animals received four-weeks of either air- or intermittent alcohol vapor exposure resulting in escalated self-administration for the vapor-exposed groups. Once responding under sham and artificial cerebrospinal fluid conditions was stable, air- and vapor-exposed animals in acute withdrawal (6 hrs into withdrawal) received intra-CeA infusions of nor-BNI, a CTOP/naltrindole cocktail or nalmefene. Nor-BNI selectively attenuated self-administration in dependent rats without impacting non-dependent self-administration, whereas the CTOP/naltrindole cocktail dose-dependently reduced responding in non-dependent rats, but had no effect in dependent rats. Therefore, a double dissociation was identified between KOR and MOR/DOR antagonists for the ability to reduce alcohol self-administration in dependent and non-dependent animals. Nalmefene dose-dependently reduced self-administration in both cohorts. Lastly, DYN A-like immunoreactivity was increased in the CeA of dependent animals in acute withdrawal. These data implicate DYN / KOR systems in excessive alcohol self-administration and identify novel targets for the treatment of alcohol dependence that should enhance treatment adherence.

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CUES ASSOCIATED WITH KAPPA-OPIOID RECEPTOR-INDUCED NEGATIVE AFFECTIVE STATES PROMOTE EXCESSIVE ALCOHOL SELF-ADMINISTRATION IN RATS

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Activation of kappa-opioid receptors (KOR) is associated with the production of negative affective states as well as escalated consumption of alcohol. Research has shown that activation of KORs can be paired with neutral stimuli and that following such pairings, the stimuli induce a negative affective state when presented alone. However, no research has been conducted to examine the effects of cues previously associated with KOR activation on alcohol self-administration. Elucidating the connection between cues reflective of negative affective states and alcohol consumption is of particular importance in order to understand the factors underlying relapse to drugs of abuse such as alcohol. This study examined whether a previously neutral cue that was associated with a negative affective-like state would be able to influence operant alcohol self-administration. Male Wistar rats were trained to self-administer 10% alcohol (w/v) in an operant self-administration paradigm before being surgically implanted with intracerebroventricular (ICV) guide cannulae. Following recovery from surgery and engaging in daily self-administration sessions until stability was reached, a neutral olfactory stimulus (almond scent) was presented prior to self-administration sessions to confirm neutrality (i.e., to not alter alcohol self-administration) and once stability of responding was again achieved, associative conditioning sessions pairing the effects of the KOR agonist U50,488 and the neutral stimulus took place. Subsequently, the animals were allowed to continue daily alcohol self-administration sessions until they stabilized their responding. Once stabilized, the cue was presented prior to self-administration sessions and was shown to be capable of inducing an escalation of operant alcohol self-administration. This result supports the hypothesis that neutral cues can be associated with negative affective states and that the cues alone can impart maladaptive regulation of alcohol consumption. The implications of these data are far reaching and provide new insights into factors that promote excessive alcohol consumption and relapse for those suffering from Alcohol Use Disorders.

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NOVEL MU-OPIOID RECEPTOR SELECTIVE ANTAGONIST NAQ SELECTIVELY REDUCES CONSUMPTION OF HIGH-CONCENTRATION ETHANOL IN MICE

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The non-selective opioid antagonist naltrexone (NTX) is one of few drug therapies approved by the FDA for alcoholism, all of which have shown limited long-term efficacy. NTX acts at mu (MOR) and kappa, and to a lesser degree delta, opioid receptors, and the role of each of these subtypes in its effects on alcohol consumption is unknown. Until recently the only mu-selective ligands available were conformation-constrained peptides with limited experimental utility. However, the recent development of a pair of small molecule MOR antagonists, NAQ and NAP, has allowed for the examination its role in alcohol consumption, with the goal of hypothesis-driven development of new pharmacological therapies for alcoholism. Toward this end C57BL/6J mice were employed in a 3-bottle-choice alcohol self-administration model, in which the effects of NAQ, NTX, and saline vehicle on ethanol consumption (g/kg/day) and preference (over water) were examined. Mice were allowed 24 hour access to 15% and 30% (v/v) ethanol and water, in 3 separate tubes. Two experiments were performed on the same mice, with all drugs administered IP 1x/day in saline. First, following 14 days of baseline ethanol access, the effects of NTX and NAQ (both at 1.00 mg/kg) were examined. Next, following 14 days of abstinence, mice were exposed to intermittent alcohol access (IAA) on a 3 day per week (M/W/F) schedule to examine the effects of prior NAQ, NTX, or saline pre-treatment (in experiment 1) on the development of elevated alcohol intake after abstinence. In the first experiment, NAQ and NTX significantly reduced total ethanol consumption compared to baseline on the first test day. On test day 2 the NTX mice had recovered to baseline consumption levels, while NAQ mice continued to show significantly decreased intake. NAQ significantly reduced consumption and preference for 30% ethanol compared to baseline on both test days, while NTX produced non-significant reductions. In the IAA model, the saline group significantly increased total ethanol preference on the first reinstatement day, while NAQ and NTX groups showed little change until week 3, and never reached the high levels of the saline group. These results show that selective MOR antagonism is sufficient to reduce alcohol consumption and preference in mice, with selectivity for high concentrations, and that NAQ may be a treatment for alcoholism with some potential benefits over NTX. This work was supported in part by NIAAA grant AA016667.

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DYNAMIC CHANGES IN THE BRAIN DUE TO ACUTE ETHANOL EXPOSURE IN NON-HUMAN PRIMATE BRAIN NETWORKS

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Neuropathological and neuroimaging studies have demonstrated morphological and functional consequences of alcoholism in humans. However, this data does not provide a clear sense of how whole-brain connectivity is affected by ethanol exposure. Network science is a valuable tool for understanding the brain as a system by showing how different regions of the brain interact with each other. Using a non-human primate (NHP) model of ethanol self-administration, we investigated the effect of acute ethanol intoxication on NHP brain network organization.

Resting state fMRI was collected in the bonnet macaque (n = 2) in the naïve state and after administration of 0.8 g/kg EtOH (equivalent to 4 drinks) over 5–8 minutes. Resting state fMRI and blood-ethanol concentration (BEC) were subsequently collected at several time points as EtOH was metabolized. Average graph metrics showed no significant difference for clustering coefficient (C), path length (L), local efficiency (E_{loc}) and global efficiency (E_{glob}); however, hub and k-core maps showed a shift of hubs in the cingulate region to the temporal lobes. In particular, global efficiency across hubs in the naïve state decreased, but increased in the temporal lobes. Community structure also showed a shift in network organization to the temporal lobe hubs forming an interconnected community.

These results suggest that acute ethanol exposure changes the organization of the brain, which is most pronounced after adminstration of the ethanol bolus. Because alcohol is disinhibitory, it is believed that it may affect connections between nodes, leading to dysfunction within the network. These results suggest that alcohol shifts the organization of the brain, but more importantly that graph metric analysis can detect dynamic changes in the brain.

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MICROGLIAL ACTIVATION IN NONHUMAN PRIMATES AND IN ALCOHOL DEPENDENCE

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Objective: Microglial activation may occur in alcoholism, and increased systemic inflammation may play a role in this. PET imaging can be used to address these questions in vivo. As an initial step we used PET imaging of the microglial marker Translocator Protein (TSPO) to detect activation of microglia by systemic inflammation in nonhuman primates. Then we scanned a man with alcohol dependence and a matched control.

Methods: Six female baboons (*Papio anubis*) received intravenous *E. coli* endotoxin (0.1 mg/kg), which induces systemic inflammation. [^{11}C]PBR28 was used to measure changes in TSPO binding from baseline (before endotoxin) to 1h and 4h after endotoxin administration. A 50 year-old man with alcohol dependence and a 50 year-old race-matched man with no substance abuse history were scanned to measure baseline [^{11}C]PBR28 binding. Total volume of distribution (V_T) of [^{11}C]PBR28 was estimated from the model fits and used as a measure of total tracer binding. Change in V_T from baseline was used as a measure of microglial activation.

Results: In each animal whole-brain [^{11}C]PBR28 binding (V_T) increased after LPS administration (F (3,6) = 5.1, p = .043). There was a 29±16% increase in binding at 1h (range 12%-47%) and a 62±34% increase in binding at 4h (range 36%-101%). Whole-brain [^{11}C]PBR28 binding in the alcohol dependent man was 27% higher than in the control subject, including frontal cortex (+34%), temporal cortex (+27%), parietal cortex (+17%), striatum (+16%) and cerebellum (+39%). Conclusions:

Systemic inflammation is associated with an increase in total binding of the TSPO radiotracer [^{11}C]PBR28 in baboons, and in one human subject with alcohol dependence, binding was higher than in a control subject, suggesting that alcohol dependence is associated with activation of microglia.

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AMYGDALA ACTIVATION DURING ALCOHOL INTOXICATION: AN EXAMINATION OF ALCOHOL'S EFFECTS IN SOCIAL DRINKERS

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Background: The amygdala is known to be involved in fear-related processes. Yet, it also contributes to a number of additional affect-related functions, spanning both negative and positive dimensions, including regulation of affective attention, value estimation, and cost/benefit analysis. Hence, studies that examine alcohol's effects on the amygdala have the potential to reveal valuable information about the neural correlates that may underlie negative behavioral outcomes associated with acute intoxication (e.g., risk taking, behavioral disinhibition, aggression). Method:

Participants included 6 social drinkers (mean age=35 years; mean AUDIT=3.5; 5 males). Our double-blind, within-subject design involved oral administration of alcohol (targeted peak breath alcohol concentration [BrAC] level of 0.06 g%) or placebo (0.00 g% BrAC) on one of 2 study days. Beverage order was randomized across subjects. Functional magnetic resonance imaging (FMRI) was used to assess brain response to positive, negative, and neutral images from the International Affective Picture System (IAPS) during the ascending phase of the BrAC curve (0.03–0.05 g%) and during placebo. We extracted mean blood oxygen level dependent (BOLD) responses within the bilateral amygdala to examine the effects of alcohol condition (placebo, alcohol) and image valence (negative, positive) on amygdala function during the IAPS task. Results:

Whole-brain voxel-wise analyses confirmed robust bilateral amygdala response to negative images (vs neutral) during placebo (p<.01, uncorrected). Analyses of mean amygdala BOLD responses revealed a significant alcohol by emotion interaction (p=.03), and trend level main effects of alcohol (p=.08, alcohol>placebo) and emotion (p=.08, negative>positive). Pairwise t-tests indicated greater amygdala response to negative images compared to positive images during placebo (p=.02). In contrast, this pattern was absent under alcohol, where a significant increase in amygdala response to positive images was observed (p=.03).

Conclusions: Moderate alcohol intoxication in social drinkers is associated with increased amygdala reactivity to positive stimuli. This apparent inability of the amygdala to discriminate between stimuli with positive and negative valance under acute alcohol, which may reflect a change in affective attention regulation or determinations of stimuli salience, could contribute to behavioral disinhibition, risk taking, and aggression during alcohol intoxication.

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NALTREXONE INCREASES ETHANOL-INDUCED FEELINGS OF INTOXICATION AND FMRI BOLD RESPONSE TO FACIAL EXPRESSIONS IN THE ANTERIOR CINGULATE AND THE INSULA

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Purpose: Evidence suggests Naltrexone (NTX) acts as a mu-opioid receptor antagonist, and blocks activation of mesolimbic dopamine neurons. Prior fMRI studies from our laboratory have shown that alcohol administration to social drinkers results in an activation of the ventral striatum. There are no studies showing the effects of NTX on ethanol-induced brain activation in treatment seeking alcoholics. Therefore, we examined whether NTX would decrease subjective effects of an ethanol infusion and blunt the fMRI BOLD response from the ventral striatum. We also examined the effects of NTX on emotional processing, as measured by responses to fearful faces on the fMRI BOLD response in various brain regions under saline/ethanol conditions.
Methods: Sixty-three hospitalized alcoholic patients (ages 21 and 50 years) were randomized following detoxification, using a double blind design, to receive either 50 mg of NTX per day or placebo for 9 days. On day nine, patients underwent an fMRI scan during which time they received a 26 minute saline infusion followed by a 36 minute infusion of 6%v/v of ethanol using a physiologically-based pharmacokinetic model designed to maintain an ethanol level at approximately 0.08g%. During the saline and ethanol infusions fMRI BOLD data with emotional facial stimuli and rating scales were collected.
Results: There was a significant increase in craving as a function of time ($F(1,55)=19.79$, $p<0.001$). There was also a significant time x treatment interaction for the rating of ''Feel High'' ($F(4,180)=3.03$, $P=0.02$). Unexpectedly, patients receiving NTX experienced higher, rather than lower, levels of subjective intoxication than subjects receiving placebo. There was no significant difference in the BOLD response in the ventral striatum between saline and ethanol infusions independent of treatment. Patients receiving the NTX showed a greater BOLD activation in response to the neutral compared to fearful faces in the insula.
Conclusion: The lack of ethanol-induced BOLD response in the ventral striatum is in contrast to our previously reported results in social drinkers, but in agreement with our prior findings in heavy social drinkers. This suggests that subjects in the later stages of the addictive process may develop a degree of tolerance to the rewarding properties of ethanol. Greater response to neutral faces under NTX in our alcoholic subjects suggests that endogenous opioid systems are involved in emotional regulation.

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FMRI OF ACUTE ALCOHOL EFFECTS ON RESPONSE INHIBITION IN HEAVY DRINKERS

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Background: Acute intoxication reliably leads to deficits in cognitive control and response inhibition, but little is known about the neural correlates of these effects. This study used fMRI to examine alcohol's effects on neural reactivity during response inhibition. We also evaluated whether these effects differ as a function of working memory (WM) capacity.
Method: Male heavy drinkers (n = 16, mean age = 26 years) completed a baseline assessment of WM capacity, followed by two fMRI sessions involving oral administration of alcohol (target BrAC = .08g%) or juice in a within-subjects, counter-balanced design. Functional imaging data were acquired during a response inhibition task (Go/NoGo). Contrasts of BOLD responses during successful inhibitions (contrast: Correct NoGo > Correct Go) and failed inhibitions (contrast: Incorrect NoGo > Correct Go) were compared across alcohol and juice sessions.
Results: Mean BrAC before and after the alcohol scan was .070g% (SD=.009) and .070g% (SD=.015), respectively. Alcohol increased the number of inhibition failures during the Go/NoGo task (p=.008). Additionally, alcohol led to reduced BOLD response (right middle/inferior frontal gyrus, right inferior parietal lobe, and posterior cingulate cortex) during failed inhibitions and greater BOLD response (left precentral gyrus, left middle frontal gyrus, and occipital cortex) during successful inhibitions (corrected p<.05). Compared to participants with high WM capacity, those with low WM capacity showed greater alcohol-induced reductions in BOLD response during successful inhibitions (supplemental motor area, left MFG, right postcentral gyrus, and left superior temporal gyrus) and during failed inhibitions (medial PFC, posterior cingulate, and bilateral lateral occipital cortex) (p<.05).
Conclusions: Alcohol-induced changes in neural activation during response inhibition are evident and could represent markers of susceptibility to alcohol-induced behavioral disinhibition. Baseline WM capacity may moderate these effects, such that alcohol-induced reductions in neural activation are greater in those with low WM capacity.

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EFFECTS OF ALCOHOL INTOXICATION ON EVENT-RELATED THETA OSCILLATIONS DURING LANGUAGE PROCESSING: ANATOMICALLY-CONSTRAINED MEG

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Language processing is commonly characterized by an event-related increase in theta power (4–7 Hz) in scalp EEG. Oscillatory brain dynamics underlying alcohol's effects on language function are poorly understood despite the evidence of impaired performance on verbal tasks, particularly those relying on semantic retrieval. To investigate how moderate alcohol intoxication modulates event-related theta activity during verbal processing, healthy social drinkers (N=22, 11 females) participated in both alcohol (0.6 g/kg ethanol for men, 0.55 g/kg for women) and placebo conditions in a counterbalanced design. They performed a double-duty lexical decision task. Subjects responded to real words with one hand while ignoring pseudowords (phonologically legal) and nonwords (nonpronounceable strings). Response conflict was induced by requiring subjects to respond with the other hand when the real words were also animals. High density whole head MEG signals were recorded from 306 channels (Elekta Neuromag) and decomposed for each trial with Morlet wavelets. Each person's cortical surface was reconstructed from high-resolution anatomical MRI scans and used to constrain noise-normalized distributed minimum norm inverse solutions for theta frequencies, resulting in ''brain movies''.
While intoxication did not affect response accuracy, it significantly increased reaction time. The overall spatiotemporal pattern is consistent with the left-lateralized fronto-temporal activation observed in language studies applying time domain analysis. The event-related total theta power increase was attenuated under intoxication overall. However, these effects were selective for the two overlapping neurofunctional systems that were engaged by the double-duty task. First, fronto-temporal event-related theta power was modulated by semantic manipulation and was attenuated by alcohol. This is consistent with the sensitivity of theta to lexical-semantic retrieval, indicating that this measure is well suited for investigating the neural basis of language functions. Furthermore, it provides insight into alcohol-induced impairment of verbal memory functions. Second, the prefrontal network comprising anterior cingulate and lateral frontal areas was sensitive to decision making and was also affected by intoxication. This finding is in agreement with previous studies indicating that alcohol's effects are particularly deleterious to executive functions. Supported by AA13402, AA016624, RR031599, MIND.

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CORTICAL DOPAMINE RELEASE DURING A BEHAVIORAL RESPONSE INHIBITION TASK IN SOCIAL DRINKERS

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Background: Alcoholism is marked by impulsive behavior and loss of control over drinking. Impulsivity is regulated, in part, by fronto-striatal circuits, and dysregulation of dopamine (DA) within this circuitry is believed to underlie cognitive processes involved in alcohol use disorders. PET imaging of D2/D3 receptors allows *in vivo* imaging of DA neurotransmission, and is used frequently to investigate the DA system in addictive disorders. To date, no one has directly demonstrated the role of cortical dopamine during tasks related to impulsivity. The goal of the current study was to determine whether a response inhibition task (stop signal) would elicit detectable extrastriatal DA release in social drinkers. We hypothesized that DA release would be detected in regions implicated in different aspects of inhibitory control, including frontal cortex, anterior cingulate cortex, and insula.
Methods: [^{18}F]-Fallypride (FAL) PET scanning was used to assess changes in cortical DA during a stop-signal task relative to a baseline ''go'' task. Six healthy, social-drinking males (23.3 ± 6.1 y.o.) underwent scanning procedures. Subjects drank an average of 1.91 ± 2.5 drinks per week and had AUDIT scores of 3.0 ± 1.7. On separate days, subjects received one FAL PET scan during a ''go'' control task and one FAL scan during the stop-signal task. Task order was counter-balanced. Parametric non-displaceable binding potential (BP_{ND}) images were generated from the dynamic FAL data and analyzed with SPM8.
Results: Preliminary voxel-wise analysis using paired t-tests ($p < 0.05$, uncorrected) revealed decreased receptor availability (indicative of DA release) during the stop-signal task relative to the ''go'' task in several cortical regions, including insula (13.3 ± 3.8% reduction), anterior cingulate cortex (11.7 ± 9.9%), dorsolateral prefrontal cortex (17.6 ± 15%), and posterior parietal cortex (15.3 ± 4.9%).
Conclusion: These data support the feasibility of using FAL PET to study the DA release during a response inhibition task. Future work will use this paradigm to investigate the relationships between DA function, impulsivity, and heavy drinking. Supported by 5P60AA007611-25.

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NEUROCOGNITIVE ACTIVATION MODERATES SIX MONTH ALCOHOL USE OUTCOMES OF A GROUP MET AMONG JUVENILE JUSTICE YOUTH

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Juvenile justice-involved youth are at high risk for alcohol use and related risky behaviors compared to their mainstream peers. Research has supported various neurocognitive mechanisms as being associated with risky behavior and a greater understanding of these neurocognitive factors involved in risky decision making could lend to the development of more effective interventions to reduce risky behavior in this population. The purpose of the current investigation was to determine the extent to which neurocognitive activation during risky decision making influenced the six month outcomes of an intervention to reduce alcohol use and associated risky sexual behavior among juvenile-justice youth. For the current investigation, we focused on activation of the right dorsolateral prefrontal cortex (DLPFC), a region associated with risk decision making and of critical importance for executive control. Adolescents in a juvenile-justice program (14–18; 75.8% male) were randomly assigned to a one-session group motivational enhancement therapy (MET) intervention targeting alcohol use and related risky sexual behavior (n = 79) or an information-based control intervention (n = 86). Prior to the intervention, participants completed the Balloon Analogue Risk Task (BART) during an fMRI scan and completed measures of current alcohol use. Participants again completed measures of current alcohol use six months after the intervention. An intervention X right DLPFC activation interaction was found (β = -.26, p = .06). Participants in the group MET intervention with greater DLPFC activation during the BART reported a greater reduction in alcohol use at six months compared to participants with lower DLPFC activation. In contrast, participants in the control condition with greater DLPFC activation during the BART reported a smaller reduction in alcohol use at six months compared to participants with lower activation. The findings suggest that neurocognitive factors associated with risky decision-making influence the response to psychosocial interventions designed to reduce risk behaviors. Researchers should take into account the role of neurocognitive factors when developing and assessing the effectiveness of risk-reduction interventions.

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NEURAL MARKERS OF RESPONSE INHIBITION IN ALCOHOL DEPENDENCE

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Deficient response inhibition, a dimension of impulsivity, has been implicated in the development and maintenance of alcohol dependence; however, little is known about the neural substrates of impulsivity in alcohol dependence. In addition, increased levels of endogenous opioids may be associated with increased impulsivity, and therefore moderate its role in the development of substance use disorders. This study investigated the relationship between alcohol dependence severity and the neural correlates of response inhibition in an alcohol dependent sample. The moderating effect of the A118G SNP of the OPRM1 gene was also tested. Twenty individuals (6 females; mean age = 29.4) with alcohol dependence were prospectively genotyped and selected from a community sample of non-treatment seeking problem drinkers. The participants were matched on ethnicity and equal numbers of male and female participants with and without the minor allele (Asp40) of the OPRM1 gene selected. Participants were evaluated in a single functional magnetic resonance imaging (fMRI) session while performing a Stop-Signal Task (SST). The blood oxygen level-dependent (BOLD) signal results were then correlated using a whole-brain approach, with the participants' scores on an alcohol dependence severity factor. Alcohol dependence severity was found to be positively correlated with neural activity during unsuccessful response inhibition (cluster-corrected at $Z = 2.3$, $p < 0.05$) in areas including the precuneus and cingulate. These areas have been previously implicated in the stopping process during unsuccessful response inhibition, suggesting individuals at higher levels of alcoholism severity are ineffectively recruiting the expected brain areas required for proper inhibition of a prepotent response. OPRM1 genotype was found to moderate this relationship with more severe homozygote A-allele alcohol dependents found to differentially recruit regions including the posterior insula during failed inhibition as compared to their G-allele carrying counterparts. Moreover, across genotype, greater alcohol dependence severity was associated with a weaker correlation between frontal regions and the putamen during both successful and unsuccessful response inhibition (cluster-corrected at $Z = 2.3$, $p < 0.05$). These findings implicate a plausible fronto-striatal pathway by which alcoholism impairs response inhibition and suggests intervention targets by which the course of the disorder may be mitigated.

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NEURAL CORRELATES OF COGNITIVE CONTROL IN OEF/OIF VETERANS WITH POST TRAUMATIC STRESS DISORDER WITH AND WITHOUT ALCOHOL USE DISORDERS

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Background: Posttraumatic stress disorder (PTSD) and alcohol use disorder (AUD) are frequently comorbid. However, the biological mechanism contributing to the maintenance and development of these co-occurring disorders is incompletely understood. Altered cognitive control has been implicated in the pathophysiology of both AUD and PTSD. Although prior studies have shown that both PTSD and AUD are associated with altered functional brain activation during cognitive control, there have been no studies investigating the neural correlates of cognitive control in individuals comorbid for PTSD and AUD. We hypothesized that PTSD individuals with PTSD and AUD relative to PTSD individuals without AUD would show inefficient utilization of brain systems involved in cognitive control.
Methods: Fourteen Operation Enduring Freedom/Operation Iraqi Freedom (OEF-OIF) male veterans with PTSD and AUD (PTSD+AUD) and 14 PTSD veterans without AUD (PTSD-AUD) matched for age, sex, education, ethnicity and severity of PTSD symptoms completed a validated stop signal task during functional magnetic resonance imaging (fMRI). Task-related brain activation was compared between the groups.
Results: The PTSD+AUD and PTSD-AUD groups showed significant differences in task-related brain activation in a network of structures, which included the prefrontal cortex (clusters >2,048microliters, voxelwise $p<.05$). The groups were not significantly different in behavioral task performance, suggesting that the differences in brain activation were not confounded by behavioral differences between the groups.
Conclusions: These results may suggest a functional brain basis of altered cognitive control in individuals comorbid for PTSD and AUD. These findings may serve as the basis for future longitudinal research aimed at determining whether differences in prefrontal activation during cognitive control represent an underlying vulnerability for the development of comorbid PTSD and AUD or are a consequence of their shared pathophysiology.
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NEURAL RESPONSES TO REAL TIME REWARDS AND PUNISHMENTS IN BINGE DRINKERS

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Previous investigations of alcohol dependence have shown evidence of altered response to cues that predict subsequent delivery of monetary gains and losses. However, few investigations have examined neural responses to cues that predict immediate delivery of real-time, non-monetary outcomes. Given that immediately available rewards and punishments play an important role in biasing behavior, it is critical to more fully understand the mechanisms by which these outcomes influence behavior. To examine the neural processes associated with automatic reactivity to cues predictive of rewarding and punishing outcomes, we examined neural responses during a modification of a monetary incentive delay task in which monetary outcomes were replaced with real-time tastant delivery in drinkers. On each trial, participants were presented with one of 5 arbitrary symbols for 250 msec, a fixation cross for variable 2000–2500 msec time period, followed by a white square that appeared for 160–260 msec, and finally a 2-second reward delivery period. Two of the symbols predicted delivery of the participant's favorite alcohol containing beverage, two predicted delivery of a mildly aversive tastant (saltwater), and one predicted water. Comparison of alcohol and saltwater cues separately to water cues revealed significant differences in nucleus accumbens, bilateral insula, dorsal ACC, suggesting overlapping circuitry for the anticipation of both rewarding and punishing outcomes. In addition, counter to expectations, AUDIT scores were negatively correlated with response in the ventral striatum in the alcohol vs. water comparison, suggesting reduced responsivity to arbitrary cues predicting alcohol in riskier drinkers. AUDIT scores were also negatively correlated with responses in lateral frontal cortex during anticipation of saltwater. The current results suggest that whereas cue reactivity for well-learned alcohol related stimuli typically shows enhanced response in more severe alcohol use disorders, arbitrary cues appear to engage reward circuitry to a less degree in individuals with higher reported hazardous drinking. Future research is needed to understand how environmental cues influence behavior in AD.

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HIGH AND LOW SENSATION-SEEKING ADOLESCENTS SHOW DISTINCT PATTERNS OF BRAIN ACTIIVITY DURING REWARD PROCESSING.

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Previous research has shown that personality characteristics, such as sensation-seeking (SS), are strong predictors of alcohol use during adolescence. However, the neural substrates of SS personality have not been studied during this time period. Since the initiation of heavy alcohol use during adolescence is a risk factor for developing an alcohol use disorder, it is important to understand neurobiological differences in reward sensitivity between youth with high and low SS personalities. To this end, we used functional magnetic resonance imaging (fMRI) to examine differences in brain activity between 27 high and 27 low SS youth, defined by the Impulsive Sensation Seeking scale of the Zuckerman-Kuhlman Personality Questionnaire (Zuckerman et al., 1993). In the scanner, participants played a decision-making task (Ernst et al., 2004), that resulted in trials with monetary Wins or No Wins. We compared age and gender matched high and low SS adolescents (mean age = 13.94 ± 1.05) on brain activity by contrasting Win versus No Win trials. Our findings indicate that high sensation-seekers show greater bilateral insular and inferior/middle frontal gyrus brain response on Win versus No Win compared to low sensation-seekers (cluster/voxelwise corrected for multiple comparisons, $p < 0.05$). Analysis of simple effects showed that while low SS youth show comparable brain activity in these areas during Wins and No Wins, high SS youth show significant differences in brain response to winning (activation) versus not winning (deactivation). Given that the insula is a region implicated in autonomic arousal, greater reactivity to rewards in this region may reflect appetitive activation. An overactive approach system in high SS adolescents may be a risk factor for the higher levels of alcohol use seen in this population. Our study suggests that fMRI can distinguish high and low SS adolescents, based on their brain activity to rewards. This neurobiological information may ultimately be helpful in establishing alcohol use prevention strategies and suggests value in further examination of the neural substrates of personality characteristics related to risky behaviors. Supported by: R01 AA017664 (Nagel), K08 NS052147 (Nagel), P60 AA010760 (Nagel), F31 AA019866 (Herting), and the OHSU Graduate Research Scholarship (Cservenka).

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THE EFFECT OF ALCOHOL DEPENDENCE ON WHITE MATTER ANISOTROPY IN HUMAN BRAIN

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Many brain imaging studies have demonstrated reductions in gray and white matter volumes in alcoholism. Recently investigators have begun to use diffusion tensor imaging (DTI) to examine white matter integrity in alcoholism, although only a few of these studies have used DTI tractography to compare alcoholics and controls. Alcoholics are known to have neurocognitive deficits in decision-making, particularly in decisions related to emotionally-motivated behavior. It is widely believed that these types of deficits are related to frontal-limbic dysfunction. Previous studies have shown abnormalities in cortico-limbic fiber degradation through fiber tracking (Pfefferbaum et al. 2009; Chanraud et al. 2009). This study quantitatively investigates this degradation through whole brain DTI analysis in normal volunteers and alcoholic patients. DTI was used to measure white matter fractional anisotropy (FA), which has been shown to be a marker for white matter integrity. Whole brain, 33** direction, DTI data was acquired using a 3T scanner of 20 healthy and 20 alcoholic subjects. Data processing included motion and eddy-current corrections (Pierpaoli et al. 2010), in addition to extensive visual inspection to remove data with severe artifacts. FA values were compared using Tract-Based Spatial Statistics (TBSS v1.2), a voxelwise analysis of multi-subject diffusion data (Smith et al. 2006). Preliminary results show significant differences in FA between alcoholics and non-alcoholic control subjects. In this whole brain analysis, several tracts, including the anterior corpus callosum, fornix, anterior commissure, and posterior cingulum bundle, showed higher FA in controls than alcoholic subjects. These areas have been implicated in the reward circuit and emotion. In general, our results appear to be similar to those recently summarized by Schulte et al. 2010. These results suggest that there may be microstructural abnormalities in white matter pathways of alcoholic brains that contribute to neurocognitive and executive functioning deficits observed in alcoholics.

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SUBCORTICAL ATROPHY IN ALCOHOL DEPENDENT SUBJECTS

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Previously, work has been done on the teratogenic effect of alcohol on cortical and subcortical brain volumes in alcohol dependent and non-dependent individuals (Mattson et al 1996). Additionally, hippocampal volume has been found to be significantly decreased in adolescent subjects with alcohol use disorders and in adult alcohol dependent subjects, (Agartz et al 1999, Wrase et al 2008). However, to the best of our knowledge, no one has yet analyzed volume differences in individually segmented subcortical structures with a population of alcohol dependent subjects. This study sought to investigate subcortical volume differences in a population of treatment seeking alcohol dependent subjects (n=130) and age and sex matched healthy control subjects (n=69). MPRAGE structural images were collected using GE scanners with a standard head coil. Alcoholic subjects were scanned 21.5±5.3 days from admission date. Subcortical volumes were obtained using FMRIB's Integrated Registration and Segmentation Tool (FIRST) (Patenaude et al 2011). The subcortical volumes were analyzed using a general linear model, which included age, sex, years of education, family history, and intracranial volume as covariates. Alcoholic subjects exhibited volume loss in following subcortical structures: left thalamus (p=0.0096), left putamen (p=0.0198), left pallidum (p=-.0358), left hippocampus (p=0.0088), right thalamus (p=0.0012), right putamen (p=0.0023), right pallidum (p=0.0092), right hippocampus (p=0.0117), right amygdala (p=0.0444), and right accumbens (p<0.001). The subcortical atrophy present in alcohol dependent subjects relative to healthy controls is consistent with the literature that suggests alcoholism causes significant brain atrophy.

Agartz I, Momenan R, Rawlings RR, Kerich MJ, Hommer DW. 1999. Hippocampal volume in patients with alcohol dependence. *Arch Gen Psychiatry* 56: 356–63
Mattson SN, Riley EP, Delis DC, Stern C, Jones KL. 1996. Verbal learning and memory in children with fetal alcohol syndrome. *Alcohol Clin Exp Res* 20: 810–6
Patenaude B, Smith SM, Kennedy DN, Jenkinson M. 2011. A Bayesian model of shape and appearance for subcortical brain segmentation. *Neuroimage* 56: 907–22
Wrase J, Makris N, Braus DF, Mann K, Smolka MN, et al. 2008. Amygdala volume associated with alcohol abuse relapse and craving. *Am J Psychiatry* 165: 1179–84

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DIFFUSION TENSOR IMAGING OF WHITE MATTER INTEGRITY IN NON-DEPENDENT ADULT ALCOHOL DRINKERS

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Background: Brain imaging has provided abundant information on structural changes related to chronic alcohol use. Specifically, diffusion tensor imaging (DTI) suggests that chronic alcohol use is associated with white matter changes involving multiple cortico-cortical and cortico-subcortical pathways. However, imaging studies of non-dependent alcohol drinkers are fewer and present less consistent results. In this study, we examined white matter integrity of non-dependent adult alcohol drinkers.
Methods: Seventy six adults participated in this DTI study. Heavy drinking was defined as greater than an average of 16/10 (men/women) drinking days per month in the prior year. We also considered age in data analyses, with 48 ''young'' (age <= 35 years, 22 heavy drinkers) and 28 ''old'' (age > 35 years, 6 heavy drinkers). Heavy and nonheavy drinkers were compared for the whole brain for each of the DTI parametric images: fractional anisotropy (FA), longitudinal eigenvalue (λ_1), perpendicular eigenvalue (λ_T), and mean diffusivity (MD).
Results: Significant λ_1 and MD differences were observed in the corona radiata and corticospinal tracks for heavy versus nonheavy young (but not old) drinkers at a corrected threshold. Simple regressions in the young group showed significant correlations with total number of drinks per month ($r = 0.40$, $p = 0.005$ for λ_1 and $r = 0.46$, $p = 0.001$ for MD) and frequency of drinking per month ($r = 0.35$, $p = 0.01$ for λ_1 and $r = 0.51$, $p = 0.0002$ for MD), in the prior year. Analysis of variance applied to the regions of interest showed significant main effects of heavy versus nonheavy drinking ($p = 0.013$) and age ($p = 0.009$) as well as interaction effect ($p = 0.01$) for λ_1. In addition, a significant interaction effect was observed for MD ($p = 0.0002$).
Conclusions: These findings suggest that non-dependent drinking is associated with significant changes in white matter integrity. This effect is particularly strong in young adults.

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GRAY MATTER VOLUME CORRELATES OF GLOBALLY POSITIVE ALCOHOL EXPECTANCY IN NON-DEPENDENT ADULT DRINKERS

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Alcohol use and misuse is known to involve structural brain changes. Numerous imaging studies have examined changes in gray matter (GM) volumes in dependent alcohol drinkers, but there is little information on whether non-dependent drinking is associated with structural changes and whether these changes are related to psychological factors – such as alcohol expectancy – that influence drinking behavior. Here, we used voxel based morphometry (VBM) to examine whether the global positive scale of alcohol expectancy, as measured by the Alcohol Expectancy Questionnaire is associated with specific structural markers and whether such markers are associated with drinking behavior in 113 adult non-dependent drinkers (66 women). The results showed that alcohol expectancy is positively correlated with GM volume of left precentrral gyrus (PCG) in men and women combined and bilateral anterior prefrontal cortices (APFC) in women alone, and negatively correlated with GM volume of the right ventral putamen in men. Furthermore, mediation analyses showed that the GM volume of PCG mediate the correlation of alcohol expectancy and the average number of drinks consumed per drinking episode in the past year, in the combined sample. When recent drinking was directly accounted for in multiple regressions, GM of bilateral dorsolateral prefrontal cortices (DLPFC) correlated positively with alcohol expectancy in the combined sample. Together, these findings support increased GM volume in the frontal cortices as a neural substrate of alcohol expectancy. To our knowledge, these results are the first to identify the structural brain correlate of alcohol expectancy and its mediation of drinking behaviors.

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OBSERVED POWER AND PROJECTED SAMPLE SIZES TO DETECT WHITE MATTER ATROPHY IN NEUROIMAGING OF ALCOHOL USE DISORDERS

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Damage to the brain's white matter is a hallmark injury of alcohol use disorders (AUD), with atrophy demonstrated in both postmortem and neuroimaging studies. A recent meta-analysis (Monnig et al., under review) investigated the magnitude of white matter volume difference between AUD and control groups in published magnetic resonance imaging (MRI) studies ($N = 19$). The result was a significant, small-to-medium-sized effect of .304 (Hedges' g) for white matter volume loss in AUD. The present study used this effect size to calculate observed power in extant studies and to project sample size necessary to detect group differences in future studies. Post hoc and *a priori* analyses were performed in G*Power 3.1.3 (Faul, Erdfelder, Buchner, & Lang, 2009) for t-tests of independent group means with $\alpha = .05$. Using the obtained effect size of .304 and average number of participants per group (34 healthy control, 35 AUD), observed power for the population of extant studies was low, at $1\text{-}\beta = .238$ for a two-tailed test and $1\text{-}\beta = .346$ for a one-tailed test. *A priori* calculations to estimate sample sizes with equal numbers per group at higher and lower levels of power varied dramatically. Specifying higher power ($1\text{-}\beta = .8$) and a two-tailed test resulted in a total sample size of 342. With lower power ($1\text{-}\beta = .5$) and a one-tailed test, the requisite sample size was 120. Because the effect size for treatment-seeking AUD samples in the meta-analysis was significantly higher than for non-treatment-seeking samples, power calculations were repeated using the effect size of $g = .433$ obtained for treatment-seeking samples. In this subpopulation, sample size of 170 would be needed for $1\text{-}\beta = .8$ using a two-tailed test, whereas a sample size of 60 would be needed for $1\text{-}\beta = .5$ using a one-tailed test. In sum, observed power in the population of MRI studies of white matter atrophy in AUD was low, at .238. At standard parameters, projected sample sizes to detect group differences in future studies were quite high, representing a considerable demand on resources. However, investigators seeking to detect AUD-related white matter atrophy could reduce requisite sample sizes by specifying lower power (e.g., $1\text{-}\beta = .5$), performing one-tailed tests, or recruiting AUD participants from the treatment-seeking subpopulation.

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DRINKING HISTORY PREDICTS WHITE MATTER INTEGRITY IN A LARGE COMMUNITY SAMPLE OF HEAVY DRINKERS

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Neuroimaging has linked alcohol use disorders (AUD) with structural brain damage, particularly to the white matter that enables communication among neurons (Kril and Halliday, 1999; Oscar-Berman and Marinković, 2007). Diffusion tensor imaging (DTI; Basser & Pierpaoli, 1996) quantifies the integrity of white matter on a microstructural level using principles of water diffusion, with higher fractional anisotropy (FA) reflecting greater directional coherence of diffusion. The objective of this study was to apply independent component analysis (ICA; Calhoun & Adali, 2006) to parcellate DTI data from 261 heavy drinkers recruited from the community (mean age = 31.0 ± 9.2; 187 male, 73 female). Seven ICA components were replicated in a split-half analysis. ICA components were located bilaterally in frontal and parietal lobes, brainstem, thalamus, and striatum. FA of white matter within most regions identified by the ICA procedure was significantly, negatively correlated with number of years drinking, total scores on the Alcohol Dependence Scale (ADS) and Alcohol Use Disorders Identification Test (AUDIT), the Failed Control subscale of the Impaired Control Scale (ICS-FC), and number of drinks per drinking day. However, FA of a subcortical component located in thalamus and putamen showed significant, positive correlations with number of years drinking and ICS-FC. These results suggest that chronic alcohol abuse decreases white matter integrity in both cerebral and subcortical white matter. In addition, cumulative experience with alcohol may increase fiber coherence in reward substrates implicated in addictions research (Koob & Volkow, 2010). Alcohol-related white matter damage in networks associated with reward and self-regulation may contribute to cognitive dysfunction, impulsivity, and loss of control over drinking.

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FUNCTIONAL CONNECTIVITY STRENGTH IN VISUOSPATIAL ATTENTION NETWORKS IN ALCOHOLISM

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Neuroadaptive changes occur in the brain's response to chronic alcoholism. The brain networks involved in these changes may differentially affect component processes of visuospatial attention. To study functional brain networks, 11 chronic alcoholics (ALC) and 13 age-matched healthy controls (CTL) underwent functional magnetic resonance imaging (fMRI) while performing a visual search task. The task assessed automatic preattentive mechanisms during single-feature pop-out search (target=red tomato; distractors=yellow tomatoes) and serial, selective attention mechanisms during color-form conjunction search (target=red tomato; distractors=yellow tomatoes and red or yellow strawberries). Feature and conjunction search conditions contained a visual load component of either 4 or 8 stimuli in a search array. As expected, visual load effects were greater in conjunction than single feature search ($p<0.002$), verifying that serial, selective attention processes are invoked in conjunction search in contrast to feature search. Behaviorally, groups performed at comparable levels in all visual search conditions. Functional connectivity analysis revealed synchronized activity among the same brain regions in ALC and CTL. Although ALC exhibited lower overall connectivity strength in both feature and conjunction search conditions, group differences in network communities of connectivity emerged only for conjunction search. Here, CTL showed both synchronized (positively correlated) activity among occipito-parietal, occipito-cerebellar, and fronto-parietal sites and anti-correlated (negatively correlated) activity among lingual gyrus, caudate nucleus, and fronto-temporal regions and between parietal (inferior parietal lobe, supramarginal gyrus) and occipital regions (calcarine, superior occipital gyri). Because this anti-correlated activity was not seen in ALC, group comparisons showed enhanced positively correlated connectivity in ALC relative to controls between lingual and fronto-temporal regions and between parietal and occipital regions. Considering comparable visual search performance in ALC and CTL, enhanced occipito-parietal and occipito-frontal cortical network synchrony in ALC relative to controls during serial conjunction search requiring selective attention may have served as a compensatory neural mechanism enabling normal performance. Support: AA018022, AA010723, AA012388, AA017168

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DIFFERENTIAL ACTIVATION OF IRRELEVANT INFORMATION IN SUBSTANCE ABUSERS AND COMMUNITY CONTROLS

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Introduction: This project proposes that an inappropriate response to irrelevance (regardless of information complexity) constitutes a fundamental substance abuse-related neurocognitive deficit. We previously demonstrated such a deficit using neuropsychological measures, tests of problem-solving, and event-related potentials. The current study extends that work, applying fMRI to examine differences in brain activation between detoxified substance abusers (SA) and community controls (CC) in an implicit memory task. In our previous work the task (DeSchepper & Treisman, 1996) shows increased P300 amplitude and latency in negatively-primed trials in CC vs. SA (Ceballos, Nixon & Tivis, 2003).
Methods: 14 SA (26–51 years old; 7 women) and 23 CC (25–49, 13 women) were recruited. Brain images were acquired using Siemens 3T MR scanner at University of Kentucky MRISC. All fMRI data were motion corrected, smoothed, and transformed into common MNI space and subjected to a standard FSL-GLM analysis (P<.05 uncorrected), comparing the activation maps for primed and negatively primed trials for each group. The task, presented using E-Prime, displayed a series of novel shapes using two shape sets, a Prime and a Probe, with equal numbers of primed and non-primed trials. Each shape set included two overlapping green and red shapes paired with a single white shape. Subjects were instructed to ignore the red shape, but to determine whether the green shape was the same as the white shape. On primed trials, previously red shapes became green shapes (probes).
Results: Preliminary analyses of a small subset of the subjects indicated differential brain activation for SA vs. CC while performing the task. These analyses indicate that substance abusers uniquely activated left frontal areas (BA 45 & BA 47) during the negatively primed trails; control subjects, however, engaged both the left and right frontal areas, as well as activating the anterior cingulate cortex (BA 32).
Discussion: These findings suggest that CC engage verbal and spatial working memory regions with the anterior cingulate during processing of primed trials, which are key areas related to executive function. In contrast, the SA may be attempting (using BA 45 & 47) to resolve primed trials solely via a verbally mediated strategy, resulting in compromised spatially oriented executive function. Though this work is preliminary, it extends our working model and may inform treatment development and early intervention.

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COMBINED EFFECTS OF ALCOHOLISM AND HIV-INFECTION ON SELECTIVE COGNITIVE AND MOTOR FUNCTIONS AND THEIR NEURAL SUBSTRATES

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HIV/AIDS infection continues to reach pandemic levels worldwide. Of even higher prevalence are alcohol use disorders, which themselves present a liability for risky behavior associated with contracting HIV infection. With the advent of improved anti-retroviral treatments, HIV-infected individuals are living longer and thus vulnerable to compounded insult from normal aging, the potential return to or initiation of alcohol misuse, and enhanced liability for functional impairment. We used a 4-group design to examine the effects of alcoholism alone (ALC), HIV infection alone (HIV), and their comorbidity (HIV+ALC) on neuropsychological functioning relative to unaffected controls. Cognitive and motor testing revealed a predominant alcohol effect on conflict processing, attentional allocation (Stroop Match to Sample Test), visual immediate memory (Block Span), reaction time, and gait and balance and a compounded effect in HIV+ALC on attentional allocation, visuospatial construction, visuospatial immediate memory, sequencing information in remote semantic memory for public figures, and finger dexterity (fine finger movement, Digit Symbol Substitution Test). Select motor deficits were related to age and lifetime alcohol consumption in the alcoholic groups, but deficits in the HIV groups were not generally associated with CD4 cell count or medication status. Investigation of neural substrates of these functional deficits in HIV+ALC revealed a number of associations. Digit Symbol performance correlated with a constellation of MRI-derived brain regional volumes representing visual memory circuitry nodes (occipital cortex, hippocampus/amygdala, and third ventricle) and nodes of attentional control (frontal sulci, insula, and precuneus), areas likely to participate in digit-symbol transcription and continuous performance. These results indicate the compounded burden of alcoholism in contributing to the neurofunctional consequences of HIV infection.
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TOBACCO AND ALCOHOL EFFECTS ON HIV-ASSOCIATED BRAIN DYSFUNCTION

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Co-morbid substance abuse is associated with reduced functional outcome in people with HIV. Alcohol exacerbates HIV-associated dysfunction, including previous findings of reduced white matter integrity on DTI among people with both HIV and alcohol abuse. Alcohol effects on liver have been postulated as the basis for these effects. Chronic tobacco use has also been linked to brain dysfunction. To date few studies have examined combined effects of alcohol and tobacco on HIV. The influence of these factors on neurocognition and structural brain indices, including diffusion tensor imaging (DTI) white matter integrity were examined in HIV-infected and seronegative controls. 145 adults (HIV+: n = 90; HIV-: n = 55) underwent comprehensive clinical, neurocognitive and neuroimaging assessments. Test battery consisted of measures sensitive to impairments in 8 cognitive domains with age/education adjusted standardized scores. A Global Deficit Score (GDS) was also derived. Cortical gray and white matter volumes for 36 R0Is were measured from T1 MRI using Freesurfer, and DTI was obtained in 64 directions. HIV-infected patients exhibited weaker performance across multiple cognitive domains compared to controls, with a reduced GDS ($p = .003$). HIV was found to be a predictor of performance on Processing Speed, Attention, Executive, Learning and Memory ($p_s < .01$). Tobacco use was associated with reduced overall cognitive performance ($p = .03$), as well as Learning and Memory. Significant interaction of tobacco by HIV was evident, with weakest performance among smokers with HIV. Significant tobacco by alcohol interaction also existed for Attention and Executive domains, with combined alcohol/tobacco use associated with weaker performance. Volumetric MRI analyses revealed reduced cortical gray matter among the HIV group. Regression revealed that current alcohol dependence and smoking were associated with reduced cortical gray matter volume as well ($p <.05$). Current alcohol use was associated with total subcortical gray matter, total cerebral white matter, hippocampal, and thalamic volumes ($P_s<.05$). Findings indicate that together with HIV status, both alcohol and tobacco are associated with reduced neurocognitive functioning as well as reduced brain volumes of the cortical gray matter, white matter, the hippocampus and thalamus. It appears that alcohol and tobacco use may exacerbate cognitive impairments associated with HIV and that the effects may be synergistic.

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ACUTE ALCOHOL INTOXICATION DOES NOT AGGRAVATE EARLY NEUROBEHAVIORAL AND NEUROINFLAMMATORY SEQUELAE POST TRAUMATIC BRAIN INJURY

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An estimated 1.7 million people sustain a traumatic brain injury (TBI) annually, which constitutes a third (30.5%) of all injury-related deaths in the United States. Evidence suggests that acute alcohol intoxication (AAI) is associated with increased risk of injury and is reported to be a contributing factor in 36% to 51% of TBI incidents. Studies suggest that the risk of injury is positively correlated with blood alcohol concentrations (BAC). However, conflicting reports from animal and clinical studies have failed to establish whether AAI significantly impacts outcomes from TBI. The aim of the study was to determine whether AAI aggravates neurobehavioral and neuropathological sequelae from TBI. Male Sprague-Dawley rats (~300 g BW) were surgically instrumented with gastric and vascular catheters prior to fitting of a female Luer-lock over a 4 mm lateral (0.3 mm posterior to bregma & 1.3 mm lateral from midline) craniotomy on the left hemisphere. After a 3 day recovery, animals received a primed (2.5 g/kg) 15 h constant (300 mg/kg/h) intragastric alcohol infusion achieving blood alcohol levels of 266±10 mg/dl. Time-matched controls received an isocaloric/isovolumic dextrose infusion. TBI was induced by lateral fluid percussion (~2.3 atm, ~30 ms) over the lateral hemisphere 30 minutes following discontinuation of the alcohol/dextrose infusion. Post TBI apnea duration (4 sec), righting reflex (7±1 min), and 24 h neurobehavioral scores (Δ 3) were not significantly different between AAI and dextrose groups. Myeloperoxidase (MPO) activity reflecting neutrophil infiltration and localized inflammation was increased in the ipsilateral (10-fold; $p<0.05$) and contra-lateral cortex (2-fold; $p< 0.05$) but not in the prefrontal cortex following TBI in both dextrose and AAI animals. These findings suggest that AAI does not aggravate neurobehavioral or neuroinflammatory sequelae from TBI. Future directions include additional measurements of inflammation and oxidative stress and more sensitive neurobehavioral assessments to determine the impact of AAI on outcomes from TBI. DOD-W81XWH-11-2-0011, NIAAA-AA7577.

5. FETAL ALCOHOL SYNDROME/DEVELOPMENT

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PRECURSORS OF AFFECTIVE DISTURBANCE IN CHILDREN WITH FETAL ALCOHOL EXPOSURE

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Prenatal alcohol exposure is associated with an increased incidence of psychopathology in children and adults. The aim of this study was to determine whether early indicators of affect disturbance are seen in infants exposed prenatally to alcohol. We hypothesized that (1) prenatal alcohol exposure is related to greater infant withdrawal and to alterations in infant temperament; (2) the effects of prenatal alcohol exposure on withdrawal and temperament are independent of each other and independent of maternal depression and postnatal maternal alcohol use, and (3) the effects of prenatal alcohol exposure on cognitive function at 5 years will be mediated, in part, by affective disturbance in infancy as assessed by withdrawal and temperament. The Cape Town Longitudinal Cohort consists of 159 mothers and infants from the Cape Coloured (mixed race) community in Cape Town, South Africa, a large proportion of whom were exposed to alcohol during gestation. Mothers were interviewed about their alcohol consumption using a timeline follow-back approach to determine frequency and amount of drinking on a day-by-day basis. The Alarm Distress Baby Scale (ADBB) of Guerdeney and Fermanian (2001), which assesses sustained affective withdrawal behaviour, was administered at 6.5 months postpartum, and the mothers were interviewed on the Buss and Plomin (1984) EAS Temperament scale at 13 months. At the 5-year follow-up, the Junior South African Intelligence Scales (IQ) assessment was administered, and the EAS interview was repeated. ADBB withdrawal was associated with reduced activity on the EAS (r = -.29, p < .01) but was not related to emotionality, shyness, or sociability. Prenatal alcohol exposure was associated with greater ADBB affective withdrawal (r = .30, p < .01) and lower EAS activity (r = -.23, p < .01). These effects were independent of each other, and both remained significant after controlling for postnatal maternal alcohol use and depression. Mediation of the effect of prenatal alcohol exposure on 5-year IQ by the ADBB fell just short of statistical significance (Sobel z = -1.34, p = .085), suggesting that affective withdrawal that is already evident in infancy contributes to poorer cognitive function at school entry. Grants from NIAAA: two supplements to RO1AA09524; U01AA014790 and U24AA014815 in conjunction with CIFASD. Also, NIH Office of Research on Minority Health; FARR; and Joseph Young, Sr., Fund from the State of Michigan.

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EXECUTIVE FUNCTIONING OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) WITH AND WITHOUT FETAL ALCOHOL SPECTRUM DISORDERS (FASD)

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Purpose of the study: The aim of the present study was to examine whether executive function can be the appropriate area to further explore the potential indicators of children with dual diagnosis of fetal alcohol spectrum disorder (FASD) and attention-deficit/hyperactivity disorder (ADHD) (i.e., dual diagnosis group) and children with single ADHD diagnosis (i.e., single diagnosis group). As such, the purpose of this study was to examine the differences between these two groups in terms of executive function that can be recognized in classrooms.
Methods: The study was conducted through a review of existing medical records. The assessment data of 149 individuals with single ADHD diagnosis and 189 individuals with dual FASD and ADHD diagnosis were gathered from raw data at a pediatric clinic in Midwest US. Inclusion criteria were individuals aged 8 to 14 years with possible comorbid disorder of disruptive behavior disorders, learning disorders, and depressive disorders. Information on the presence and level of prenatal exposure to alcohol and chemicals, age, gender, ethnicity, IQ scores, socioeconomic status, comorbid disorders, and the number of foster or adoptive placements was collected in addition to the scores on the Behavior Rating Inventory of Executive Function (BRIEF: Gioia, Isquith, Guys, & Kenworthy, 2000).
Results: Preliminary analysis revealed that children in both single and dual diagnosis groups in the present study exhibited significant problems in two areas of executive function, behavioral regulation and metacognition, that were in the clinical range. However, for behavioral regulation, the results indicated that there were statistically significant differences between the two groups due to the presence of FASD (i.e., single or dual diagnosis) on the basis of parent ratings. This finding agreed with previous findings indicating that children with dual diagnosis exhibited more significant externalizing behavior problems than those with single diagnosis by teacher and parent ratings (Someki et al., in preparation). In contrast, for metacognition, there was no significant difference between the two groups.
Conclusion: Demographical differences between children with dual FASD and ADHD diagnosis and children with single ADHD diagnosis, details of differences between the two groups regarding executive function, and the implications for the future research will be discussed at the presentation.

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PRENATAL ALCOHOL EXPOSURE AND ADOLESCENT ADVERSITY: LONG-LASTING EFFECTS ON COGNITION AND DRUG RESPONSE

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In humans, prenatal alcohol exposure (PAE) produces a range of behavioural and cognitive disorders including mental retardation that ranges from mild to severe. Indeed, cognitive impairments are one of the most pervasive and persistent consequences associated with all levels of PAE. In addition, individuals often show an increased predisposition for the development of secondary disorders, including addiction. Of interest, deficits in the prefrontal cortex (PFC), a brain region associated with executive functions such as attention, working memory, and inhibitory control, has been implicated in each of these disorders. This suggests that the PFC is especially vulnerable to the teratogenic effects of PAE. Importantly, the PFC continues to develop through puberty. Thus, as postnatal development is largely influenced by experience, the PFC remains vulnerable to adverse environmental factors into adulthood.
To investigate possible differential effects of early stress in PAE individuals, we used male offspring from dams assigned to: 1) Alcohol (PAE), *ad libitum* liquid alcohol diet; 2) Pair-fed (PF), isocaloric-control liquid diet; or 3) Control, *ad libitum* pelleted control diet. In adolescence, half of each group underwent a 5 day period of chronic mild stress (CMS) or were left undisturbed. As adults, rats were first tested in the T-Maze task, followed by the more taxing 5-choice serial reaction time task. Once performances were stable, rats were reassessed under three doses (0.3, 0.6 & 1.0mg/kg) of amphetamine (AMPH) or saline. Rats were then assessed drug-free for 4 days before being sacrificed.
The results indicate a learning-related deficit in PAE-CMS rats that was evident only in more challenging test trials. In addition, the AMPH challenges produced a differential effect on performance; at lower doses decreasing premature responding in Control-CMS rats while producing deficits at higher doses in both CMS and Non-CMS groups. In contrast, PAE-CMS rats showed a marked decrease in premature responding at high AMPH doses. Of interest, the changes in premature responding correlated with accuracy of performance in the Control but not PAE rats, with the latter showing no changes in performance over the test days. These results indicate PAE-related behavioural alterations in response to adolescent experience, which may impact subsequent adult experiences such as drug use.
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EFFECTS OF THREE-DAY BINGE ETHANOL VAPOR EXPOSURE IN NEONATAL NSA MICE ON LOCOMOTOR ACTIVITY

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In humans, a brain growth spurt happens during the third trimester of pregnancy. The third trimester equivalent in rodents is approximately during the first two weeks of postnatal development. Binge exposure to ethanol in rodents during this brain growth spurt period results in reduced brain mass, degeneration of cortical and subcortical structures, and behavioral changes [Goodlett et al., 1987; Wozniak et al., 2004]. Wagner and Goodlett [2008] reported subcutaneous (SC) ethanol injections during postnatal days 7-9 in C57BL/6 mice produced spatial learning deficits when assessed at 30 and 70 days of age. To extend these findings to another behavior using a different exposure method, the present experiment examined postnatal binge ethanol vapor exposure on dam weight and litter growth, and pup locomotor activity. Eighteen NSA dams and litters were placed in inhalation chambers (La Jolla Alcohol Research, Inc.) and either exposed to ethanol vapor (n=11) or air (n=7), which served as the control group. Exposure took place on postnatal days 7-9 for 9 hours. Dam blood ethanol content (BAC) averaged less than 100 mg/dl, while pup BACs averaged 373 mg/dl across days 7 to 9. Ethanol-exposed dam and litter weights showed similar increases to their respective control groups across days 7 to 9. Locomotor activity was measured by placing individual mice within an AccuScan activity monitor and recording total distance traversed. Activity was recorded in three 5-min blocks on four consecutive days beginning at 35 and at 150 days of age. Pup activity did not differ between treatment groups at 35 days of age, but was significantly higher in ethanol compared to air control groups at 150 days of age (p<.01). This study shows ethanol vapor inhalation can be used for postnatal mouse litter and dam exposure, and results in significant changes in behavior without affecting growth. Ethanol inhalation is less stressful than SC, intraperitoneal or intragastric methods and should provide uniform exposure across multiple genotypes. Supported by: UNCs Office of Sponsored Programs; a Provost Fund award; the Faculty Research and Publication Board; and a Summer Graduate Research Assistant Award.

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BEHAVIOR IN A COMPLEX ENVIRONMENT FOLLOWING VOLUNTARY EXERCISE IN RATS EXPOSED TO ALCOHOL NEONATALLY

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Developmental alcohol exposure is accompanied by permanent structural changes in various brain regions, including the hippocampus and frontal cortex, and produces functional impairments in many aspects of behavior, including learning and memory. The hippocampal dentate gyrus is one of two brain regions where adult neurogenesis occurs. Neonatal alcohol exposure has long-term detrimental effects on the maturation and survival of progenitor cells. Further, neonatal alcohol exposure produces long-term deficits in hippocampus-dependent learning and memory. Exposure to a complex environment (EC) enhances both hippocampal adult neurogenesis and performance on hippocampus-dependent tasks. The present study investigates how animals behave when placed in EC, following a 12-day exposure to voluntary exercise, and determines whether alcohol-exposed animals respond differently to the various components (interaction with the toys and with other rats, movement and exploration of the cage). During PD4-9, pups were intubated with alcohol in a binge-like manner (2 feedings, 2 hours apart, 5.25g/kg/day), sham-intubated, or reared normally. Adolescent rats received 24 hours access to running wheels on PD30-42 followed by exposure to EC (WR/EC; 9/cage) for an additional 30 days (PD42-72). Each animal was marked with a distinct non-toxic paint color in order to record individual rat behavior. Sessions were videotaped during the first two hours following the onset of the light cycle on PD42, PD48, PD56, PD62 and PD68. Behavior was coded for total movement, exploration of the environment, social contact and interaction with enrichment items. Data from PD42 indicate all rats are moving significantly less in the second hour compared to the first hour. However, they are interacting with their environment the same manner throughout the session as exploration of the toys and social behaviors remain unchanged. Furthermore, in the second hour, AE animals explore the different quadrants of the cage significantly less than control animals; however, their level of movement during the second hour (measured as whether the rats are in motion at specific time points during 30 minutes) remains similar to that of controls. These data together with other findings in our lab suggest that although alcohol-exposed rats still benefit from life in the EC, this benefit may be limited and may produce more subtle changes in behavior and brain morphology than in normal animals. Supported by NIAAA 09838.

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DIFFERENTIAL EFFECTS OF SOCIAL INTERACTIONS ON COGNITIVE PERFORMANCE IN ADULT RATS FOLLOWING PRENATAL ALCOHOL EXPOSURE

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Prenatal alcohol exposure (PAE) is characterized by a range of deficits across the lifespan, including cognitive and behavioral abnormalities, such as impaired executive function and social behavior that may be exacerbated by postnatal stress. Our previous data suggest that social status in early life may impact cognitive performance in adulthood, with submissive PAE animals showing more errors on the radial arm maze (RAM) than controls. Moreover, post-stress basal corticosterone (CORT) levels were shown to be positively correlated with mean total errors in a T-Maze task in PAE but not control or pair-fed, males and females.

Although intact executive function may be a requirement for normal social behavior, the interplay between higher cognitive function and social behavior is complex, and more research investigating this relationship is needed. To investigate further the effects of social interaction on cognitive function, we evaluated the effects of adolescent stressful experience and adult social interactions in modulating cognitive function in PAE and control animals. Pregnant rat dams were assigned to: 1) PAE – liquid ethanol diet *ad libitum*; 2) Pair-fed (PF) – liquid control diet paired to PAE consumption; or 3) Control – lab chow *ad libitum.* To emulate postnatal exposure to stress, we utilized a chronic mild stress (CMS) paradigm. In adulthood, rats were assessed on the Win-Shift task using an 8-arm RAM to evaluate executive function. Animals were first evaluated using a 20 min delay between training and testing. The next day, animals repeated the task with the introduction of an unfamiliar rat (social distractor) into the holding cage during the 20 min delay.

Preliminary analysis indicates that errors were increased in PAE and PF females on the Win-Shift task. Moreover, the introduction of a social distracter during the 20 min delay increased the number of errors in animals from all groups. In males, however, no differences there were no effects of either prenatal group or presence of a social distractor on number of errors in the RAM.

These data suggest sexually dimorphic effects of prenatal group and social test condition on executive function. Further analysis is needed to determine the role of changes in key brain areas, such as the prefrontal cortex and amygdala, in mediating the outcome observed. Supported by NIH/NIAAA R37 AA007789 and NeuroDevNet to JW.

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ROLE OF HPA HYPERREACTIVITY IN MEDIATING DEPRESSIVE-/ANXIETY-LIKE BEHAVIORS FOLLOWING PRENATAL ALCOHOL EXPOSURE AND CHRONIC MILD STRESS

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Prenatal alcohol exposure (PAE) may produce a range of physical, cognitive, neurological, and behavioral deficits. Those affected may also develop secondary disabilities later in life, which include a high incidence of depression and anxiety disorders. One potential mechanism that may mediate the connection between PAE and depressive/anxiety disorders is fetal programming of the hypothalamic-pituitary-adrenal (HPA), or stress, axis, by PAE. Previous work has shown that PAE reprograms the fetal HPA axis, resulting in increased HPA tone and hyper-reactivity (e.g. elevated corticosterone [CORT] and/or adrenocorticotropin [ACTH] levels) to subsequent stressors throughout life. Moreover, work from our lab found that exposure to chronic mild stress (CMS) produces, in a sexually dimorphic manner, greater depressive- and anxiety-like behaviors in PAE than control rats. We hypothesized that the increased propensity to depressive/anxiety disorders in individuals prenatally exposed to alcohol may be related to the fact that stressors experienced over the life course act on a sensitized or hyperresponsive HPA axis. As such, it is proposed that normalizing HPA activity would attenuate some of the adverse effects of chronic stress on behavior and emotionality in PAE rats. Using our rat model of PAE, adult male and female offspring from prenatal alcohol (36% ethanol-derived calories), pairfed (nutritional control), and ad libitum-fed control groups underwent sham surgery or adrenalectomy (ADX) with replacement of CORT at low basal levels (25 ug/ml in males; 75 ug/ml in females) in drinking water (0.2% ethanol; 0.9% saline) at postnatal 55-65 days of age. Following recovery, animals were either exposed to CMS or left undisturbed (non-CMS). Animals were weighed on days 1 and 5 of CMS, and 1 day post-CMS, as a non-invasive measure of stress responsivity. Depressive- and anxiety-like behaviors were then assessed on the open field, elevated plus maze, and Porsolt forced swim tests. Plasma CORT levels prior to ADX, pre- and post-CMS exposure, and 30-min post-FST were measured. Preliminary findings indicate a sexually dimorphic effect of prenatal treatment and/or CMS on weight gain and a modulation of PAE- and/or stress-induced anxiety-like behavior following normalization of CORT levels. These findings suggest a role for HPA activity in mediating the effects of PAE and CMS on behavior.

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EFFECTS OF PRENATAL ALCOHOL EXPOSURE AND ADOLESCENT CHRONIC MILD STRESS ON ANXIETY- AND DEPRESSIVE-LIKE BEHAVIORS IN ADOLESCENT RATS

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Prenatal alcohol exposure (PAE) can induce a variety of cognitive, physiological, morphological, and neurobehavioral deficits, including dysregulation of the stress system. Besides these primary effects, PAE also increases vulnerability to the development of secondary disabilities such as anxiety and depression. Clinical and animal literature has shown that pre-existing dysregulation of the stress system may be a major factor underlying the development of depression and anxiety disorders, particularly if the individual is exposed to stressors later in life. As the onset of many psychopathologies often occurs around adolescence, here we explore the links between dysregulation of the stress system and increased vulnerability to anxiety-/depressive-like behaviors using a chronic mild stress (CMS) paradigm during adolescence in rats following PAE. Pregnant rats were assigned to either Alcohol (PAE) – liquid alcohol diet, *ad libitum*; Pair-fed – liquid control diet paired to PAE consumption; or Control – lab chow, *ad libitum.* Offspring were exposed to 10 days of CMS starting at postnatal day 31 (females) or 37 (males). On the last day of CMS, basal blood samples were collected (tail nick) to measure corticosterone (CORT) levels. After CMS, rats were tested first in the open-field (anxiety) and then in the forced swim test (depression). Thirty minutes after FST, rats were decapitated and blood was collected to measure CORT. Our results show that CMS increased basal CORT levels and decreased CORT response to stress (FST) in males and females from all prenatal groups. In the open field, we found that males exposed to CMS showed an increase in distance traveled in both center and periphery and overall movement, irrespective of prenatal group. In females, however, PAE modified open field behavior; specifically, both non-CMS and CMS PAE females spent more time in center and showed an increase in distance traveled. Finally, in the FST, both PAE and pair-fed males spent more time immobile as compared to control animals, suggesting some effects of restricted feeding in addition to the effects of PAE. CMS reduced time spent immobile and increased the latency to immobility in all male groups. No significant effects of either prenatal group or CMS were observed in females during FST. Our results indicate that PAE and CMS influence anxiety- and depressive-like behaviors in a sexually dimorphic manner.

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BETA-ENDORPHIN NEURON TRANSPLANTATION IN THE HYPOTHALAMUS ATTENUATES CORTICOSTERONE RESPONSE AND ANXIETY-LIKE BEHAVIORS IN FETAL ALCOHOL EXPOSED RATS

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The adverse effects of fetal alcohol exposure (FAE) on physiological and behavioral stress reactivity are primarily due to the susceptibility of the hypothalamic-pituitary-adrenal (HPA) axis to developmental perturbation. Stress related neurobiological cascades result in the release of hypothalamic peptides, including corticotropin-releasing hormone (CRH) and proopiomelanocortin (POMC) gene expression, which is further cleaved. Of these, beta-endorphin (BEP), primarily acting by negative feedback, is implicated in the hyper-responsiveness of the HPA axis in FAE offspring. Previously, we have shown BEP neuron transplantation effectively reduces the FAE associated hyper-response of hypothalamic CRH neurons in response to an immune stressor. In these experiments, we sought to explore whether a reduction of BEP neuronal activity is involved in mediating this stress hyper-responsivity phenotype in FAE rats, and whether it may translate to alterations in anxiety-like behaviors. FAE male Fischer rats were injected bilaterally into the paraventricular nucleus of the hypothalamus (PVN) with BEP cells differentiated *in-vitro* from fetal neural stem cells. Following 4-6 weeks of recovery, rats underwent an acute behavioral stressor consisting of 60 min of physical restraint. In order to assess corticosterone (CORT) response over the stress period, tail blood was collected at regular time intervals during and following restraint. BEP transplantation in FAE rats significantly attenuated the CORT response during and following restraint stress. We aimed to determine if these changes due to BEP transplantation corresponded to reduced gene expression of CRH and associated receptor, CRHR1, or, neuropeptide Y (NPY) in the PVN and amygdala (AMY) in FAE rats. Indeed, reductions in gene expression levels of CRH, but not CRHR1, in the PVN were observed in BEP FAE rats. Unexpectedly, CRH and CRH1 expression was significantly reduced in the AMY of BEP FAE rats. NPY remained unchanged in all groups. Rats were also assessed for anxiety-like behaviors in the elevated-plus maze (EPM) and open-field (OF) arenas. Interestingly, BEP transplantation reversed the behavioral alterations seen in FAE rats, suggesting an involvement in behavioral responses to acute stress. Together, these data suggest low BEP mediates the hyper-response to acute stress observed in FAE rats, which may be partially remedied by restoration of BEP hypothalamic systems. (Supported by NIAAA grant R37 AA0875715).

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NEONATAL ALCOHOL EXPOSURE IMPAIRS THE CONTEXT PRE-EXPOSURE FACILITATION EFFECT IN JUVENILE RATS: EFFECTS OF EXPOSURE WINDOW AND SHOCK INTENSITY

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Neonatal alcohol exposure from postnatal day (PD) 7-9 abolishes spatial learning during the context pre-exposure facilitation effect (CPFE, Murawski & Stanton, 2011). The current experiment extends this finding by examining narrower windows of alcohol exposure and the effects of shock intensity on context freezing. In Experiment 1, rats received a single binge dose of alcohol (5.25g/kg/day) on either PD7, 8, 9, 7-9, or were sham intubated (SI). On PD31, rats were either pre-exposed for 5 minutes to either Context A (Pre group) or Context B (No Pre). On PD32, all rats were subsequently trained in Context A, using an immediate 1.5mA, 2s footshock. On PD33, conditioned freezing was tested for 5 min in Context A. SI and PD9 animals pre-exposed to the training context showed the CPFE: exposure to Context A facilitated contextual conditioning to the immediate shock relative to rats exposed to Context B. PD8 rats showed a marginal CPFE, owing to the high variability in the pre-exposure group compared to the No Pre animals. PD7-alcohol exposed pups showed impaired performance, whereas PD7-9 exposed animals showed complete absence of the CPFE. In Experiment 2, rats received a single binge dose of alcohol (5.25g/kg/day) on PD7 or were SI. The same protocol was used as Experiment 1, except a No Pre group was not included, and pups were trained with either a 0.0, 0.5, 1.0, or 1.5mA 2s immediate footshock. SI and PD7-alcohol exposed rats trained with a 0.0 or 0.5mA footshock showed no conditioning to the context. SI and PD7 pups trained with a 1.0mA footshock showed comparable amounts of freezing and increased levels of freezing compared to the lower shock intensity groups. SI rats differed from PD7 rats when trained using a 1.5mA shock, freezing more than the ethanol exposed animals and replicating the findings from Experiment 1. The behavioral and neural processes that mediate performance on the CPFE appear to be particularly sensitive to ethanol exposure during the latter portion of the brain growth spurt (PD7-9 in the rat), with a narrower window of vulnerability emerging on PD7.

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BEHAVIORAL AND HORMONAL RESPONSES TO STRESS IN PRENATAL ETHANOL- AND PRENATAL STRESS-EXPOSED ADULT FEMALE LONG-EVANS RATS

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Ethanol (EtOH) exposure during prenatal development has been shown to impair learning in adult offspring. Similarly, prenatal stress during gestational development has also been shown to produce learning deficits in adult offspring. However, the interactive effects of these two developmental teratogens on behavioral outcomes have not been systematically evaluated. We combined an established moderate prenatal EtOH consumption paradigm where Long-Evans rat dams voluntarily consume either a 0% or 5% EtOH solution in 0.066% saccharin water (resulting in a mean peak maternal serum EtOH concentration of 84 mg/dL) with a novel prenatal stress paradigm. Pregnant rat dams were exposed to 3% TMT (2,3,5-trimethyl-3-thiazoline) for 20 minutes a day on Gestational Days 13, 15, 17, and 19. Exposure to the TMT elevated maternal serum corticosterone approximately two fold higher than controls. The combined exposure paradigm did not alter maternal weight gain, ethanol consumption, maternal reactivity to predator scent, litter size, pup birth weight, or pup weight gain up to weaning. Previously, we had demonstrated a prenatal ethanol exposure effect on adult female offspring's capacity to learn a hippocampal-sensitive Two-Trial Trace Conditioning task, with no effect of prenatal stress exposure and no combined effect [two-way ANOVA ($F(1,44)=4.88$, $p < .05$]. Preliminary measures of stress reactivity in the adult female offspring from this paradigm demonstrated a trend toward altered patterns of hormonal responses to footshock across a two hour time-course. Based on the altered hormonal response to stress, we predict that adult female offspring from this combined prenatal exposure paradigm will demonstrate deficits in the Two-Trial Trace Conditioning task when learning occurs under stressful conditions. Further behavioral and biochemical assessment of the female offspring in this paradigm is needed to better understand the interactive effects of the two prenatal insults. Funded by 1 P20 AA017068, T32 AA 014127, and F31 AA 2070210.

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AN ETHANOL BINGE ON POSTNATAL DAYS SIX PLUS EIGHT RESULTS IN A DOSE DEPENDENT BEHAVIORAL CHANGE IN YOUNG RATS

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Women who drink during pregnancy frequently drink in a periodic binge pattern typifying weekend drinking. Dose dependent behavioural changes occur in animal models following a single binge ethanol exposure on postnatal day six (PN6). This study exposed rat pups to an ethanol binge, on each of PN6 and PN8, to mimic a weekend drinking session, and assessed activity and anxiety in the offspring.

On PN6 and PN8 Long Evans rat pups in treatment groups; E4, 4.5g/kg/day; E5, 5.25g/kg/day or E6, 6.0g/kg/day, received ethanol in an artificial milk solution via intra-gastric intubation in two feeds two hours apart. A sham intubation (SI) group acted as a control for the effects of ethanol and pups reared normally by the dam were suckle controls (SC). Open field testing was carried out at PN7, PN16/17 and PN27/28. Elevated T-maze testing began on PN75. All testing was carried out under sodium lighting, darkness, during the 'dark cycle' of the animals' day.

Ethanol treatment had a dose dependent effect on distance travelled on PN6, ($F[4,22]=9.172$, $p<.001$. Distance travelled in the open field was greater on PN17 than PN16 in E6 animals, ($p<.01$) with no other group differences.

Ethanol had a significant effect on avoidance ($F[4,128]=7.206$, $p<.0001$) but not the escape component in the T-maze.

This ethanol exposure regimen produced behavioral effects on both activity and learned fear, adding to our understanding of what behaviors may be characteristic of children with Fetal alcohol spectrum disorder. This data has implications for understanding the effects of intermittent drinking during the third trimester of human pregnancy.

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PERSISTENT DOSE-DEPENDENT CHANGES IN BRAIN STRUCTURE IN YOUNG ADULTS WITH LOW-TO-MODERATE PRENATAL ALCOHOL EXPOSURE

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Many children with heavy exposure to alcohol *in utero* display characteristic alterations in brain size and structure. However, the long-term effects of low-to-moderate alcohol exposure on these outcomes are unknown. Using voxel-based morphometry and region-of-interest analyses, we examined the influence of lower doses of alcohol on gray and white matter composition in a prospectively recruited, homogeneous, well-characterized inner-city cohort of alcohol-exposed (n=11, age 19.5±0.3 yr) and control (n=9, age 19.6±0.5 yr) young adults. A large proportion of the exposed individuals were born to mothers whose alcohol consumption during pregnancy was in the low-to-moderate range (0.11-0.99 oz absolute alcohol/day). T1-weighted 3D structural brain images were collected on a Philips 3T Achieva MRI using an 8-channel SENSE head coil. Voxel-based morphometry (VBM) was used to test for structural differences between brains of the alcohol exposed and control subjects. There were no differences in total brain volume, total gray or white matter volume, or regional white matter volume between the exposed and control groups. However, gray matter volume was reduced in alcohol-exposed individuals in several areas previously reported to be affected by high levels of exposure, including the left cingulate gyrus, bilateral middle frontal gyri, right middle temporal gyrus, and right caudate nucleus, all ps < 0.001. Notably, this gray matter loss was dose-dependent (r^2=0.37–0.50, p<0.005), with higher exposure producing more substantial losses. The results were not altered by statistical adjustment for gender, maternal smoking or drug use during pregnancy, or current alcohol and drug use by the participant. Some recent studies suggest that fetal alcohol exposure is associated with a developmental delay in cortical pruning. These data identify local deficits in cortical gray matter volumes in young adulthood once earlier phases of brain development are complete. Thus, these results suggest that even at low doses, alcohol exposure during pregnancy impacts brain development and that these effects persist into young adulthood.

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SALIVARY CORTISOL LEVELS ARE ELEVATED IN THE AFTERNOON AND AT BEDTIME IN CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDER

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Objectives: Prenatal alcohol exposure can cause dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, and this may underlie some of the behavioural and adaptive problems in individuals with Fetal Alcohol Spectrum Disorders (FASD). Infants prenatally exposed to alcohol show increased basal and post-stress cortisol levels, but it is unknown if this persists beyond infancy. We have completed a 3-year study on the effects of a strength-based, motor skill development program for children with FASD. Our hypothesis is that improvements in the motor domain will extend to other domains, and affect behaviour and adaptive functioning, possibly through effects on the HPA system. Our objectives were to determine the effect of the program on the HPA system (as indicated by salivary cortisol levels), and to compare cortisol levels of children with FASD to that of control children.
Methods: Twenty-seven children (age 6–14 y) participated in an 8-week motor skill development program consisting of 2 x 1.5 hour sessions/week. Salivary cortisol levels were measured in 24 children (FASD group) and compared at 4 time points: before, immediately after, 2 months, and 1 year after program completion. Cortisol levels were also compared to 32 control children (C group, no FASD) to evaluate the long-term effects of prenatal alcohol exposure on HPA regulation. For each time point, saliva was collected on each of 2 days at 3 times in the diurnal cycle: wake-up, after school, and just before bedtime.
Results: Salivary cortisol levels showed significant (p's<0.05) diurnal variation in all children, being higher at wake-up, compared with after school and bedtime, and higher after school compared to bedtime. Cortisol levels did not vary significantly over the 4 time points in the C or FASD groups, indicating that there was no effect of the motor skill program on cortisol levels. When the time points were combined, cortisol levels were significantly higher in the afternoon (p=0.033) and at bedtime (p=0.026), but not at wake-up, in children with FASD, compared with controls.
Conclusions: These results indicate that cortisol levels are elevated throughout the day in children with FASD, possible due to increased basal levels and/or an increased response to daily stressors. Importantly, these results indicate that prenatal alcohol exposure has long-term effects on the HPA system in humans, which could increase vulnerability to mental health issues and chronic disease.

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SACCADIC EYE MOVEMENT CONTROL AND PSYCHOMETRIC TESTING IN THE ASSESSMENT OF COGNITITVE DYSFUNCTION IN CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS

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Background: Prenatal alcohol exposure is a major, preventable cause of neurobehavioural and cognitive deficits in children. The developing brain is the principal target organ for gestational alcohol exposure. The full spectrum includes several diagnostic subgroups, and is collectively referred to as Fetal Alcohol Spectrum Disorders (FASD). There is a clear need to develop new tools for assessing brain function in the FASD population. Measurement of eye movement control is a powerful tool for assessing cognitive, sensory and motor function.
Objective: To utilize standardized psychometric tests and measures of saccadic eye movement control to identify brain dysfunction in children with FASD.
Methods: In this multi-centre study, each child completed a battery of psychometric tests and a set of structured saccadic eye movement tasks. The psychometric battery measured executive function, working memory, short-term memory, visuospatial skills, language and math ability. Depending on age, each child completed structured eye movement tasks that assessed sensory motor integration, response inhibition, cognitive flexibility and spatial working memory.
Results: Preliminary analysis of both sets of tasks revealed significant differences between children with FASD and typically developing children. In both the pro- and antisaccade tasks, the children with FASD display significantly more hypometric initial saccades, which required a greater number of additional saccades per trial to arrive at the target. Also in the prosaccade task, the accuracy of the saccades were significantly poorer in children with FASD compared to controls. The children with FASD made significantly more direction errors in the antisaccade task. In the memory guided task, the children with FASD made significantly more timing errors, and also exhibited decreased accuracy in the task. Analysis of the data from the psychometric battery has revealed that the children with FASD scored significantly lower on every subtest administered except the NEPSY-II arrows task, a test of visuospatial processing. This result suggests that the deficits in eye movement control cannot be attributed to a general deficit in visuospatial processing capability.
Conclusions: This study will provide greater insight into the motor and cognitive domains that are assessed using eye movement tasks, and will generate new knowledge that better defines the relationship between brain injury and behaviour in children with FASD.

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BRAIN DYNAMICS OF ADOLESCENTS WITH FASD

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Brain regions known to be impacted in FASD include midline cortical areas, medial prefrontal cortex, hippocampus and cerebellum. Cortico-cerebellar networks that include medial temporal areas are critical for effective learning and memory function. We utilized a magnetoencephalographic (MEG) array to record spatio-temporal patterns of brain dynamics from 13 adolescents and young adults with FASD and age- and sex-matched controls during an aversive trace conditioning paradigm. Trails included 1) visual (CS+) stimuli followed after a delay by aversive (US) sounds (1/3 of trials), 2) the same CS+ unpaired with US (1/3 of trials) and 3) a different set of visual stimuli (CS-) never paired with US (1/3 of trials). Source analysis of the data was based on individual MR images and then projected onto a standard Colin27 brain. Spatio-temporal activation patterns were examined for significant differences between FASD and controls (paired Students t-test: p<0.05). Marked differences were observed across all conditions and epochs. Activity in occipital and inferior temporal cortex was stronger in adolescents with FASD than in controls. The converse was true for activity in parietal and prefrontal cortex. For CS+ paired trials, activity prior to the US was stronger in medial temporal cortex for controls than for FASD. Activity within right amygdale and right hippocampus at 100-150 ms after the US was stronger for FASD than controls. In contrast, activity within left hippocampus at 200–450ms after the US was larger for controls than FASD for both CS+ paired and unpaired trials. Early processing of sensory input occurred in left Crus II of cerebellum at <90ms following CS stimuli and was stronger in controls compared to FASD. Sustained activation of this area was then stronger for FASD than controls until the termination of the delay period. Differential activation continued for an additional ~1s. Differential activation was also observed for regions in left/right lobule VI/Crus I, components of a cerebellar WM network identified by Stoodley et al. (2009). The observation of distinct spatio-temporal activation patterns in adolescents with FASD compared to age- and sex-matched controls during an aversive conditioning paradigm suggest either abnormal and/or delayed development of fronto-cerebellar networks in adolescents with FASD.

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NEURAL CORRELATES OF FORCE REGULATION IN CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE

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Children with histories of heavy prenatal alcohol exposure show reduced control of isometric (IM) and isotonic (IT) force as well as brain structural abnormalities in regions known to be involved in motor control, including the cerebral cortex, cerebellum, basal ganglia, and corpus callosum. However, the relationship between regulation of motor force and neuroanatomical impairments has not been explored in children with fetal alcohol spectrum disorders (FASD). Prior studies have evaluated deficits in force regulation in children with heavy prenatal alcohol exposure, and this study extended those studies by examining regional brain volumes associated with IM and IT force regulation in the same cohort of participants. Children with (ALC=9) and without (CON=7) histories of heavy prenatal alcohol exposure, who previously received assessment of force regulation, underwent structural magnetic resonance imaging. Measures of force regulation previously reported to differ between groups—response accuracy, response variability, and signal complexity—were correlated with regional brain volume after correcting for total intracranial volume; significant correlations were followed-up with multiple regression to control for age. In the ALC group, greater IM signal complexity was associated with smaller volume of the inferior parietal (IP) region, and greater IT response variability was correlated with larger volume of the anterior midbody of the corpus callosum. In the CON group, greater IT response variability and signal complexity was related to larger volumes in the genu and splenium of the corpus callosum, respectively. Findings provide a link between brain structure and force regulation and suggest altered influences of brain development on force production in alcohol-exposed children. Reductions in brain volume as a result of prenatal exposure to alcohol likely contribute to deficits in regulation of motor force in this clinical population. Force regulation is an important control parameter involved in complex movement, and the continued use of neuroimaging methods will help elucidate the relationships between brain and motor development in children with FASD.

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PROGRAMMING OF NEURAL GENE EXPRESSION RESPONSE TO ADJUVANT-INDUCED ARTHRITIS BY PRENATAL DIET IN A RAT MODEL OF PRENATAL ALCOHOL EXPOSURE

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Prenatal alcohol exposure (PAE) results in alterations in numerous physiological systems, including neuroendocrine and neuroimmune systems. This study's purpose was to determine whether PAE results in fetal programming of neural gene expression, particularly in genes related to neuroendocrine and neuroimmune function. Utilizing our well-established animal model of PAE, ethanol was administered to pregnant Sprague-Dawley dams throughout gestation in a liquid diet, *ad libitum* (36% ethanol-derived calories). Maltose-dextrin was isocalorically substituted for ethanol in a liquid control diet for a pair-fed (PF) group, and a control (C) group received a pelleted control diet, *ad libitum*. Female offspring were injected in adulthood with complete Freund's adjuvant to induce an inflammatory response (adjuvant-induced arthritis [AA]) and elucidate dysregulated neuroimmune pathways. A saline-injected cohort assessed the effects of prenatal treatment alone. PAE animals demonstrated increased incidence and severity, and prolonged course of AA compared to C and PF controls. Gene expression was analyzed in the prefrontal cortex (PFC) and hippocampus at both the peak and resolution of AA using whole genome gene expression microarrays. Adjuvant injection altered expression of numerous genes in both the hippocampus and PFC, in animals both with and without clinical signs of AA. C and PF females demonstrated greater changes than PAE females, which may be indicative of a failure to mount an appropriate neural response to the immune challenge. Changes in response to prenatal ethanol exposure were greatest in the PFC, with 37 genes differentially expressed in PAE compared to control females; 8 of these genes were also significantly different between PAE and PF females. In the PFC, 16 genes also demonstrated changes resulting from an interaction between adjuvant injection and PAE. Gene ontology analysis revealed numerous Biological Processes enriched in genes that score high for expression differences between PAE and control animals, *eg.* system development, cell adhesion, and antigen processing and presentation. Several of the genes differentially expressed with PAE have been validated using RT-qPCR (Nhej, Atp6ap1, and Vdac2), and are considered candidates for epigenetic reprogramming to be analyzed for changes in DNA methylation. Supported by: NIH/NIMH MH081797 (Project 2) to JW, GGM, MSK; NIH/NIAAA R37 AA007789 to JW; and CFRI/NeuroDevNet Graduate Studentship to KAS.

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ALTERATIONS IN NUCLEUS ACCUMBENS DENDRITIC MORPHOLOGY AFTER VOLUNTARY ETHANOL CONSUMPTION IN ADULT RATS EXPOSED TO MODERATE LEVELS OF ETHANOL IN UTERO

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Recent reports from our lab indicate that moderate prenatal ethanol exposure 1) results in reductions in measures of dendritic morphology in the nucleus accumbens (NAc) shell, and 2) these rats voluntarily consume more of a 10 and 20% ethanol solution in adulthood. In order to further establish a link between the NAc and ethanol consumption, fetal ethanol and saccharin exposed rats that voluntarily consumed both 10 and 20% ethanol solutions at 6 months of age were analyzed for changes in dendritic length and branching in the NAc using Golgi-Cox staining and *camera lucida* imaging techniques. Moderate fetal ethanol exposure was achieved using a two-bottle choice voluntary consumption paradigm. Dams received either 0 or 5% ethanol in saccharin throughout gestation, resulting in blood ethanol concentrations around 82 mg/dL. At six months of age, male offspring were individually housed and given access to two bottles containing either 10% ethanol in tap water or tap water. Consumption was measured at 4 and 24-hour time points, and the bottles were made available on Monday, Wednesday, and Friday at the start of the dark cycle. The ethanol solution was ramped up to 20% for the latter aspect of the study. At the conclusion of the last ethanol consumption session, rats were sacrificed and brains were removed and immersed in a Golgi-Cox solution. These brains were left in solution for 2 weeks, and were then cut on a vibratome at 200 microns and mounted on slides for microscopic analysis of dendritic length and branching in medium spiny neurons sampled from the NAc core and shell. Ten cells (5 per hemisphere) were drawn from each region for each rat. Results indicate that fetal ethanol exposed rats had significant reductions in the NAc core for both dendritic length and branching, and that, for all animals, alterations in the NAc served as significant predictors of voluntary ethanol consumption. Further analysis of other regions, including the NAc shell and the dorsal striatum, are underway in our lab. These findings suggest that changes in reward circuitry as a result of fetal ethanol exposure are related to ethanol consumption later in adulthood, and that deficits resulting from fetal ethanol exposure can have a domino effect that starts in the NAc shell and spreads to other regions of the striatum after adult ethanol exposure.

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PRENATAL ETHANOL ALTERS THE POSTNATAL EXPRESSION OF ETHANOL-INDUCED APPETITIVE AND AVERSIVE REINFORCEMENT

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Prenatal ethanol has a permissive effect on later alcohol consumption, yet the mechanisms underlying this phenomenon are poorly understood. Little is known about the impact of prenatal ethanol on the sensitivity to ethanol's reinforcing effects. One possibility is that prenatal ethanol exposure makes subjects more sensitive to the appetitive effects of ethanol or less sensitive to ethanol's aversive consequences. The present study assessed ethanol-induced second-order conditioned place preference and aversion and ethanol-induced conditioned taste aversion (CTA), with varied ethanol doses, in infant rats derived from pregnant rats administered vehicle or 2 g/kg ethanol during gestational days 17–20. The involvement of the kappa opioid receptor system in the aversive effects of ethanol was also explored. When place conditioning occurred during the rising limb of the blood-ethanol curve (Experiment 1) pups exposed to ethanol in-utero, but not controls, exhibited conditioned place preference. Conditioning during a later phase of the intoxication (30–45 min post-administration, Experiment 2) resulted in place aversion in control pups but not in those that had been exposed to ethanol in-utero. Ethanol readily induced conditioned taste aversion (Experiment 3), which was fairly similar across pups treated with vehicle or ethanol during gestation. The administration of a kappa antagonist (norbinaltorphimine) 24 hrs before conditioning did not alter ethanol-induced CTA. These results suggest that a relatively brief exposure to a moderate ethanol dose during late gestation tilts the balance between ethanol's appetitive and aversive effects, promoting the expression of ethanol-mediated conditioned reinforcement and blocking the acquisition of conditioned aversion by ethanol. This altered pattern of motivational reactivity to ethanol could be one of the mechanisms underlying the permissive effect that prenatal ethanol exerts in later ethanol acceptance.

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ETHANOL EXPOSURE CAUSES INCREASED BUT DISORIENTED DENDRITIC GROWTH DURING EARLY CORTICAL DEVELOPMENT

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Prenatal ethanol exposure disrupts cortical neurite initiation and outgrowth, but prior findings have shown both ethanol-dependent growth promotion or inhibition, depending on experimental context. For example, the inclusion of astrocytes has been shown to change the embryonic neuronal response to ethanol in vitro. To better approximate in vivo conditions we examined neuronal morphology using a whole hemisphere explant model developed in our lab. In this model, layer 6 cortical neurons migrate, laminate and extend neurites in an organotypic fashion. To label a subpopulation of cells for complete morphological reconstruction we performed ex utero electroporation of a GFP expression construct on E13 and allowed the explants to develop for 2 DIV (days in vitro) before fixation and analysis. The explants were exposed to ethanol (400mg/dL) at either 4 or 24 hours prior to fixation. The explants were then embedded, sectioned and imaged using confocal microscopy and complete 3D reconstructions were made of >80 cells in each condition. We found a modest (~15%) increase in total dendritic length subsequent to both 4 and 24 hour ethanol exposure ($P<0.01$) but no differences in total dendritic branch number under any conditions. Surprisingly, we also found a consistent disorientation of the cell body and primary dendrite with respect to the pial surface that was especially pronounced after 24 hours of ethanol exposure. While the primary dendrites of control neurons had an orientation angle of 38±2.0° from the pial surface with respect to a normal, the primary dendrites of ethanol exposed neurons were found at an average of 60.5±3.6° ($P<0.001$). These findings establish that layer 6 neurons are sensitive to ethanol during a critical early point in cerebral cortex formation and show that ethanol exposure may have an unexpected influence on cellular orientation and the mechanisms underlying the establishment of neuronal polarity.

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EFFECTS OF PRENATAL ETHANOL EXPOSURE ON CORTICOTHALAMIC NEURONS

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Fetal Alcohol Spectrum Disorder (FASD) is the umbrella term used to describe the broad range of cognitive and physical defects resulting from prenatal exposure to alcohol. Sensorimotor deficits observed in human FASDs likely result from malformations during axon tract development. Candidate axons to be affected by prenatal ethanol exposure are those connecting the thalamus and cortex because these are essential for normal sensation and perception. In addition to effects on axon formation, prenatal ethanol exposure affects the fate, proliferation, and survival of neurons that extend these connections. Previous studies have shown that prenatal ethanol exposure does not affect thalamocortical neuron proliferation and survival. Therefore, for this study we examined corticothalamic neurons. Ethanol was administered to pregnant Swiss Webster mice via injection or a voluntary drinking protocol during critical time points of thalamo-cortical development, either embryonic days (E) E12.5 to E14.5. Age-matched controls received phosphate buffered saline (injection protocol) or tap water (voluntary drinking protocol). Bromodeoxyuridine (BrdU) was injected at E12.5 in order to analyze corticothalamic neuron proliferation via BrdU birthdating of postnatal embryos. To study axons, we analyzed postnatal offspring because corticothalamic axons (CTAs) should have reached their targets by this time. Immunostaining was used to visualize axon tracts with L1 antibodies labeling CTAs and neurofilament labeling all axons. Immunostaining with T-box brain 1 (Tbr1) antibodies was used to analyze corticothalamic neuron fate within the cortex and cleaved caspase 3 antibodies were used to identify apoptotic cells. Nissl staining was also used to investigate nervous system cytoarchitecture. Using binning analysis to compare position and number of Tbr1+ neurons within the cortex, we found their position shifted in the cortical plate, closer to the ventricular zone, of mice prenatally exposed to ethanol. Additionally, there were more Tbb1+ neurons in the deep layers of the cortical plate. Finally, the qualitative size of fiber bundles in the internal capsule appeared larger. From these studies, we conclude that prenatal ethanol exposure increases number of corticothalamic neurons within the cortical plate and axons within the internal capsule. These effects may contribute to sensorimotor deficits observed in human FASDs.

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EFFECTS OF CHRONIC EARLY GESTATIONAL ETHANOL EXPOSURE ON THE DEVELOPING BRAIN: A MAGNETIC RESONANCE MICROSCOPY STUDY

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Magnetic resonance microscopy (MRM - high resolution magnetic resonance imaging) has previously been utilized to examine mice acutely exposed to ethanol during discrete stages of early development. These studies have demonstrated that even short, binge-like exposures to high doses of ethanol on a single early gestational day (GDs 7, 8, 9, 10 or 11) can result in exposure stage-dependent neuroanatomical abnormalities including holoprosencephaly, cortical heterotopias and hypothalamic hamartomas as well as volumetric and shape changes in the striatum, hippocampus and cerebellum. The current study was designed to extend the previous analyses with determination of the neuroanatomical effects of chronic ethanol exposure during the entire GD 7-11 period. For this, female C57Bl/6J mice were acclimated to a liquid diet containing 4.8% ethanol. After the acclimation period, the mice were bred and then, from days 7–11 of pregnancy were provided liquid diet containing ethanol or an isocaloric amount of maltodextrin. This ethanol exposure paradigm results in daily peak maternal blood ethanol concentrations of about 200–220 mg/dl. Fetuses were removed on GD 17 and immersion fixed in Bouin's fixative containing the contrast agent, Prohance (Bracco Diagnostics). Randomly selected fetuses were imaged at the Duke Center for In Vivo Microscopy using a solenoid radio-frequency coil specifically designed for MRM. Image arrays were acquired using 3-D spin warp encoding. The resulting high resolution scans (29 mm isotropic) were manually segmented using the program, ITK-SNAP, in order to determine volumes of specific brain areas. Comparisons of the brains of ethanol-exposed and control specimens did not reveal any overall microencephaly. Similar to the acute early effects of ethanol, the chronic, lower-dose of ethanol employed in this current study resulted in significant ventricular and pituitary enlargement. Additionally, the GD 7-11 chronic ethanol exposure significantly decreased the size of the pons and medulla, a deficit not observed in the previous acute, single day exposure studies. In addition to extending our understanding of the range and type of defects that result from early gestational ethanol exposure, these results aid in defining the exposure pattern and dosage dependency of ethanol-induced neuroanatomical alterations. This work was supported by NIH grants AA011605, AA017124, NCRR/NCI P41 05959.

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ROLE OF PROGRAMMED CELL DEATH 4 (PDCD4) IN ETHANOL-INDUCED DYSREGULATION OF NEUROGENESIS

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Background: Ingestion of ethanol during pregnancy can induce grave abnormalities in developing fetal brain. Recent studies have demonstrated that ethanol inhibits the proliferation and promote premature differentiation of neural stem /progenitor cell. However, the molecular mechanism involving ethanol's toxicity on proliferation and differentiation of neural cells are still unclear. Our preliminary data suggest the importance of Programmed Cell Death 4 (PDCD4), a tumor suppressor gene in normal prenatal and postnatal brain development. In accordance with our preliminary observation, we postulate that PDCD4 could be a potential candidate by which ethanol impairs the proliferation and differentiation of neural cells. The goal of the present study is to investigate the possible role of PDCD4 in ethanol-induced abnormalities in proliferation and differentiation of neuroblasts.
Methods: To test the hypothesis, rat brain neuroblasts spontaneously established from 17 day fetal cerebral cortices characterized for primitive neuronal nestin, NF68 and on differentiation with dibutyryl-cAMP, expressing neuronal markers neuron specific enolase (NSE) and NF-200 were utilized. Ethanol's effect on neuroblast proliferation was assessed by cell counting using Vi-Cell viability analyzer and BrdU incorporation assay. For the differentiation studies, neuroblasts were treated with or without dibutyryl-cAMP containing 0 or 86 mM ethanol. Expression levels of mRNA and protein were analyzed by RT-PCR and immunoblotting.
Results: Ethanol exposure significantly decreased cell proliferation as demonstrated by cell counting and BrdU incorporation. Moreover, message as well as protein levels of PDCD4 were significantly increased with ethanol treatment. Ethanol exposure further potentiated the expression of the neuronal marker NSE on addition of dibutyryl-cAMP.
Conclusion: Ethanol inhibits proliferation and induces early differentiation of cortical neuroblasts associatedly increasing PDCD4 expression. SiRNA mediated downregulation of PDCD4 and adenovirus mediated overexpression of PDCD4 strategies will be employed in our study to explore the involvement of PDCD4 in ethanol inhibited proliferation and immature differentiation of neuroblasts. The present study addressing the current perspectives on how alcohol can produce neuroteratogenic effects might explain the neurodevelopmental anomalies associated with Fetal Alcohol Syndrome (FAS).

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EFFECT OF LIPID RAFT DISRUPTION ON ETHANOL INHIBITION OF L1 ADHESION

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Alcohol causes fetal alcohol spectrum disorders in part by disrupting the function of the neural cell adhesion molecule L1. Alcohol inhibits L1-mediated cell-cell adhesion by interacting with a binding pocket at the Ig1-Ig4 interface of the L1 extracellular domain (Dou *et al.*, J Biol Chem 2011). Ethanol also inhibits L1-mediated neurite outgrowth in cerebellar granule neurons (CGN). A recent report (Tang *et al.*, J Neurochem 2011) indicates that ethanol induces the translocation of L1 into CGN lipid rafts and that disruption of lipid rafts prevents ethanol inhibition of L1-mediated neurite outgrowth. Of note, the same butanol-pentanol cutoff was noted for alcohol-induced translocation of L1 into lipid rafts as was reported for alcohol inhibition of L1 adhesion (Ramanathan et al. J Cell Biol 1996). These observations raised the question of whether ethanol inhibits L1 adhesion by inducing the translocation of L1 into lipid rafts. We tested this hypothesis in a well-characterized ethanol-sensitive NIH/3T3 cell line, 2A2-L1, which is stably transfected with human L1. Lipid rafts were characterized by measuring the distribution of caveolin, a protein marker of lipid rafts, between a detergent (Triton-X100)-soluble and detergent-insoluble fraction of whole cell lysates. In control 2A2-L1 cells, 16.6 ± 4.3 % of caveolin was distributed within the detergent-soluble fraction. In contrast, treatment for one hour with 5 μg/ml filipin, an agent known to disrupt lipid rafts, markedly increased the percentage of caveolin in the detergent-soluble fraction (45.5 ± 3.4%; $p = 0.0003$, n=8). In control 2A2-L1 cells, 25 mM ethanol did not affect the distribution of caveolin within detergent-soluble and insoluble fractions ($p=0.18$, n=8) but did decrease L1 adhesion by 37.4 ± 3.3 %. Disruption of lipid rafts with filipin did not significantly reduce either L1 adhesion (control, 34.5 ± 1.4% adhesion; filipin-treated, 33.9 ± 2.0% adhesion; $p=0.7$; n=8) or ethanol inhibition of L1 adhesion (30.5 ± 5.6 % inhibition, $p = 0.16$, n=8). These findings indicate that ethanol inhibition of L1 adhesion does not require the integrity of lipid rafts.
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RHYTHMIC LICKING BEHAVIOR IS ALTERED IN ADULT RATS THAT RECEIVED POSTNATAL ETHANOL EXPOSURE

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Ethanol exposure to rats during the postnatal (PN) vulnerable period (days 4–6) has been shown to produce significant decreases of Purkinje cells (PCs) and decreased innervation from olivary climbing fibers to the surviving PCs. For the present study, the functional capacity of the cerebellum was assessed by analysis of rhythmic licking behavior. Rhythmic licking movements are believed to be controlled by brainstem pattern-generating circuits, and it has been demonstrated that the olivo-cerebellar system is essential for controlling the timing of the licks. Therefore, we hypothesized that the timing aspects of rhythmic licking would reflect alterations in cerebellar activity in rats that were ethanol exposed verses controls. Rats (E group) were treated by intragastric intubation with a daily dose (4.5 g/kg) of ethanol on PN4-6. Control rats received sham intubations. The licking behavior was analyzed in adult rats following 4 hours of water deprivation. The rats were allowed access to a water bottle connected to a standard analog/digital converter and the animal was connected to ground via a metal wire grid on the cage floor. A current (< 1 mA) was passed through the drinking spout of the water bottle and is undetectable by the rat. Individual licks were recorded and the interlick interval was analyzed by frequency analysis. The mode of the interlick interval was altered in the E-group resulting in a significantly faster rate of licking by these rats. This alteration in licking behavior was consistent in adult animals irrespective of age. This simple behavioral method provides a means for indirectly assessing cerebellar function that is linked to damage resulting from postnatal ethanol exposure.
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IN-SCHOOL STUDY OF PREVALENCE OF FETAL ALCOHOL SPECTRUM DISORDER IN EAST TAIWAN

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Background: Fetal Alcohol Spectrum Disorders (FASD), including Fetal alcohol syndrome (FAS) and Fetal Alcohol Effect (FAE) resulting from prenatal alcohol exposure has been well-documented in the Western world. With protective genetics (e.g., ADH2*2) in place, how FASD prevails in Eastern world has not been clear. We aim to report a prevalence study of FASD in East Taiwan.
Methods: This study was performed in-school in Hualien County in East Taiwan which includes Taiwanese with ancestor of Chinese Han and aborigines with ancestor of Malaysia descent. From 1996 through 1998, data from 3817 students in 87 schools including 847 students from special schools, between 3 to 15 years old were enrolled. A three-stage evaluation process was used, including stage one: background history collection including birth weight & height, and maternal alcohol- or substance-use history during pregnancy; stage two: pediatric physical and neurological assessment including physical dysmorphism. A total of 3817 students complete the first two stages. Children with positive maternal alcohol consumption history and pre- or post-natal growth delay or facial/body dysmorphic characteristics, received stage three:-developmental or cognitive assessment. All the subjects were reviewed by pediatric geneticists, neurologists and psychologists on the same day.
Results: Among participants with reported alcohol exposure during pregnancy, we confirmed seven children (1.83 per 1000 live births, 4 boys and 3 girls) with severe form described in fetal alcohol syndrome (FAS), and fifteen (3.93 per 1000 live births, 9 boys and 6 girls) with alcohol related neurodevelopmental deficit without all facial dysmorphic features. With 300-character space, do you plan to add the numbers in special schools? Children with FAS had smaller head circumstance, lower body weight and lower body height than those with FAE. Also, children with FAS scored lower on intelligence tests than did children with non-FAS FASD.
Conclusion: Using active case ascertainment in general schools and special schools, this study reported estimates of the prevalence of FASD in East Taiwan. Although with protective gene in Asian population, a comparable prevalence of FASD in East Taiwan is observed comparable to that of the Western world.

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THE RELATIONSHIP BETWEEN LIFE EVENTS AND ALCOHOL USE DISORDERS TREATMENT OUTCOME: OPERATIONALIZATION MATTERS

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Life events have been implicated in contributing to poor alcohol use disorders (AUDs) treatment outcomes. However, this relationship has not received consistent empirical support. This may be due, in part, to differences in how life events and treatment outcomes are operationalized across studies. The purpose of this study was to demonstrate how the use of different operational definitions of life events and AUD treatment outcomes affects the life events-AUD outcome relationship.
A total of 495 treatment-seeking AUD adults completed the Life Experiences Survey for the previous six months. Participants rated the desirability/undesirability of each endorsed event on a Likert-type scale from -3 to 3, where -3 = *extremely negative* and 3 = *extremely positive*. Based on the literature, life event data were operationalized in the following ways: number of endorsed events, negative events, positive events, all extreme events, extremely negative events, extremely positive events, presence of any extremely negative event, and total health-related events. Daily alcohol use data were collected for the subsequent six months. AUD treatment outcomes were computed for the two-month and six-month timeframes following the life events assessment, and included occurrence of relapse, drinks per drinking day (DDD), and percentage of days abstinent (PDA).
Regressions indicated that negative events were associated with greater likelihood of relapse and DDD for both timeframes. Extremely negative events were associated with greater likelihood of relapse during the two-month timeframe, and greater DDD and lower PDA for both timeframes. Presence of extremely negative events predicted greater DDD and lower PDA for both timeframes, but was unrelated to relapse. Extremely positive events predicted lower likelihood of relapse for the two-month timeframe. Both positive and extremely positive events were associated with lower DDD at two months, and greater PDA for the two- and six-month timeframes. Total events and health-related events were unrelated to all outcomes. These results suggest that although there are general trends in the data, the direction and significance of the life event-AUD treatment outcome relationship differs across operationalizations of the two constructs, which may account for inconsistencies in the literature. Selecting operational definitions that fit within the theoretical framework that is guiding the hypotheses may better elucidate this relationship.

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ETHNIC/RACIAL DIFFERENCES IN THE RELATIONSHIP BETWEEN DEPRESSIVE SYMPTOMS, STRESSFUL LIFE EVENTS, AND ALCOHOL USE IN YOUNG ADULTS

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There is growing evidence supporting a significant relationship between heavy drinking and depressive symptoms (Hasin et al., 2007), as well as stressful life events (Keyes et al., 2011). However, less is known about potential ethnic/racial differences in these associations. Thus, the goal of the current investigation was to examine the pattern of relationships between depressive symptoms and stressful life events with alcohol use among Caucasians, African Americans, and Asian Americans.

The sample consisted of 190 nonalcoholic young adults who did not have an Axis I or II disorder participating in the Chicago Social Drinking Project; there were 147 Caucasians, 20 African Americans, and 14 Asian Americans. Assessments were taken at baseline, as well as yearly follow-ups at 1, 2, 4, and 5 years using the Stressful Life Events Scale (SLE), BDI, QFI, and AUDIT.

Analyses with Caucasians demonstrated a significant positive relationship between alcohol use and greater depression, both concurrently (significant *r*s ranged from .17 to .53) as well as longitudinally (significant *r*s ranged from .22 to .35), with depression predicting higher levels of drinking across a one-to-two year lag. Neither African Americans nor Asian Americans demonstrated consistently significant relationships between drinking and depression, concurrently or longitudinally. Regarding stress, no significant relationship was found with drinking for Caucasians or Asian Americans. However, for African Americans, there was a strong positive relationship between drinking and stressful life events, both concurrently (almost all *r*s ranged from .32 to .54), as well as longitudinally (almost all *r*s ranged from .26 to .62), with stress predicting higher levels of drinking across a one-to-two year lag.

Overall, the results demonstrated significant associations between heavier alcohol use and both depressive symptoms and stressful life events, but there were different patterns among ethnic/racial subgroups. Heavier drinking was associated with higher depressive symptoms over time for Caucasian young adults, but greater stressful life events for African American young adults. Results with Asian American young adults were largely nonsignificant for both depression and stress. Interpretation of this data should be made with caution as the sample size for minority subgroups was small; however, the results highlight the importance of considering potential ethnic/racial differences in future alcohol research.

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BELIEFS IN PERSONAL CONTROL: DIRECT & INDIRECT EFFECTS OF GOD MEDIATED, EXAGGERATED INTERNAL, & EXTERNAL CONTROL ON DEPRESSION & ALCOHOL PROBLEMS

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Berrenberg's (1987) multidimensional model of personal control proposes three distinct dimensions related to psychological adjustment variables: an exaggerated sense of internal control (e.g. continuing to strive for goals long after most individuals would have given up), a generalized external control (e.g. success or failure as a matter of luck or knowing the right people), and God mediated control (e.g. the belief in the ability to succeed but only with God's help). While correlational work has been conducted regarding several psychological adjustment variables such as depression (Berrenberg, 1987), little is really known regarding if these beliefs in personal control may directly or indirectly influence pathological reasons for drinking (e.g. drinking to cope), frequency of drunkenness, or alcohol-related problems. A multiple group structural equation model with 581 university students (317 women, 264 men) was examined. Tests of structural invariance revealed that there was moderation by gender. For instance, God mediated control was found to be directly linked to pathological reasons for drinking, frequency of drunkenness, and alcohol-related problems only among women. Three path mediational analyses were conducted within each gender group. Higher levels of beliefs in an exaggerated internal control were indirectly linked to increased frequency of drunkenness through more depressive symptoms and pathological reasons for drinking among both genders. In addition, higher levels of exaggerated internal control were indirectly linked to more alcohol-related problems through more depression and pathological reasons for drinking among both genders. In contrast, generalized external control indirectly reduced both drunkenness and alcohol-related problems via the same mechanisms. Moreover, higher levels of God mediated control were indirectly linked to more alcohol-related problems through increased pathological reasons for drinking and frequency of drunkenness among women only. Our results suggest that God mediated control may be a more important direct and indirect link to alcohol-related outcomes for women than for men.

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LAGGED RELATIONS BETWEEN DRINKING FREQUENCY AND DEPRESSED MOOD IN ADOLESCENCE

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Depression and alcohol use among adolescents are great public health concerns due to negative consequences from adolescence into adulthood. Most previous studies have used cross-sectional designs and examined unidirectional associations between alcohol use and depressive mood. Studies focused on the relationship between depression and alcohol use are equivocal as to whether depression influences alcohol use or vice versa; however, the nature of these relationships is less known and needs to be investigated. Therefore, this study examined cross-lagged relationships between depressed mood and alcohol use among youth in mid-adolescence and late-adolescence.

Using a subsample derived from the Project on Human Development in Chicago Neighborhoods (n=693), we examined longitudinal relationships between alcohol use and depressed symptoms. Data on depressed mood were drawn from the depression subscale of the Child Behavior Checklist. Alcohol use was measured by the days of drinking alcohol in the past year. We estimated a cross-lagged SEM model to test the relationships between depressed mood and alcohol use at a single cohort group in two different waves (i.e., ages 15 and 18).

Model fit indices, (except χ^2) suggested adequate fit for both the measurement ($\chi^2(349)=696.04$, $p=.000$; CFI&TLI=.95; WRMR=1.22) and structural models ($\chi^2(479)=592.20$, $p<.001$; CFI=.97; TLI=.96; RMSEA=.02). The findings from the measurement model supported the one-factor structure as appropriate, which is consistent with the previous studies. There was a weak correlation between depressed symptoms at ages 15 and 18 in the CFA model ($r=.33$, $p<.001$), whereas it has a strong coefficient in the structural model ($\beta=.81$, $p<.001$). Depressed mood and alcohol use at age 15 were associated with further increases in those behaviors at age 18. Depressed mood at age 15 were associated with lower levels of alcohol use at age 18, whereas alcohol use in mid-adolescence was not affect the level of depressed mood in the late-adolescence.

Consistent with previous studies, prior depressed symptoms and alcohol use are associated with later depressive mood and alcohol consumption. Alcohol use contributed to a strong relationship between depressive mood at ages 15 and 18. The results of this study differ from others in that it appears that depressed youth may not choose drinking as a way to cope with depressive symptoms. This may be a counter-argument for the prevalent notion of ''self-medication''. Further studies should consider a more comprehensive developmental model of depression and alcohol use and gender differences to clarify the relationships between these problems.

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CHILD MALTREATMENT, ALTERED SELF-CAPACITIES, COPING MOTIVES, AND ALCOHOL PROBLEMS IN A SAMPLE OF EMERGING ADULT WOMEN

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The maltreatment of children is a common and costly problem with consequences for its survivors throughout the lifespan, including alcohol abuse and dependence. Recently, researchers have begun to examine the specific relationship between CM, alcohol use and alcohol problems during emerging adulthood, a transitional period marked by identity development, instability, and involvement in high risk behaviors, including substance use (Arnett, 2000; 2010). For emerging adult women who have experienced CM, this developmental stage may be particularly difficult due to impairments in three primary areas, collectively referred to as self-capacities: identity development, affect regulation and interpersonal relationships (Briere, 2000; 2002; Briere&Rickards, 2007). In addition, the relationship between these primary areas of functioning and alcohol use may be heightened among young women who drink to cope with negative affect. The purpose of the current study was to explore the psychological mechanisms that underlie the link between CM, alcohol use and alcohol problems in a sample of young women. Participants were 81 young women making the transition out of the child welfare system who completed questionnaires assessing: alcohol and other drug use and problems, drinking motives, and difficulties in affect regulation, identity development and interpersonal relationships (Inventory of Altered Self-Capacities; IASC; Briere, 2000). Preliminary analyses revealed significant relationships between CM and several of the IASC subscales, particularly those related to difficulties with identity and affect control. In addition,coping motives were associated with difficulties in interpersonal relationships, identity and affect control, and with alcohol problems. Finally, with the exception of identity impairment, all of the altered self-capacities were associated with alcohol problems. Separate hierarchical regression analyses examined the contribution of coping motives to alcohol problems over and above CM history and each of the three IASC domains. Results highlight the significant contribution of coping motives (R^2 change ranging from .14-.16) even when accounting for CM and other important CM-related psychological mechanisms.

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A STUDY OF THE RELATIONSHIP BETWEEN PARTICIPATION IN ALCOHOLICS ANONYMOUS AND ANXIETY

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Evidence exist that anxiety disorders precede alcoholism in over 90% of alcoholics and individuals with alcohol related disorders may use alcohol to self-medicate comorbid anxiety disorders (Ham, 2009; Schmidt, Buckner, & Keough, 2007). Understanding how treatment of alcoholism impacts anxiety may provide information for the development of more effective treatment modalities for alcohol related disorders. Alcoholics Anonymous (AA) has been established as an important psychosocial intervention for the treatment of alcohol related disorders (Groh, Jason, & Keys, 2008). However, due to the anonymous nature of the AA program, there is little research that explains who it will benefit or why it is effective.
The goal of the present study was to explore the relationship of AA participation with symptoms of anxiety. It was hypothesized that continuous long-term participation in AA (5+ years) would be associated with lower levels of anxiety compared to short-term participation (>5 years).
Participants were recruited using a social media website (i.e. individuals who "liked" pages related to AA received an advertisement for participation in a study investigating AA). The study consisted of 314 participants who self-identified as a recovering alcoholic and met criteria for 'problem drinker' measured by the Brief Michigan Alcohol Screening Test. Participants also completed the Mood and Anxiety Symptom Questionnaire and the Social Interaction Anxiety Scale.
Bivariate correlations found participants with 0-5 years of AA participation reported significantly higher levels of social anxiety, anxious arousal, and depression compared to participants with 6+ years. Length of continuous sobriety was highly correlated with regular attendance of A.A. meetings.
The results of this study support the research hypothesis that predicted lower levels of anxiety with longer participation in AA. These results support the research hypothesis and suggest that the structure of the AA program provides a safe supportive environment that potentially facilitates aspects of exposure therapy for anxiety in social situations. These results provide avenues for future research to further explore how treatment approaches that utilize integrated interventions for both symptoms anxiety and alcoholism may improve the overall efficacy of treatment for alcohol related disorders.

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PSYCHOMETRIC CHARACTERISTICS AND UTILITY OF THE SOCIAL ANXIETY DRINKING SCALE

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Introduction: The comorbidity between social anxiety disorder (SAD) and alcohol use disorders (AUD) is well-established. Theory and research in this area have pointed to the central importance of drinking to cope in understanding joint SAD-AUD, yet validated assessment options for this key variable are limited. Toward this end, we describe the psychometric characteristics and clinical utility of the Social Anxiety Drinking Scale (SADS). The SADS is a self-report survey of the deliberate use of alcohol to cope with social anxiety, with stem and follow-up questions grouped across three timeframes (before, during, and after social situations).
Method: Assessment batteries were completed with 109 treatment-seekers from three university-based outpatient substance use treatment clinics, as part of a parent study of the impact of anxiety on treatment participation. Diagnoses were obtained in a subsample of 55 participants using the Structured Clinical Interview for DSM-IV. To test convergent and discriminant validity, correlations with established measures similar and dissimilar to the SADS were compared across three domains (drinking motives, alcohol expectancies, and psychiatric symptoms). The clinical utility of the SADS was examined via classification statistics measuring the ability of the three stem items to separate individuals with and without comorbid SAD-AUD.
Results: Convergent-discriminant analyses showed a pattern of graded correlation coefficients, with higher correlations between the SADS stem items and similar measures, compared to correlations with dissimilar measures. This pattern was found both across (mean convergent r = .57 > mean discriminant r = .31) and within instrument domains (mean convergent r = .58 > mean discriminant r = .47). Classification analyses showed that the three stem items had good sensitivity (.80 - .93), but mixed specificity (.53 - .73) in identifying comorbid individuals. Receiver operating characteristic analyses showed areas under the curve for the stem items = .71 to .76.
Conclusion: The SADS has desirable psychometric properties supporting its use as a measure of drinking to cope with social anxiety. Also, stem items assessing the presence of drinking to cope with social anxiety before, during, and after social situations may be useful as screening questions to identify individuals with comorbid SAD-AUD among those seeking outpatient substance use treatment.

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DOES EXTRAVERSION PREDICT SUBSTANCE USING BEHAVIOR IN ALCOHOL DEPENDENT INDIVIDUALS?

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Extraversion, a biologically-based personality factor, appears to be a key factor in the engagement in alternative pleasant activity in patients with substance use disorders. Yet a controversy exists regarding whether extraversion is a unitary construct; it has been suggested that the extraversion dimension may also contain sociability and impulsivity components. Building upon this assumption it has been posited that impulsivity, characterized by a loss of inhibitory control, plays a prominent role in the development and maintenance of addiction. The current study hypothesized that extraversion would not only predict non-substance related activities, but also substance-related activities. The present research examined the impact of extraversion on the rewarding value of both alcohol/non-alcohol related activities, and subsequently their activity ratios (proportion of substance-free activities and substance-related activities), all in terms of frequency and enjoyability as proximal indices of reinforcement. Fifty-two actively drinking alcohol dependent patients who were admitted for inpatient treatment and 32 healthy controls were recruited from the same community; Utrecht, the Netherlands. These participants completed the extraversion scale of the NEO-FFI, the Dickman Impulsivity Inventory (DII), and an adapted version of the Pleasant Activity List (PAL). It was found that extraversion and functional impulsivity were moderately correlated, but the correlation between extraversion and dysfunctional impulsivity was not statistically significant. In the collapsed sample, extraversion was positively correlated with frequency and enjoyability scores of substance-free activities and both the frequency and enjoyability ratio indices. However, extraversion was virtually unrelated to substance-related indices. Functional impulsivity was positively correlated with the frequency and enjoyability scores of substance-free activities and both ratio indices, while it was negatively related to these outcomes on substance-related activities. Dysfunctional impulsivity was positively related to substance-related activities, but virtually unrelated to substance-free activities. Moreover, dysfunctional impulsivity was negatively linked to both ratio indices. Thus, our hypothesis was not confirmed. Although extraversion may contain some aspects of impulsivity (i.e., functional), extraversion clearly appears to be linked to non-substance related activities.

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THE IMPACT OF SEXUAL ASSAULT ON THE PREDICTION OF EXTERNALIZING AND INTERNALIZING BEHAVIORS FROM PERSONALITY

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Sexual assault is a considerable source of concern for clinicians and researchers. For some women, the experience of being sexually assaulted leads to increases in problem drinking behavior; for other women, the experience of being assaulted leads to increases in internalizing distress like depression or anxiety. It is possible that pre-assault personality traits interact with a sexual assault to predict internalizing or externalizing distress; this study tested such a model. We hypothesized that negative urgency will interact with sexual assault to predict problem drinking but not anxiety or depression, while trait anxiety and depression will interact with sexual assault to predict anxiety or depression but not drinking. We surveyed 759 women during the summer prior to their freshman year at a large public university. When asked about any sexual assault since the age of 14, 14% reported unwanted touching, 5.7% reported attempted intercourse, 4.6% reported being verbally pressured into intercourse, and 8.4% reported being forced into intercourse. Of all women surveyed, 38.3% reported experiencing at least one drinking problem, ranging from having a hangover after drinking to being arrested while drinking. In a cross-sectional linear regression, drinking problems were only significantly predicted by negative urgency (β=.28, p<.01) and previous sexual assault (β =.28, p<.01); however, sexual assault alone was no longer predictive when the interaction between negative urgency and sexual assault was included (β =.54, p<.01). Similarly, internalizing distress (clinical anxiety and depression) was only significantly predicted by trait anxiety and depression (β =.55, p<.01) and sexual assault (β =.15, p<.01); again, sexual assault was no longer predictive when the interaction between trait anxiety and depression and sexual assault was included (β =.51, p<.01). These results suggest that people who are high on negative urgency, an externalizing personality trait, are more likely to exhibit drinking problems than clinical depression or anxiety, especially after a sexual assault. Also, people high on internalizing personality traits, such as anxiety and depression, are more likely to be high on measures of clinical anxiety and depression and not of drinking problems, especially after experiencing a sexual assault. The current results will be of great use when determining the best recourse for survivors of sexual assault who differ on measures of personality traits.

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THREE-YEAR TRAJECTORIES OF DRINKING BEHAVIOR IN A SAMPLE OF ALCOHOLICS
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Aims. To identify trajectories of drinking behavior change over 3 years in a sample of adults with alcohol dependence.
Methods. Secondary analyses of data from the Life Transitions Study (LTS) were carried out. The LTS is a longitudinal survey of 364 individuals with SCID-verified alcohol dependence. Respondents were followed for 2½ to 3 years, with in-person interviews every 6 months. The sample was 66% male; about 82% Euro-American, 10% African-American, and the remainder other ethnicities, including self-identified multi-ethnicities; mean age was 44 years and mean education was over 14 years. To identify drinking trajectory classes, a zero-inflated Poisson model was specified for drinks per drinking day over the past 90 days at T1-T6.
Results. Results from latent class growth analyses indicated that a 4-class solution was optimal. We used the intercepts and slopes to label the four trajectory classes: 1) the Moderate Intercept-Stable Drinking group (39.6%) started with a moderate level of drinking (about 4 drinks per drinking day) that remained relatively stable over time; 2) the High Intercept-Heavy Drinking group (25.2%) started with a high level of drinking (about 13 drinks per drinking day) that declined initially then remained relatively stable and high (about 10 drinks per drinking day) over time; 3) the High Intercept-Stable Abstinence group (24.0%) started with a high level of drinking (about 9 drinks per drinking day) and reported abstinence starting at 6-months post-baseline and continuing for the duration of the study; and 4) the High Intercept-Steep Decline group (11.1%) had the highest level of drinking at baseline (about 20 drinks per drinking day) followed by a rapid decline to 2 drinks per drinking day at 1-year post-baseline, eventually reaching abstinence starting at 2.5-3 years post-baseline.
Conclusions. There is substantial variability in drinking behavior change over time among treated and untreated alcoholics, but discernible patterns can be identified. Consistent with previous work, some groups show systematic declines in alcohol involvement over time. Yet a high-risk trajectory group characterized by heavy drinking that remained relatively stable over time was also identified. Targeting this high-risk group could enhance screening and treatment efforts.
This project was supported by Grant R01 AA014442 from the National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health.

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ASSOCIATION BETWEEN ILLNESS-SPECIFIC WORRY AND COMORBID ALCOHOL ABUSE IN HIV-POSITIVE OUTPATIENTS
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Alcohol abuse remains prevalent in HIV-positive patients, compared to the general population, in spite of its known negative impact on medication adherence and effectiveness, and overall disease progression. To date, the reasons why patients living with HIV are more prone to engage in risky drinking remain poorly understood. This study sought to test the hypothesis that HIV-positive patients use alcohol to cope with affective symptoms by examining the strength of the association between alcohol abuse and illness-specific worry.
Participants (n=110; 36.4% female, 60.0% African-American) completed an anonymous self-report questionnaire assessing illness-specific worry using the recently developed Worry Inventory Specific to HIV/AIDS (WISH). The WISH is a four-factor measure indexing worries about daily "Coping" with and the long-term "Impact" of living with HIV, as well as the effects of HIV on "Intimacy" concerns and "Relationships." Alcohol abuse was assessed using the CAGE screen.
Mean (i.e. divided by the total number of survey items, range: 0–10) total worry scores (M=4.41, SD=2.49) suggested the presence of significant illness-specific concerns in the patients surveyed. Mean (i.e. divided by the total number of items loading on each of the four factors, range 0–10) factor scores indicated that worries about daily "Coping" were most pronounced (M=5.17, SD=3.09), followed by concerns about "Intimacy" (M=4.83, SD=3.11), the long-term "Impact" of HIV (M=4.36, SD=2.78), and "Relationships" (M=3.75, SD=3.03). About one quarter of respondents (24.1%, n=21) screened positive for alcohol abuse, as per the CAGE. These patients reported significantly more overall worry (p=.02), as well as significantly higher ratings on the "Impact" (p=.01) and "Intimacy" (p=.03) subscales, compared to respondents who did not indicate problems related to alcohol use.
Findings suggest a significant positive association between illness-specific worry and comorbid alcohol abuse in HIV-positive patients. Further analysis is needed to determine the direction of this association. Results point to specific areas of concern related to living with HIV/AIDS that may put patients at an increased risk for developing and/or maintaining risky drinking behaviors. Addressing these concerns in treatment may be a useful step in preventing or reducing the negative effects of alcohol misuse on HIV disease progression.
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AN EXPERIMENTAL EXAMINATION OF THE EFFECTS OF EATING RESTRAINT ON DRINKING FOLLOWING MOOD INDUCTION
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Restrained eaters frequently report consuming more alcohol than non-restrained eaters on retrospective self-report measures of alcohol consumption, such as the Timeline Followback (TLFB; Stewart et al., 2000). One possible reason for greater drinking among restrained eaters is drinking to regulate negative affect (Anderson et al., 2006). However, eating restraint also is associated with self-report of drinking *less* (i.e., restraining their drinking) due to weight and shape concerns (Robinson et al., 2011), raising the question of whether eating restraint truly is associated with greater drinking – potentially in an effort to regulate negative affect. In this study we examined if eating restraint affected drinking quantity during an experimental task following negative mood induction. Male (n = 82) and female (n = 62) 21- to 30-year-old social drinkers completed self-report surveys of drinking (30 day self-report TLFB) and eating restraint, as well as an experimental drinking task, preceded by a negative, neutral, or positive mood-induction. A hierarchical regression, controlling for gender, body mass index, and drinking quantity, was conducted to examine if mood induction and eating restraint interacted to affect total alcohol consumed. Overall, eating restraint was not associated with increased alcohol intake (β = -.05, p = .63). Further, there was no interaction between eating restraint and the mood conditions, ΔR^2 = .002, p = .851, suggesting eating restraint did not affect the amount of alcohol consumed following either negative, neutral, or positive mood inductions. To our knowledge, this is the first study to examine the association between eating restraint and drinking during an experimental alcohol administration study. The results suggest individuals higher in restraint do not drink more during an experimental task and do not drink more following a negative mood induction. One reason for this may the time-limited nature of the experimental task. Those higher in restraint may initially restrain their drinking; but given more time they may drink more, potentially due to intoxication overriding weight or shape concerns. Although previous findings suggest eating restraint may be associated with greater drinking to regulate affect, our findings do not support this.

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A COMPARISON OF METHODS FOR INDUCING CRAVING FOR ALCOHOL
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The purpose of the present study was to compare methods for inducing craving for alcohol in response to stress. These methods comprise the Trier/Cue Reactivity (Trier/CR) paradigm and guided imagery scripts (Scripts) paradigm. Both methods evaluate change in stress and craving over time, following presentation of a stressor.
The sample included 52 individuals, all of whom were diagnosed with alcohol dependence, participating in a four week inpatient study at NIAAA. All subjects underwent both paradigms, and subsequently completed the same questionnaires to measure both stress and craving for alcohol. The Trier/CR procedure was completed during the third week, while the scripts were presented over three days during the fourth week. Baseline measures were gathered and biological and behavioral data collected at regular intervals up to 90 minutes post-stressor. Procedures were carried out by trained research assistants; scripts were edited by a single individual to ensure fidelity. Outcomes included the Alcohol Urges Questionnaire (AUQ), Spielberger State Trait Anxiety Inventory (state version, STAI), Subjective Units of Distress Scale (SUDS), and serum levels of ACTH and cortisol.
Results indicated an increase in alcohol craving during both the Trier/CR and Scripts as measured by the AUQ. Peak craving was observed at 40 minutes during the Trier/CR, after the cue reactivity procedure, and at the 5 and 15 minute time points during the Scripts. For the Scripts, there was also a significant main effect of script type, with both the alcohol and stress scripts inducing higher levels of craving than the neutral script. Similar patterns were found for anxiety (STAI) and subjective stress (SUDS), which both increased in response to the Scripts and Trier/CR. Only the stress script induced higher levels of anxiety and stress ratings compared to the neutral scripts. Although the Trier/CR resulted in significant increases in ACTH and cortisol, the Scripts did not elicit any changes in the endocrine stress response. We found that both methods increased stress and craving for alcohol, but only the Scripts paradigm affords the ability to decouple craving related to stress from that related to alcohol cues. Moreover, the lack of endocrine response during the Scripts procedure demonstrates a dissociation of HPA axis activity and craving. These findings suggest different mechanisms may be responsible for cravings, thus necessitating specific interventions to reduce cravings.

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ASSESSING THE BIS-PATHWAY TO ALCOHOL USE: MEASURING THE RELATIONS BETWEEN ANXIOUS MOOD, IMPULSIVE RESPONDING AND IN-LAB DRINKING

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Background: Gray's Reinforcement Sensitivity Theory posits that persons with a strong behavioural inhibition system (BIS) over-attend to threat, leading to high anxiety and the inhibition of behaviour. The role of elevated BIS in alcohol use is complex, as anxiety may lead to self-medication drinking while attention to threat may be a protective factor. For a high BIS person to misuse alcohol, they must no longer focus on alcohol threat cues. High BIS individuals, when anxious, may temporarily disregard alcohol's possible negative outcomes, and thus may act more impulsively in drinking contexts (e.g., binge drinking). The goal of the current study was to test this possibility.
Hypotheses: Following an anxious mood induction, *only* high BIS persons will show increases in impulsive responding on a computer task. We further expected that these increases would be positively correlated with in-lab alcohol consumption.
Method: 165 students were randomly assigned to a positive or anxious musical mood induction condition. At baseline, participants completed a self-report measure of BIS strength. A Go/No-Go Task was administered pre/post mood induction to assess changes in impulsivity. On the Go/No-Go Task, participants had to learn by trial and error to press a key when presented with reward stimuli, and learn to withhold responses for punishment stimuli. More commission errors (responding to punishment targets) and faster reaction times on reward trials indicate an impulsive response style. Next, alcohol consumption was assessed using a taste-rating task. Peak blood alcohol level (BAL) was the primary measure of consumption.
Results: Simple slopes analyses revealed that a high BIS was not significantly associated with increased impulsive responding on the Go/No-Go Task in the anxious condition. Further, pre-post differences in impulsivity were not significantly correlated with BIS and peak BAL.
Conclusions: Our hypotheses were not supported. However, our results have implications for improving the laboratory assessment of BIS in alcohol use. A more ecologically valid anxious mood induction may be needed to push high BIS individuals to disregard negative outcomes and behave impulsively. Also, the present study suggests that shifts in impulsivity may not be central to the BIS-pathway to alcohol use. Consistent with the extant literature, there may be other individual difference factors (e.g., coping styles) that moderate the relation between BIS and drinking.

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UNDIFFERENTIATED AFFECT AND IMPULSIVITY AMONG DRINKERS WITH AFFECTIVE DYSREGULATION

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Previous research has suggested that an inability to describe or differentiate emotions is a risk factor for alcohol use (Kashdan et al., 2010). Using ecological momentary assessment (EMA), undifferentiated or ''mixed'' negative affective states were examined as a possible risk factor for alcohol consumption in a sample of individuals characterized by emotional dysregulation. Specifically, 91 drinkers with borderline personality disorder (BPD) or depressive disorder diagnosis carried around an electronic diary for 28 days and reported on their mood and impulsivity approximately 6 times per day (in response to random prompts). Impulsivity was assessed using 6 binary items (i.e, ''since the last prompt, I have acted on impulse''). Mixed negative affective states were defined as the intraclass correlation coefficient of fear, sadness, and hostility ratings across the 28 days for each subject (at the trait level). The standard deviation of these ratings at each assessment was used to represent mixed negative affective states at the momentary (or state) level. Higher intraclass correlation coefficients meant less differentiation between different affective states. In contrast, higher standard deviations meant more differentiation between affective states. There was no significant difference between the BPD and DD drinkers in terms of intraclass correlation coefficients (trait mixed affect). Using hierarchical linear modeling, mixed affect was used to predict momentary impulsivity. State and trait mixed affect were entered as random and fixed effect predictors, respectively. Diagnostic group was also entered into the model. Results suggest that state mixed affect (standard deviation) significantly predicted self-reported impulsivity at each assessment. There was a trend for a significant interaction between trait and state mixed affect. However, the main effect of trait mixed affect (intraclass correlation) was not a significant predictor of impulsivity. Thus, the results of the current study suggest that from moment to moment, affectively dysregulated drinkers are more likely to behave impulsively when they experience undifferentiated or mixed affect. Further, drinkers who experience more mixed affect overall are possibly even more likely to behave impulsively in a mixed affect experience. These findings extend previous research and suggest that undifferentiated emotion among drinkers can lead to other risky behaviors in addition to increased alcohol use.

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SELF-REPORTED DISABILITY IN RELATION TO ALCOHOL AND OTHER DRUG USE AND MENTAL HEALTH AMONG EMERGING ADULTS: AN INTERNATIONAL COMPARISON

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The ATLAS Project is a longitudinal study of 17- to 19-year-old high school students in the US and Sweden. The present study includes baseline data from 2867 students (77.8% from Sweden, 22.2% from US) and evaluates the relationships among self-reported disabilities, alcohol use, other substance use, and psychosocial adjustment. There were 114 (4.6%) ''hard-of-hearing'' (HH) students, 129 (5.2%) reported visual disabilities, 33 (1.3%) reported motor disabilities, 223 (9.0%) reported a reading/writing disability, and 97 (3.6%) reported they had ''other'' disabilities. Of these, 70 (14.1%) reported more than one disability. Presence of a disability was significantly higher among Sweden students (<!–[endif]–>^{2}(1)=19.93, p< 0.001), with 19.1% of Sweden students and 11.5% of US students reporting at least one disability. Reporting any type of disability was associated with significantly greater alcohol use frequency, intensity, and related problems (all p < 0.02), significantly more mental health symptoms and conduct problems (p < 0.005), and significantly greater likelihood of illicit and prescription drug use (all p < 0.001). With respect to specific disabilities, individuals with motor disabilities reported the highest levels of alcohol use and mental health symptoms, whereas individuals who reported ''other'' disabilities had higher rates of illicit drug use and conduct problems. Further, there was a significantly positive correlation between the number of disabilities and intensity of alcohol use, mental health symptoms, conduct problems, illicit and prescription drug use, and alcohol related problems (all p < 0.001). The association between conduct problems and disability (any disability and number of disabilities) was moderated by country of origin, gender, and drinking for coping reasons on the Drinking Motives Questionnaire. Participants in Sweden, males, and those who drank for coping reasons were more likely to report a relationship between disability and conduct problems (p < 0.001). Participants who drank for coping reasons were also more likely to report a relationship between disability and alcohol related problems (p=0.001). These findings indicate students with disabilities are an important risk group for preventive interventions for alcohol, substance, and mental health problems, and may benefit from interventions which target healthy coping skills. This research was supported by NIAAA # 5R01AA018276 awarded to Drs. Larimer & Berglund.

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EFFECTS OF DRINKING CONTEXT ON THE EFFECTIVENESS OF A PLACEBO ALCOHOL MANIPULATION

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A recent meta-analysis by Schlauch et al. (2010) indicates that placebo manipulations in alcohol administration studies demonstrate limited effectiveness, particularly at higher breath alcohol concentrations (BrACs). On measures of subjective intoxication, the mean effect size for differences between alcohol and placebo conditions was 1.44. This is an important issue as ineffective placebo manipulations make it difficult to determine if differences in behavioral outcomes between placebo and alcohol conditions are a result of alcohol expectancies or pharmacological alcohol effects. One proposed method for improving the effectiveness of placebo manipulations is to use naturalistic drinking contexts (e.g. simulated bars). Although there are a number of simulated bar labs in the U.S., systematic evaluation of the impact of a naturalistic context on placebo manipulations has not been conducted. Unfortunately, the meta-analysis by Schlauch et al. (2010) was unable to examine this potential moderator of placebo response, because only 4 of the 44 studies reviewed were conducted in simulated bar labs. The current study addresses this gap in the literature using a 2 (alcohol vs. placebo) by 2 (traditional lab vs. simulated bar) design with subjective intoxication (participant's estimates of their BrAC levels) as the outcome measure. Participants were 146 young adult social drinkers (Mean age = 22.6 (SD = 2.26); 42.2% female) who were randomly assigned to one of the four conditions; all participants consumed their drinks in groups of 2 to 4. A 2 X 2 ANCOVA with gender as a covariate identified a significant beverage by context interaction (p = .02). When the interaction was decomposed by context, the effects size for the difference between alcohol and placebo conditions within the traditional lab context was 1.58 (Cohen's d), consistent with the average effects size identified in the Schlauch et al. meta-analysis. In contrast, within the simulated bar context, the effect size was only .54, suggesting a much stronger placebo response. In terms of percentage response to placebo relative to alcohol, there was a 39.5% response in the traditional lab context, and a 69.5% response in the simulated bar context. The results demonstrate a robust effect of physical context on placebo response and indicate that the use of a simulated bar context can yield a highly effective placebo manipulation even at BrACs approaching the legal limit for intoxication.

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GENDER DIFFERENCES IN ATTENTIONAL BIAS TO ALCOHOL-RELATED STIMULI IN ALCOHOL-DEPENDENT ADULTS

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Growing evidence indicates that gender is an important variable in several aspects of alcohol abuse. One vulnerability factor that is highly predictive of relapse but has yet to be studied in men and women is sensitivity to alcohol-related cues. The purpose of the present study was to examine gender differences in attentional bias to alcohol-related cues. Sixty men and forty women receiving inpatient treatment for alcohol dependence were compared on a computerized dual-task procedure that consisted of digit and word (alcohol-related or neutral) classification trials. During experimental trials digits and words were presented simultaneously. Participants were instructed to first classify the centrally presented digit as even or odd by pressing the appropriate computer key and to subsequently classify the peripheral stimulus as a word or nonword (anagram); half of the words were alcohol-related and the other half were neutral (i.e., gemstones). Reaction time (in milliseconds) in classifying stimuli and the number of classification errors were recorded for each participant. All participants took longer to classify alcohol-related words (M = 600 ms) compared to neutral words (M = 565 ms) suggesting that the meaning of the alcohol words caused disruption in task performance. However, this effect was significantly related to gender: women took significantly longer to make word/nonword decisions to alcohol words (M = 619 ms) compared to neutral words (M = 528 ms) whereas men did not show this effect (M = 588 vs. 591 ms). There were no gender differences in RTs to classify digits as a function of word type. With respect to classification errors, men made significantly more errors than women in classifying neutral words (M = 0.67) as opposed to alcohol words (M = 0.22) in the lexical decision task. The two groups did not differ on any other error types. Taken together, the results suggest that women may be more likely than men to show an attentional bias toward alcohol-related stimuli. The relationship between gender and sensitivity to alcohol-related cues lends support to the development of gender-specific treatment strategies in alcohol dependence.

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GENDER DIFFERENCES IN THOUGHT CONTROL STRATEGIES AND THEIR RELATION TO IMPLICIT ALCOHOL COGNITIONS AMONG SOCIAL OR HEAVY DRINKERS

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Drinking patterns and reasons for drinking among men and women differ. For example, women are more likely to drink in response to some negative moods (Sell et al., 2001). Certain aspects of gender role norms may predispose men and women to use alcohol differentially to cope with emotional distress. For instance, men are highly motivated to avoid expressing emotion and may prefer to drink as a method of coping with emotional distress (Wang et al., 2009). In contrast, women are motivated to express emotions with others, and may drink alcohol when interpersonal problems limit open emotional expression. The aim of this research was to examine gender differences in ways of controlling unpleasant thoughts and their relation to alcohol-approach attitudes using an implicit association task. The sample consisted of 69 social to heavy drinking men and women. Participants completed the Thought Control Questionnaire (TCQ), which measures ways of dealing with unwanted thoughts, including: engaging in distraction, engaging in cognitive punishment, re-appraisal of negative thoughts, worry, and social connection. Participants also completed an Implicit Association Task (IAT) designed to measure implicit alcohol cognitions by measuring the strength of the association between alcohol/water pictures and ''approach/avoidance'' words. Gender was significantly and negatively correlated with TCQ social (r=-.344, p=.004) and TCQ reappraisal (r=-.273, p=.022), suggesting that women were more likely than men to cope with unwanted thoughts by talking to others and cognitively re-evaluating thoughts. There was also a significant cross-over interaction of Gender X Distraction (β=*1.355*, p=.025). Explication of the interaction showed that that the use of distraction as a method of coping with unwanted thoughts was positively related to motivation to drink for women (β=.333); but negatively related to motivation to drink in men (β=-.235). Distraction coping strategies are related to increased risk for drinking motivations among women, but associated with decreased risk among men, counter to expectations. Treatment programs should be developed to educate men and women about how gender-relevant coping strategies in response to unpleasant thoughts may influence alcohol use behavior.

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INCENTIVE SENSITIZATION THEORY IN HEAVY AND LIGHT SOCIAL DRINKERS: A PROSPECTIVE STUDY

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The incentive sensitization theory of addiction proposes that repeated drug use sensitizes the neural systems that mediate the motivational process of incentive salience, resulting in a disassociation of motivational (wanting) effects for a drug and hedonic (liking) effects. Little support for this theory has been dedicated to prospective, alcohol-based research in non-dependent humans. The Chicago Social Drinking Project (CSDP) examined alcohol liking and wanting during initial alcohol challenge testing and again at a five-year re-test. The analysis included the n=156/190 (82.1%) of participants who returned after five years for retest sessions in CSDP. At baseline, participants (average age 25.6) met criteria for either heavy social drinking (n=86, 57% male, 10+ drinks/week, 1-5 binge episodes weekly) or a light drinking control group (n=70, 49% male, <5 drinks/week, rare/no binges). In the laboratory, each participant consumed a high dose of alcohol (0.8 g/kg) or placebo dose beverage under double-blind conditions and in random order. Visual analogue scales (scored 0–100) were administered for ratings of ''like'' and ''want more'' of the beverage at peak breath alcohol concentration (+60 min. following consumption). Five years after the original testing, participants returned to the laboratory for two repeat laboratory sessions under identical conditions as baseline. At original testing, alcohol increased ratings (Δ from placebo) of both liking (+13.4) and wanting (+22.4) in heavy drinkers (ps<0.001), but not in light drinkers (liking: +1.3; wanting: +6.1, ps=ns). Similarly, at five-year re-test, alcohol continued to produce significant liking (+10.1) and wanting (+27.3) increases relative to placebo in heavy drinkers (ps<0.001) but not in light drinkers (liking: -4.1; wanting: +1.3, ps=ns). Across both periods, positive correlations between ratings of liking and wanting after alcohol were evident for both groups (rs=0.51–0.75, ps<0.001). Analyses of the changes in liking and wanting over time revealed increased wanting but decreased liking in heavy drinkers, and decreases in both wanting and liking in light drinkers (F=5.34, p< 0.05). In sum, these preliminary longitudinal results support the development of incentive salience among young adult heavy drinkers over time.

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FURTHER VALIDATION OF AN ALCOHOL PURCHASE TASK FOR ASSESSING THE INCENTIVE VALUE OF ALCOHOL

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In experimental research, one method of measuring the relative value of alcohol is an Alcohol Purchase Task (APT), which assesses estimated consumption of standard drinks at escalating levels of price and generates several different indices of value, such as Intensity (i.e., consumption when alcohol is free), Omax (i.e., maximum expenditure for alcohol), and breakpoint (i.e., first price suppressing consumption to 0). In the current study, we examined the relationship between these indices of demand for alcohol and the Quantity-Frequency subscale and Hazardous Drinking subscale of Alcohol Use Disorders Identification Test (AUDIT).

Participants were 964 individuals recruited for an assessment in one of two locations (Athens, GA; Aiken, SC). For this study, the primary sample comprised 728 drinkers (mean age of 29.8). Racial composition was: White (68.3%), African American (23.9%), mixed race (3.6%), Asian (2.7%), Other (1.0%), American Indian/Alaskan Native (0.5%). The gender composition was 60.4% male, 38.6% female, and 1.0% unreported. The mean total score on the AUDIT was 10.7.

Correlation analyses indicated significant, positive associations between the demand indexes of Omax and AUDIT-QF, r = 0.43, p <.01, as well as a significant relationship between Omax and AUDIT-HZD, r = 0.30, p <.01. Intensity showed the strongest, significant, positive association to AUDIT-QF, r = 0.52, p <.01, and AUDIT-HZD, r = 0.37, p <.01. Additionally, breakpoint showed significant positive associations with AUDIT-QF, r = 0.23, p <.01, and AUDIT-HZD, r = 0.16, p <.01. Demographic variables of race, pretax income, years of education, age, and sex were analyzed along the demand indices. Significant, negative associations were found between intensity and sex, r = -0.20, p <.01 (with females drinking less than males), and Omax and sex, r = -0.12, p <.01 (with females exhibiting lower maxima compared to males). No significant correlation (p <.01) was present in the other demographic variables along these indices of demand.

Multiple significant positive correlations between demand indices and both alcohol consumption and hazardous drinking support a robust relationship between these aspects of drinking and overvaluation of alcohol. Also, as predicted, female participants exhibited significantly lower demand as measured by Intensity and Omax. This study replicates previous findings and extends them to a larger, more diverse sample of adults.

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PSYCHOSOCIAL PREDICTORS OF IMPULSIVITY IN ALCOHOL-DEPENDENT PATIENTS

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Impulsivity is an important risk factor of severe course of alcohol dependence. However, the significance of environmental determinants of impulsivity has been underestimated. The aim of the study was to identify psychosocial factors increasing the level of impulsivity in alcoholics. Levels of impulsivity were measured in 304 alcohol-dependent patients. Stop-signal task was used to assess behavioral impulsivity, and Barratt Impulsiveness Scale to measure global and cognitive impulsivity. Correlations between impulsivity and psychosocial variables were examined. A significant association between level of impulsivity and severity of psychopathological symptoms were observed. Patients who reported childhood sexual or physical abuse, lower social support, more severe course of alcohol dependence were more impulsive, especially in cognitive domain. When entered into a linear regression analysis model, severity of alcohol dependence, psychopathology and childhood physical abuse remained significant. These results suggest that psychosocial variables are important factors associated with high levels of impulsivity in alcohol-dependent patients.

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DIMENSIONS OF IMPULSIVITY AMONG HEAVY DRINKERS, SMOKERS, AND HEAVY DRINKING SMOKERS: SINGULAR AND COMBINED EFFECTS

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Alcohol use and cigarette smoking commonly occur together. The role impulsivity may play as an underlying mechanism in alcohol use and cigarette smoking is of particular interest due to emerging evidence of it being a critical component across multiple forms of addiction. Impulsivity can be examined through several constructs including, risky decision-making, response inhibition, and delay reward discounting. Impulsivity and each of these specific constructs play significant roles in regards to the initiation of drug use, continued use despite negative consequences, and potential to relapse. This study used three behavioral tasks to measure risky decision-making (Balloon Analog Risk Test; BART), response inhibition (Stop Signal Task (SST), and delay reward discounting (Delay Discounting Task; DDT). This study aimed to advance research on impulsivity and substance use by parsing out the various components of impulsivity and examining them across three groups. The three participant groups consisted of heavy drinkers only (HD) (N =107), smokers only (S) (N=67), and heavy drinking smokers (HDS) (N=213). Following an initial phone screen, participants were invited to the laboratory for an in-person screening session in which they completed questionnaires, interviews, and neurocognitive tasks including the SST, BART, and DDT. Analyses revealed initial evidence of an additive effect of alcohol and nicotine use in delay reward discounting. Heavy drinking smokers displayed steeper delay discounting of small rewards than did both smokers only ($p < .05$) and heavy drinkers only ($p < .05$). This additive effect of smoking and drinking was not observed for risky decision-making and response inhibition, suggesting specificity of the effects for delay reward discounting. This study's findings indicate that those who both drink heavily and smoke cigarettes daily have increased delay reward discounting, than those in the S and HD groups. This group of heavy drinking smokers tends to value smaller, immediate rewards over larger, more distant rewards. This is the first study of its kind to investigate the combined effects of smoking and drinking on dimensions of impulsivity. Future studies should examine these constructs longitudinally, as well as incorporate genetic and/or a neuroimaging component to these group comparisons.

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ALCOHOL-RELATED STIMULI REDUCE BEHAVIORAL CONTROL IN DRINKERS

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Poor behavioral control and heightened attentional bias toward alcohol-related stimuli have independently received considerable attention in regard to their roles in alcohol abuse. Theoretical accounts have begun to speculate as to potential reciprocal interactions between these two mechanisms that might promote excessive alcohol consumption, yet experimental evidence is lacking. For the current study, we sought to integrate these two lines of research through the development of a novel laboratory task that examines the degree to which alcohol cues serve to disrupt mechanisms of behavioral control. Fifty adult drinkers were recruited to perform the Attentional Bias-Behavioral Activation (ABBA) task. The ABBA task, an adaptation of traditional cued go/no-go tasks, is a reaction time model that measures the degree to which alcohol-related stimuli can increase behavioral activation of a drinker and reduce the ability to inhibit inappropriate responses. Participants also completed a novel measure of attentional bias, the Scene Inspection Paradigm (SIP), that measures fixation time on alcohol content imbedded in complex scenes. As hypothesized, the proportion of inhibitory failures on the ABBA task was significantly higher following alcohol images compared to neutral images. Additionally, correlational analyses showed that heightened attentional bias on the SIP was associated with greater response activation following alcohol images on the ABBA task. These findings suggest that alcohol stimuli serve to disrupt mechanisms of behavioral control, and that heightened attentional bias is associated with greater disruption of control mechanisms following alcohol images.

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MOTIVATION DIFFERENCES BETWEEN ALCOHOLICS AND CONTROLS IN A MONETARY INCENTIVE EFFORT TASK

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Personality factors, and in particular motivation, have been implicated in individuals who are vulnerable to alcoholism. For this reason, we created a new fMRI paradigm, called ''Effort Task,'' to assess the motivation for efforts put forth to both win (gain trials) and avoid the loss (loss avoidance trials) of money in control subjects and alcoholic inpatients. In this task, participants were asked to press a button a certain number of times, as indicated by a cue. If participants pressed the button at least as many times as indicated, they received a reward of $0.50 in the gain trials, and they would avoid losing $0.50 in the loss avoidance trials. We also included a ''mystery'' condition where participants were unaware of how many presses were needed to win money (positive condition) or prevent the loss of money (negative condition). We predicted that alcoholic participants would be more sensitive to both rewarding and negative cues, and particularly in regions associated with decision making (frontal lobes) and emotion (insula).

To measure differences between alcoholics and controls, we used EPI fMRI images that were collected using a 3Tesla GE scanner. fMRI scans of 39 right-handed subjects, including 21 alcohol dependent participants (8 female) and 18 controls (9 female) were analyzed. Data processing was performed using the restricted (or residual, or reduced) maximum likelihood (REML) and mixed-effect multilevel analysis (MEMA) of AFNI (National Institute of Mental Health, created by R.W. Cox) for individual subjects and group analysis, respectively. Preliminary results confirm that there are significant differences in the BOLD response of alcoholics vs. controls in the Effort Task (corrected $p < 0.01$). When we looked at the feedbacks from winning in gain trials vs. losing in the loss avoidance trials, in a comparison of alcoholics vs. controls, there was more activation in alcoholics only in the right middle frontal gyrus. When we looked at winning in the positive mystery condition vs. losing in the negative mystery condition, we saw an increase in activation in the alcoholics in many areas, across the frontal right and left hemispheres. Based on this result, it seems that alcoholics use more brain activation in tasks with uncertain results than do controls. In the future, fMRI studies assessing connections between these regions and their relationship to motivation may be helpful to further understand the neurological effects of alcoholism.

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INHIBITORY CAPACITY IN EMERGING ADULT BINGE DRINKERS: INFLUENCE OF FACIAL CUES

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Binge alcohol consumption has been associated with alterations in cognitive functioning, behavioral self-control and the ability to ascribe emotional significance to stimuli. In the current study, response inhibition was examined in emerging adult binge alcohol drinkers and light alcohol drinkers, using two Go No Go (GNG) behavioral paradigms, one that required response inhibition to shapes and one that required response inhibition to threat or safety cues present in the expression of facial stimuli. Percent accuracy data for GNG trials were acquired from 8 binge drinkers (BD) aged 21.5 ± 1.1 years and 10 light drinkers (LD) aged 22.2 ± 1.5 years. For shapes GNG, although no group differences were observed, LD exhibited similar accuracy on Go and No Go trials, whereas BD performed worse on No Go trials than on Go trials (p=.020). For faces GNG, significantly better accuracy was observed on Go trials for safe faces than for threatening faces in both LD (p=.016) and BD (p=.028). For faces No Go trials, LD demonstrated better accuracy on threat (p=.038) and safe trials (p=.009) than BD, whereas BD performed worse on No Go Trials regardless of facial cue. BD displayed significantly faster reaction times on faces Go trials, regardless of facial cue (p<.05), but not on shapes Go trials. These findings suggest that binge alcohol consumption is associated with impaired inhibitory capacity particularly in the presence of facial cues of threat and safety. These data also indicate that while facial cues do not differentially influence the poor response inhibition observed in BD, the presence of a safe stimulus serves to enhance inhibitory capacity in LD. Thus, drinking pattern-related differences in the ability to discriminate and utilize social information may compromise inhibitory capacity in binge drinkers, which may in turn impair social decision-making. Supported by K01AA014651 & R01AA018153 (MMS).

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ANTICIPATORY DIFFERENCES BETWEEN ALCOHOL DEPENDENT SUBJECTS AND NORMAL VOLUNTEERS IN EFFORT TASK

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Personality factors, and in particular motivation, have been implicated in individuals who are vulnerable to alcoholism. For this reason, we created a new fMRI paradigm, called ''Effort Task,'' to assess the motivation for efforts put forth to both win (gain trials) and avoid the loss (loss avoidance trials) of money in control subjects and alcoholic inpatients. In this task, participants were asked to press a button a certain number of times, as indicated by a cue. If participants pressed the button at least as many times as indicated, they received a reward of $0.50 in the gain trials, and they would avoid losing $0.50 in the loss avoidance trials. We also included a ''mystery'' condition where participants were unaware of how many presses were needed to win money (positive condition) or prevent the loss of money (negative condition). We predicted that alcoholic participants would require more effort than controls in response to cues requiring greater effort and would likewise exhibit increased activation.
To measure differences between alcoholics and controls, we used EPI fMRI images that were collected using a 3Tesla GE scanner. fMRI scans of 39 right-handed subjects, including 21 alcohol dependent participants (8 female) and 18 controls (9 female) were analyzed. Data processing was performed using the restricted (or residual, or reduced) maximum likelihood (REML) and mixed-effect multilevel analysis (MEMA) of AFNI (National Institute of Mental Health, created by R.W. Cox) for individual subjects and group analysis, respectively.
When looking at the BOLD response, we saw increases in brain activation (corrected for number of button presses) in several brain regions including the right and left cingulate gyri, the right superior temporal gyrus, and the left insula, in the alcoholics compared with controls on the positive mystery condition (corrected $p < 0.01$). Despite increases in activation, the alcoholic subjects also earned less money on the task. This indicates that while alcoholic participants anticipated expending a greater amount of effort (as shown by the increased BOLD response) in response to the cues, they did not perform the required task as effectively as the controls. This in turn may indicate a delayed and diminished motor response to the targeted number of presses. In the future, we hope to use this information to further assess the motivational differences between alcoholics and controls in relation to planning and executing tasks.

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DUTCH STUDENT SURVEY: REASONS FOR ENERGY DRINK CONSUMPTION AND MIXING WITH ALCOHOL

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Introduction: Recent surveys raised concerns that students mix alcohol with energy drinks, to be able to consume more alcohol or to sober up. Aim of this survey was to assess reasons for energy drink consumption, alone and mixed with alcohol.
Methods: An online survey was conducted among Dutch students. In addition to demographic data and alcohol and energy drink consumption questions, several neutral and negative reasons for consumption of energy drinks, alone or mixed with alcohol, were assessed.
Results: Of N=6002 students who completed the survey, N=173 consumed energy drinks only (ED-group), N=917 consumed energy drinks and alcohol without ever mixing these (AED-group), and N=1239 occasionally combined energy drinks with alcohol (AMED-group). A total of N=2329 students consumed energy drinks. Reasons for consuming energy drinks (without alcohol) included 'I like the taste' (59%), 'To keep me awake' (54%), 'It gives me energy' (44%), 'It help concentrating when studying' (34%), 'It increases alertness' (29%), 'It helps me concentrate better' (21%), and 'It makes me less sleepy when driving (14%)'. Main reasons for mixing energy drinks with alcohol were neutral and included 'I like the taste' (81%), 'I wanted to drink something else' (35%), and 'To celebrate a special occasion' (15%). A minority of students reported negative reasons to consume AMED such as 'To get drunk' (8%), because 'It feels like energy drinks reduce the negative effects of alcohol' (7%), 'It feels like I can drink more alcohol' (6%), 'To prevent getting drunk' (4%), 'To sober up' (3%), or 'To prevent next-day hangover' (2%). Reasons for mixing alcohol with energy drinks are not related to overall alcohol consumption. The alcohol consumption pattern (frequency and quantity) of a subset of the AMED group (N=257) that acknowledged to mix alcohol with energy drinks for 'negative' reasons did not differ from those who consume AMED for neutral reasons (N=982). When compared to occasions when consuming alcohol alone, both groups show a significant decrease in alcohol consumption on occasions when they consume AMED.
Conclusion: The majority of students who consume energy drinks (without alcohol) do so because they like the taste, to keep them awake or because it gives them energy. Neutral reasons are more important than negative ones for mixing alcohol with energy drinks. Reasons for mixing are not related to overall alcohol consumption.

1108

DEVELOPMENT OF A NEW MEASURE REGARDING EXPECTANCIES CONCERNING ENERGY DRINKS AND MIXING ALCOHOL WITH ENERGY DRINKS

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Mixing alcohol and energy drinks has become the new trend on college campuses (Oteri, Salvo, Caputi, Calapai, 2007; Kapner, 2007). Yet, little is known regarding why college students consume so many energy drinks or why they so frequently select to mix them with alcohol. With the exception of Heinz et al. (2009), measures concerning expectancies regarding energy drinks are sparse. Thus, a new measure of energy drink expectancies as well as energy drinks mixed with alcohol was developed on 321 university students (243 women, 78 men). The EEDS or Expectancies for Energy Drinks Scale version one consists of 46 items measuring expectancies for energy drinks as well as 46 items for measuring expectancies for mixing energy drinks with alcohol. Exploratory Factor Analysis in Mplus 6.0 was utilized to examine factors of attention, persistence, coordination, alertness, irritableness (negative expectancies), and increased drug use. Comparisons between our measure and the existing Heinz et al. (2009) scale are made as well as existing alcohol expectancies scales (e.g., Fromme, Stroot, & Kaplan, 1993). Focus group discussions of items we may have left off this initial version of the scale will also be discussed. In general, our results suggest researchers may need to consider measuring expectancies regarding energy drink consumption and expectancies regarding mixing energy drinks with alcohol separately.

1109

MARIJUANA USE, DRIVING, AND RELATED COGNITIONS

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Acute marijuana use adversely impacts driving ability and motor vehicle crash risk, with impairment increasing at higher doses (Ramaekers, et al, 2004). Cognitive factors, such as risk perceptions, social norms, and expectancies can contribute to marijuana use, related problems (Grube et al., 1996; Schafer et al., 1991; Simons et al., 2007; Simons et al., 2006), and driving while high (DWH) (McCarthy et al., 2007). We hypothesized greater negative expectancies and marijuana-related driving cognitions (i.e., peer disapproval, perceived danger, perceived negative consequences), would be associated with decreased DWH. Participants were recruited from introductory psychology classes at a large public university who reported ever having used marijuana (n = 597). The majority of the sample were Caucasian (90%) and in their first year of college (80%). Mean age was 18.77 years and approximately 50% were female (n = 300). Participants completed paper-and-pencil surveys assessing demographic information, frequency of marijuana use, and driving behavior. Participants indicated the number of times in the past three months they drove within two hours of smoking marijuana (DWH). Marijuana expectancies were assessed with the Marijuana Effect Expectancy Questionnaire—Short Form (MEEQ: Aarons, et al. 2001). Questions assessing DWH cognitions were adapted from Grube et al. (1996).
Zero-inflated Poisson (ZIP) regression models were estimated with Mplus Version 4 (Muthén & Muthén, 2006) to account for smokers not reporting DWH or RWHD. In univariate ZIP models, results indicated engagement in DWH and frequency of DWH was significantly reduced for smokers with stronger negative expectancies, OR = .62, $p < .01$, 95% CI [.33, .91], and β = -.30, $p < .001$, 95% CI [-.38, -.22], respectively. However, in multivariate ZIP models, perceived danger and social norms were significantly associated with engagement in DWH, above and beyond negative marijuana expectancies, perceived negative consequences, gender, and marijuana use frequency (OR = .63, $p < .01$, 95%CI [.45, .87], and OR = .75, $p < .05$, 95%CI [.58, .98], respectively. All cognitive predictors were significantly associated with decreased frequency of DWH. Findings suggest perceived peer approval and perceived danger are a stronger influence on decisions to DWH than general negative expectancies and perceived negative consequences, which may inform and augment intervention efforts for driving under the influence.

1110

DRINKING MOTIVES MEDIATE THE ASSOCIATION BETWEEN RS2236781 IN GABRB1 AND FREQUENCY OF DRINKING TO INTOXICATION

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Purpose: The Motivational Model of Alcohol Use states that alcohol's perceived incentive value–the changes in affective state anticipated to be brought about by consuming alcohol compared to not consuming alcohol, such as drinking for ''enhancement'' or to ''cope''—is involved in the final decision about whether or not alcohol is consumed. The model also states it is through drinking motives that distal factors, such as genetic influences, impact drinking behaviors. In this study, we tested whether drinking motives mediated the association between rs2236781 in *GABRB1* and frequency of drinking to intoxication (INTOX).
Method: Data were drawn from the Missouri Adolescent Female Twin Study. Genotypic data and phenotypic data collected via interview (INTOX) and mailed self-report questionnaire were available on 829 young adult females (Mn age= 22.1, Range 18–27) who reported drinking on 6 or more instances lifetime. First, a candidate gene association study was conducted to identify SNPs significantly associated with enhancement and coping motives. Second, structural equation models (path analyses), were used to test whether drinking motives mediated the association between rs2236781 and frequency of drinking to intoxication.
Results: Of the 1014 SNPs genotyped, 62 SNPs were associated with enhancement at p-values less than 0.05; however, only one SNP (rs2236781 in *GABRB1*) survived correction for multiple testing (p =.00002). Although no associations with coping survived correction for multiple testing, the p value for rs2236781 was .011. Regression analysis indicated that rs2236781 also was significantly associated with INTOX (b=.18, p= .016). Path models that adjusted for covariates including zygosity, age, mood problems and externalizing problems, indicated that the association between rs2236781 (or rs4109288, a functional SNP, that according to 1000 Genomes Pilot 1, is in high LD [r^2=0.84]) and frequency of drinking to intoxication was mediated by enhancement (indirect effect = .055, p=.002) but not by coping (indirect effect =.015, p=.13).
Conclusion: Our results indicate that rs2236781 in *GABRB1* is associated with frequency of drinking to intoxication via self-reported motivation to drink in order to enhance positive affective state. Previously, *GABRB1* has been implicated in the development of alcoholism, and our findings suggest one etiologic mechanism might involve the *GABRB1*–enhancement motive–INTOX pathway.

1111

ALCOHOL CUES, APPROACH BIAS, AND INHIBITORY CONTROL: APPLYING A DUAL PROCESS MODEL OF ADDICTION TO ALCOHOL SENSITIVITY

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Low sensitivity to the acute effects of alcohol, or needing a relatively large amount to feel alcohol's effects, is a risk factor for developing AUDs and related problems. Dual processing models of addiction posit that decisions to engage in substance use are governed by the relative strength of two different modes of information processing: an implicit, approach-motivational process, and an explicit, cognitive control process regulating approach tendencies. The current study had two main aims: (1) to test for differences in alcohol approach bias among high- and low-sensitivity drinkers, and (2) to investigate the neural and behavioral consequences of this bias for inhibitory control in the presence of alcohol cues. Sixty-four social drinkers were recruited on the basis of their responses to the Alcohol Sensitivity Questionnaire (O'Neill et al., 2002). The final sample included 58% men and 52% LS individuals. Participants completed an Alcohol Approach-Avoidance Task (AAT; Wiers et al., 2009), in which they responded to images (alcoholic beverages, non-alcoholic beverages, and other liquids) by pulling or pushing a joystick, depending on the image tilt. Participants also completed a Cued Go/No-Go Task (e.g., Abroms et al., 2003) while brain electrical activity (ERPs) and behavioral responses were measured. On each trial, a target that required either the commission or withholding of a behavioral response, depending upon its color, was preceded by an alcohol or nonalcohol image prime. Critical trials were those in which alcohol primes preceded ''no-go'' targets, during a block in which alcohol primes typically preceded ''go'' targets. A significant Group x Target interaction in the Alcohol-AAT indicated that, as predicted, LS participants showed an approach bias for alcohol cues that was not present among HS participants. Additionally, LS participants made somewhat more inhibition errors than HS participants for alcohol-primed, no-go targets, but this trend was not significant. However, LS participants showed an enhancement of the N2 component of the ERP on such trials, indicating greater conflict associated with inhibiting the behavioral response, compared to HS participants. Taken together, these data indicate that alcohol cues elicit an approach bias among LS individuals, which translates into greater difficulty inhibiting behavioral responses in the presence of such cues, a pattern generally supportive of dual process models of substance use.

1112

DRINK-RELATED SELF-EFFICACY AS A MODERATOR OF THE RELATIONSHIP BETWEEN ALCOHOL-RELATED IMPLICIT ATTITUDE AND DRINKING BEHAVIOR

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The present study evaluated self-awareness in the relationship between implicit attitudes and behaviors. Our hypothesis was that self-awareness would moderate the link between alcohol-related attitudes and behaviors. Self-awareness was expected to correlate positively with drinking, but only among those with more positive (or less negative) implicit associations with drinking. Consistent with previous research, we measured self-awareness via the Self-Consciousness Scale. We expected that self-awareness would moderate the relationship between alcohol-related attitudes, measured via three separate alcohol-related implicit association tests (IATs), and alcohol-related behavior, measured via self-report questionnaires. Participants included 218 undergraduate students who completed self-report alcohol-related measures and the alcohol-related IATs. Multiple hierarchical regression analyses were conducted. The alcohol consumption variables were significantly and positively correlated with each other and with the three IATs. Contrary to expectations, results did not suggest that self-awareness is a moderator of the relationship between alcohol-related attitude and drinking behavior. Results were not meaningfully different when gender and presentation order were controlled. However, exploratory analyses revealed multiple three-way interactions when drink refusal self-efficacy was included as a moderator of the association between alcohol-related implicit attitudes and drinking behavior. Results revealed that high implicit drinking identity was associated with greater drinking frequency when private self-consciousness was low, but only for participants low in drink refusal self-efficacy. Findings further revealed that high implicit drinking identity was associated with greater drinks per week and peak drinks when public self-consciousness was low, but only for participants low in drink refusal self-efficacy. This suggests that there may be parameters wherein implicit measures such as the IAT are useful in predicting drinking. This research indicates that alcohol-related IATs may be a useful tool in predicting drinking frequency, drinks per week, and peak drinks, particularly among those low in public or private self-consciousness and low in drink refusal self-efficacy.

7. CONSEQUENCES OF ALCOHOL CONSUMPTION IN HUMANS

a. Social harms (family, financial, legal or work problems) 149–162/1113–1126

1113

THE INFLUENCE OF SOCIAL DRINKING GROUP CHARACTERISTICS ON AGGRESSION IN NIGHTCLUBS

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Purpose: Research has focused on individual characteristics that predict aggression in bars/clubs. However, most patrons attend clubs in social groups, not alone. These analyses examine group characteristics that predict same-night experiences of physical and sexual aggression, accounting for individual characteristics.
Methods: Data were collected from club patrons as they entered and exited clubs featuring Electronic Music Dance Events. During the summer of 2010, data were collected from 38 different events in 8 clubs. A total of 368 patron groups were included (968 individuals). Using portal methodology, self-report data were collected anonymously at entrance and exit. As well as demographic data, we collected information on expectations for self and group members' drinking that evening, as well as 30-day prior experiences of sexual (grabbing/fondling) and physical (pushing/punching) aggression in clubs. Aggregate data were created using all group responses to form group characteristics, such as average age of the group members. A discrepancy score for drinking expectancy was calculated by subtracting the lowest expectation score in the group from the highest. Multilevel mixed modeling was used to account for data nested at the club, event, and group levels.
Results: Of the groups, nearly two thirds are composed of dyads, about half are single sex, slightly more than half are exclusively heterosexual, and nearly half have an average age under 30. About 28% of groups have one or more members who report experiences of physical aggression and the same percentage who report sexual aggression at the event. Group characteristics that significantly predict physical aggression experiences at the event include: younger mean age, lower percentage of students, greater discrepancy for expectations of group members' drinking, higher 30-day average experience of physical and sexual aggression experiences. Group characteristics that significantly predict sexual aggression experiences at the event include: higher percentage of gays/lesbians/bisexuals and higher 30-day average experience of sexual aggression.
Conclusions: Results indicate that there are unique characteristics of social groups that can contribute to an individual's experience of physical and sexual aggression outside of their own characteristics. We recommend that prevention efforts address social groups as a target of intervention for their role in aggression victimization.

1114

CHILD PROTECTIVE SERVICES, SINGLE MOTHERS, AND SUBSTANCE MISUSE

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Background: When caregivers misuse alcohol and/or drugs, children are more likely to experience physical, developmental, intellectual, social, and emotional problems. When single mothers misuse alcohol and/or drugs, the situation is compounded. Children who reside with a single parent (most often the mother) experience abuse at twice the rate of children who live with two parents. This study examines family structure and alcohol/drug misuse in a sample of Child Protective Service (CPS)-involved families.
Hypothesis: CPS-involved families with supported mothers who do not misuse alcohol/drugs will demonstrate more positive outcomes than families headed by single mothers who misuse alcohol/drugs.
Methods: This study is a secondary analysis of The National Survey of Child and Adolescent Well-Being.
Sample: The sample consists of over six thousand children who had contact with the child welfare system within a fifteen-month timeframe. Four family groups are analyzed: Single mothers or supported mothers; mothers who misuse alcohol/drugs (MU) or who do not misuse alcohol/drugs (no MU).
Results: Children in families headed by single mothers with MU demonstrate higher externalized behavior problems compared to children in families headed by supported mothers with no MU ($b=1.24$, $t=2.14$, $p<.05$) Children in families headed by single mothers with MU demonstrate significantly lower social skills when compared to supported mothers with no MU ($b=-3.27$, $t=-1.96$, $p<.05$).
When compared to supported mothers who are not misusing alcohol/drugs, both supported mothers ($b=.75$, $t=2.43$, $p<.01$) and single mothers who misuse alcohol/drugs use more social services ($b=.45$, $t=2.17$, $p<.05$).
Conclusion: Over time, children demonstrate more positive behavior outcomes and social skills in families in which there is no alcohol/drug misuse. Single mothers who misuse alcohol/drugs appear to be accessing the most mental/behavioral health services and child welfare services. This study adds to research that supports a link between MU and CPS involvement.

1115

A DOSE-RESPONSE RELATIONSHIP OF DRINKING VENUE UTILIZATION ON PHYSICALLY ABUSIVE PARENTING PRACTICES

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Objective. Despite well-known associations between heavy drinking and child physical abuse, little is known about the exact risk of drinking amounts and use of drinking venues on the use of physically abusive parenting practices. The current study examines how dose-response relationships of drinking in various venues are related to frequency of physically abusive parenting practices.
Methods. Data were collected via a telephone survey of parents in 50 cities in California resulting in 2,163 respondents who reported drinking in the past year. Child physical abuse and corporal punishment was measured using the Conflict Tactics Scale, Parent Child version. Drinking behaviors were measured using continued drinking measures. Data were analyzed using zero inflated Poisson models.
Results. The frequency of drinking at bars or homes and parties increases the use of physically abusive parenting practices while drinking more often at restaurants is related to less use of physically abusive parenting practices. The frequency of having one drink at home/parties and in bars was positively related to increased use of corporal punishment while restaurants were negatively related.
Conclusions. Use of drinking venues, particular bars and at home or parties, increases use of punitive parenting practices placing children at risk for being abused or neglected. These findings suggest that developing interventions that take into account parents' alcohol use at drinking venues is an important avenue in preventing child maltreatment from occurring.

1116

POSITIVE PARENTING HAS GREATER EFFECTS ON ANTISOCIAL BEHAVIOR FOR CHILDREN IN NON-ALCHOLIC FAMILIES THAN THOSE IN ALCOHOLIC FAMILIES

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This study examined the relationship between child's experience of positive parenting and the child's antisocial behavior (ASB), while controlling for parent's use of spanking.
Two subsamples from the Michigan Longitudinal Study were used: A high-risk community sample recruited based on the father's drunk driving conviction and a community comparison sample recruited by canvassing in the same neighborhoods as the high-risk families. 221 of the children had no alcoholic parents and 329 children had an alcoholic father. Parents were interviewed regarding how frequently they used spanking with their child, at preschool, age 6–8, and age 9–11. At ages 9–11 and 12–14, children were given an interview which inquired about their experience of their parent's positive behavior towards them: e.g. talking to them and comforting them when they felt bad. The child's ASB was rated by a clinician who had spent several hours with the child. Path modeling was used to study the relationship between positive parenting, child ASB and parent's spanking across four time points spanning preschool to age 12–14.
Spanking was common in the preschool period, but declined dramatically throughout childhood. There were higher levels of spanking in the preschool period for alcoholic families. For all families, path models showed positive relationships between parent's spanking and future ASB. Path models also showed an inverse relationship between child's experience of positive parenting at age 9–11, their concurrent ASB, and their ASB at age 12–14, but only in non-alcoholic families.
The relationship between positive parenting and ASB suggests that parent's good relationships with children can be beneficial in managing negative child behaviors. However, children in alcoholic families have a higher risk load (genetic risk for ASB, stress and chaos in the family) such that a positive relationship with a parent may not be sufficient to ameliorate their propensity to antisociality.
Supported by NIAAA grant R37 AA07065 to RA Zucker

1117

RELATIONSHIP-SPECIFIC ALCOHOL EXPECTANCIES AS A MODERATOR OF DAILY DRINKING WITH ONE'S PARTNER AND RELATIONSHIP FUNCTIONING IN ADULT ROMANTIC COUPLES

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Research shows that drinking with one's partner (DWP) in romantic relationships is associated with positive relationship functioning (e.g., increased intimacy), whereas drinking apart (DA) from one's partner is associated with negative relationship functioning (e.g., increased negative behaviors/events; e.g., Levitt & Cooper, 2010; Homish & Leonard, 2005). However, much is still unknown about these processes at the daily level, particularly factors that can moderate these processes. Relationship-specific alcohol expectancies (e.g., Derrick et al., 2010; Leonard & Mudar, 2004) are one such factor that should illuminate when and for whom these processes are more positive or negative. The current study tested positive relationship-specific alcohol expectancies (e.g., DWP will enhance intimacy) as a moderator of the effects of daily DWP (vs. DA) and alcohol consumption on both positive (e.g., love, getting along) and negative (e.g., arguing, anger toward partner) relationship functioning outcomes in a sample of mostly married, moderate-drinking adult couples. Both members of 96 couples completed daily diary reports of alcohol use and relationship functioning for up to 56 days. Multilevel, time-lagged models were estimated using the Actor-Partner Interdependence Model (APIM). Results corroborated previous research showing that positive relationship functioning was higher on days following DWP compared to DA or not drinking, although this effect was limited to days of heavier consumption. Negative relationship functioning was higher on days following DA compared to DWP or not drinking. However, as predicted, positive relationship-specific alcohol expectancies moderated the effects of DA on negative relationship functioning, such that negative relationship functioning was worse on days following DA for those with strong positive expectancies. Expectancies did not moderate DWP or alcohol use effects on positive relationship functioning. These results support prior research on DWP, and extend it by showing that positive relationship-specific alcohol expectancies moderate the effects of DA on negative relationship functioning. These findings have implications for future research and theory on expectancy violations as they pertain to alcohol use and romantic relationship functioning processes.

1118

THE DYNAMIC INFLUENCE OF ALCOHOL USE, GENDER, TRUST, AND RELATIONSHIP SATISFACTION IN DATING AND MARRIED COUPLES

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For couples in romantic relationships, alcohol use may serve as a source of pleasure or tension. Previous research regarding how one person's drinking affects his or her partner's relationship adjustment is complex and dependent on several factors. Further, due to the difference in prevalence rates of drinking problems between men and women, the research is unclear on whether the partner effect differs by gender. The current research sought to examine the relationship among alcohol use, gender, trust, and relationship satisfaction among couples. Inclusion criteria involved romantic commitment with one's partner for at least three months and at least one partner being an undergraduate. Both members of couples (N = 78 dyads) completed an online survey in exchange for research credit. Alcohol measures included drinks per week, drinking frequency, typical quantity, and drinking problems. Relationship measures included relationship satisfaction and trust. The Actor-Partner Interdependence Model was used to account for the nonindependence resulting from analyzing dyadic data. Results revealed a partner effect of drinking on relationship satisfaction such that as one's partner consumed more, relationship satisfaction declined. This effect was moderated by gender such that it was stronger for males. Further, two significant interactions between (a) gender and satisfaction and (b) gender and trust suggested that females who are less satisfied with and trusting of their partner tend to drink more. Future research may examine whether this is occurring as a coping mechanism. Finally, a significant partner trust by gender interaction revealed that especially among males, as partner trust decreases, drinking increases. Overall, these results convey a compelling and interconnected story of the detrimental effect alcohol may have on close relationships. Implications and future directions are discussed.

1119

ALCOHOL RELATED DATING SCENARIOS: PREDICTING LIKELIHOOD AND AMOUNT OF ALCOHOL INTAKE IN RISKY DATING SITUATIONS

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Risky sex prevention programs encourage women to determine when risks are greatest and drink less or abstain in those situations. Otherwise, women are less likely to notice risks, coerced sex is more common (Muehlenhard & Linton, 2007) and they tend to stay in hazardous situations, even if noticing risks (Gidycz, et al, 2006). To understand specifically how previous drinking behavior predicts drinking in risky situations, we focused on women's projections of likelihood to drink and amount of alcohol they would consume in risky dating scenarios. Heterosexual women from an Intro Psychology class (N=175; M age=19.13, SD=1.75; 88.6% Caucasian and 75% freshman or sophomore) completed a Quantity Frequency Inventory to assess frequency and quantity of liquor, beer and wine consumption and a survey of dating behavior in the last 90 days. They reported 17.8 mean drinking days in the last 90 (SD=17.8) with 11% abstinent. Then they viewed nine scenarios, in counterbalanced order, involving a main character (''you'') being pressured to drink by a man who was presented as attractive, complimentary and interesting, but in a risky situation (e.g. the couple is isolated in a home). These scenarios were previously validated as ''risky'' (Heaton, et al 2011). After each viewing, participants rated the likelihood and amount they would drink. Linear regressions showed that for all nine scenarios, the likelihood and the amount of alcohol consumption were both significantly predicted by the frequency and/or amount of specifically hard liquor consumption in the past 90 days. Beer consumption was occasionally predictive while wine consumption and previous dating behaviors were never significant predictors. Review of QFI data shows that overall the participants reportedly drank about equal amounts of beer, wine and hard liquor (a median of 1 – 3 days per month, 3 – 4 standard drinks per occasion), but only hard liquor consumption was a consistent predictor for likelihood and amount of drinking in sexually risky situations. This is consistent with literature showing women who binge drink (4+ drinks in a setting) are more likely to drink in risky sexual situations, but our more fine-grained analysis suggests that liquor specifically is a consistent predictor. Perhaps previous hard liquor use could be the best indicator of drinking in a risky sexual situation because it might be a marker of more involvement in binge drinking than just overall quantity and frequency of drinking.

1120

DAILY ASSOCIATIONS BETWEEN ALCOHOL CONSUMPTION AND DATING VIOLENCE PERPETRATION: AN EXAMINATION OF THE EFFECTS OF SELF-REGULATION AND TRAIT ANGER

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Alcohol use has consistently been implicated in the perpetration of dating violence (DV). Not everyone who consumes alcohol, however, becomes aggressive. Self-regulation difficulties and high levels of trait anger have been found to moderate the effect of alcohol intoxication on the perpetration of aggression. Although daily alcohol consumption is related to DV, it is not known whether self-regulation and trait anger moderate this daily association. Therefore, we examined the moderating effects of self-regulation and trait anger on the daily associations between alcohol use and DV. College-aged individuals (N = 150; 51% female) in dating relationships participated in a larger study that included an assessment of self-regulation and trait anger as well as an interview administration of the Timeline Followback to assess the occurrence of DV and the amount of alcohol consumed for each of the past 90 days. Estimates of blood alcohol content (eBAC) were calculated for each day as well as an average for the 90 days. A generalized estimating equation using a binomial distribution and logit link function was used to examine these data. A significant interaction between self-regulation and average eBAC suggests that poor self-regulation was associated with an increased likelihood of DV, however, as average eBAC increased, the likelihood of DV decreased overall. In addition, there is a significant interaction between average and daily eBAC. Higher daily eBACs were associated with an increased likelihood of DV, especially among those with lower compared to higher average eBACs. Trait anger exerted a main effect with individuals high in trait anger more likely to perpetrate DV than those low in trait anger. Results suggest that self-regulation difficulties are associated with DV, especially among those who are overall lighter drinkers. And, overall lighter drinkers are more likely to perpetrate DV as their daily level of intoxication increases. This may be related to tolerance, as individuals who are typically lighter drinkers may be especially vulnerable to alcohol's pharmacological effects. Although high levels of trait anger were associated with DV, trait anger did not moderate the daily association between alcohol and DV. Findings highlight the importance of educating individuals regarding the risk for DV associated with increasing their level of intoxication above and beyond their average level, and improving self-regulation skills.

1121

IMPULSIVITY MEDIATES RELATIONSHIP BETWEEN PROTECTIVE BEHAVIORAL STRATEGIES AND NEGATIVE OUTCOMES IN COLLEGE STUDENT DRINKING GAME PARTICIPANTS

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Drinking games have been identified as a risk factor for increased binge drinking and alcohol-related negative consequences among college students (Cameron et al., 2010). Harm-reduction interventions for college students have incorporated strategies that students can engage in to limit their alcohol consumption as well as the risks associated with their drinking (Dimeff et al., 1999). These strategies, known as protective behavioral strategies (PBS), have been shown to be inversely related to negative consequence (Martens et al., 2004). To date PBS's haven't been investigated in samples of students who participate in drinking games. The current study tested whether PBS's are predictive of negative consequences among drinking game participants. Because PBS's (Donovan, 2009), negative consequences (Simons et al., 2005), and drinking game participation (Silvestri et al., 2011) have also been linked to impulsivity, we also tested a model in which PBS's mediated the relationship between impulsivity and consequences.

Participants were 225 undergraduates (69% female) who endorsed playing a drinking game in the past 28 days. Each subject completed an online survey that included the Rutgers Alcohol Problems Index (White & Labouvie, 1989), the Protective Behavioral Strategies Scale (PBSS; Martens et al., 2005), and the Barrett Impulsivity Scale (Barratt, 1994). Structural Equation Modeling was performed using maximum likelihood to test the meditational model.

The hypothesized model included the variable impulsivity as an exogenous variable with paths to PBS's and negative consequences, and PBS's as an endogenous variable with a path to negative consequences. The fit of the meditational model was good, Chi-square (24, N = 225) = 28.35, p = .25, RMSEA = .03, CFI = .99. All direct and indirect paths in this model were significant, suggesting that the predictive value of impulsivity on negative consequences is partially mediated by PBS's. The model accounted for 26% of the variance in negative consequences and 8% of the variance in PBS's. These results suggest that students that are high on measures of impulsivity are at greater risk for negative consequences, and this risk is in part due to decreased use of PBS's. Research on interventions designed to increase the use of PBS's in students who play drinking games is warranted.

1122

RISK AND PROTECTIVE FACTORS FOR DRINKING AND DRIVING AMONG HEAVY DRINKING COLLEGE STUDENTS

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Young adults account for the highest number of alcohol-related traffic accidents and fatalities each year. College students, specifically, are a population with increased likelihood to engage in binge drinking and other risky behaviors, placing them at particular risk for driving while under the influence of alcohol or drugs. Uncovering risk and protective factors for drinking and driving (DAD) is a vital step for effective prevention. Many previous studies concluded that there is a linear relationship between alcohol consumption and DAD. The purpose of the current study was to identify risk and protective factors for college students' self-reported DAD while controlling for alcohol consumption. The participants were 207 undergraduate students (53.1% female; Age, M = 19.50, SD = 1.99; 64.7% Caucasian, 26.1% African American) who reported at least one heavy drinking episode (≥ 5/4 drinks in one occasion for a man/woman) in the last month. Of the 207 participants, 45% (n = 91) reported having ever driven a vehicle after knowingly consuming too much alcohol. Participants completed questionnaires that measured alcohol consumption, alcohol-related consequences, sensation-seeking, depression, protective behavioral strategies, and family history of alcohol-related problems. Controlling for alcohol consumption, partial correlation analyses indicated that self-reported DAD was significantly correlated with age (p =.008), year in school (p = .003), and residence ($p \leq .001$). Those participants aged 21 years and older were significantly more likely to report ever DAD (p = .001), as were those participants living off campus ($p \leq .001$). In contrast to previous findings, neither gender, family history, ethnicity, nor age when first drunk were significantly correlated with DAD. Greek affiliation, depressive symptoms, and sensation-seeking were also unrelated to DAD after controlling for drinking behavior. Protective behavioral strategies (p = .005), specifically knowing when to stop drinking ($p \leq .001$) and attempting to avoid negative drinking consequences (p = .003), were protective against DAD. These findings provide support for prevention efforts that promote responsible drinking behaviors as a protective component against DAD.

1123

CHILDHOOD ATTENTION DEFICIT HYPERACTIVITY DISORDER, IMPULSIVITY, AND DRINKING AND DRIVING IN YOUNG ADULTS: A LONGITUDINAL EXAMINATION

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Drinking and driving poses serious health risks for young adults. Risk for experiencing a fatal motor vehicle accident is higher at any BAC for youth and increases more sharply for younger people as BAC increases (Zador et al., 2000). In 2009, 19% of 16–20 year olds killed in motor vehicle accidents had a BAC at or above .08 (NHTSA, 2010). Impulsivity predicts drinking and driving (e.g., Ryb et al., 2006). However, research has not examined drinking and driving in individuals with Attention Deficit Hyperactivity Disorder (ADHD), a population marked by elevated levels of impulsivity. An exception is a cross-sectional finding from a portion of the current sample that did not find group differences (Thompson et al., 2007). Research has not examined change in drinking and driving over time for young adults with and without a childhood diagnosis of ADHD or examined the indirect association that childhood ADHD may have with drinking and driving through impulsivity.

Data were used from the Pittsburgh ADHD Longitudinal Study, an ongoing study of individuals with and without childhood ADHD. The current sample was restricted to individuals with a driver's license at one or more timepoints during the assessment period. This reduced sample included 359 young adults aged 18–20 years (n = 181 non-ADHD; n = 178 ADHD; 90% male; 87% White). Self-reported frequency of drinking and driving after 1 or 2 drinks was assessed annually while self-reported impulsivity was assessed at age 18.

An unconditional latent growth curve model of drinking and driving fit the data well (χ^2=0.14, p = .71; CFI = 1.00). Drinking and driving behavior significantly increased between ages 18 and 20 (M_s = .50, p = .01). Childhood ADHD did not directly predict change in drinking and driving over time (β = -.10, p = .36), but it predicted impulsivity at age 18 (β = -.22, p < .001). Moreover, age 18 impulsivity was significantly associated with sharper increases in drinking and driving (β = .30, p = .04). A significant indirect effect of childhood ADHD on change in drinking and driving through impulsivity was found (β = -.12, p = .03). Taken together with MacKinnon et al's (2002) recommendation that mediation may be established without a direct effect from the predictor to the outcome, these findings highlight the possibility that persistence of inhibitory control problems in children with ADHD may increase their risk for a very high-risk behavior with potentially expensive and tragic consequences.

1124

RACE AND GENDER DIFFERENCES IN ALCOHOL-RELATED NEGATIVE CONSEQUENCES AMONG COLLEGE STUDENTS

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In the US, college students have the highest prevalence of high risk drinking, which can lead to many alcohol problems. Previous studies have found that White students drink more than Blacks. However, it has been suggested that Blacks suffer from more alcohol problems when they do drink. Few studies however, have examined whether the relationships among race, alcohol use, and consequences differ by gender. The purpose of this study was to examine race and gender differences in alcohol problems among college students. Data for this study came from Project INTEGRATE, an integrative data analysis study aimed at examining mechanisms of change by combining and analyzing data from 22 independent intervention studies. We limited analysis to current drinkers (i.e., drinking in the past month) and Black and White students. The sample for this study consisted of 604 Blacks and 7,575 Whites (M age = 19.1, 57% women, 53% 1st year students). For alcohol problems, we examined the Rutgers Alcohol Problem Index, an18-item self report questionnaire. The typical number of drinks per week was 13.2 with Whites drinking more than Blacks (Whites, M = 15.1; Blacks, M = 10.2). Also, Whites were more likely to endorse alcohol consequences than Blacks (Whites, M = 4.3; Blacks, M = 3.6). The types of the negative consequences experienced by White and Black students were similar. Multiple regression analysis was conducted to examine (1) whether Blacks experienced more negative consequences when controlling for their drinking and (2) whether the racial difference in alcohol problems differed for men and women. The results revealed that when alcohol use was statistically controlled, Black and White students were similar in their number of alcohol problems. There was a significant three-way interaction effect between race x gender x drinking on alcohol problems. For men, at high levels of alcohol consumption, Blacks experienced more alcohol problems than Whites; while at low levels of alcohol consumption Whites endorsed more alcohol problems than Blacks. On the other hand, for women, at high levels of alcohol use, Whites experienced more alcohol problems than Blacks; while at low levels of alcohol use, Blacks endorsed more alcohol problems than Whites. Thus alcohol interventions should be targeted towards Black men and White women who drink at high levels.

1125

A POLYTOMOUS GRADED ITEM RESPONSE THEORY ANALYSIS OF THE RUTGERS ALCOHOL PROBLEM INDEX BASED ON A SAMPLE OF COLLEGE STUDENTS

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The Rutgers Alcohol Problem Index (RAPI) is one of the most widely used screening measures of alcohol-related consequences in college students. Extensive psychometric evaluation of the RAPI has indicated it to be both reliable and valid as well as a good predictor of brief intervention outcomes in heavy drinking college students. The majority of research has validated this instrument using classical test theory approaches, which has several limitations relative to innovative statistical approaches, such as Item Response Theory (IRT). IRT improves upon classical test theory by providing a more in-depth analysis of how items function across an underlying latent-trait continuum. Few studies have examined the item characteristics of the RAPI using methods from IRT. Given this background, the present study applied polytmous graded response IRT models to examine the unique item characteristics of the RAPI in a sample of heavy drinking college students. Participants (N = 854; 36.4% Male; 75.8% White) were recruited from Introductory Psychology courses and consumed alcohol, on average, 19 days out of the prior 90. Each was asked to fill out a battery of questionnaires that assessed for alcohol use and related correlates. The RAPI was used to assess for 23 alcohol-related negative consequences (0 = never to 3 = 10 or more times) that occurred during the prior year. IRT analyses generated item discrimination and severity threshold parameters for each item. Results indicated that the item discrimination parameters were high and ranged from 1.52 (#4 ''went to school high or drink'') to 4.74 (# 22 ''felt physically/psychologically dependent on alcohol''). The item severity thresholds revealed that the RAPI items covered the more severe end of the latent-trait negative consequences severity continuum. The items with the highest item severity thresholds were #7 ''relatives avoided you'', #20 ''felt you were going crazy'', #22 ''felt psychically and psychologically dependent on alcohol'', and #10 ''had withdrawal symptoms''. These findings were further confirmed by the total information curve, which indicated that the RAPI is most reliable at the more severe end of the latent-trait continuum. Collectively, our findings indicate that the RAPI items have good discrimination and capture the more severe end of the latent-continuum. Future research should consider identifying items that cover the lower end of the latent-trait continuum.

1126

THE RELATIONSHIP OF INDIVIDUAL VERSUS COMORBID SUBSTANCE USE TO GAMBLING OUTCOMES AMONG EMERGING ADULTS

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Emerging adulthood is marked by engagement in various risk behaviors, including frequent/heavy use of alcohol, use of other substances, and gambling. Gambling is the most prevalent of these behaviors, with 85% of college students reporting at least one gambling occasion in the past year (Lesieur et al., 1991); approximately 79%, 33% and 17% of students report at least one occasion of alcohol use, marijuana use, and another illicit substance over the same time period, respectively (Johnston et al., 2011). Evidence suggests there is considerable overlap between these behaviors both within individuals (i.e., the same person uses both alcohol and marijuana) and within occasions (e.g., drinking while gambling). A wealth of research documents the harms associated with these individual behaviors; however, less is known about the consequences when these behaviors overlap. Thus, the purpose of this study was to examine the association between substance use and gambling outcomes among emerging adults who report only alcohol use versus alcohol use and concurrent use of either marijuana or cocaine. These were selected as they are the illicit drugs most commonly reported among pathological gamblers (Burge et al., 2006).
College students (N=1769; 57.4% female; Age: *M*=19.75, *SD*=1.26) completed a web-based screening survey as part of a longitudinal randomized clinical trial; 56% had gambled in the past 6 months; 86%, 48%, and 8% reported lifetime use of alcohol, marijuana, and cocaine, respectively, and 92%, 75%, and 45% of those reported use of the respective drugs in the past 3 months. Individuals reporting use of alcohol and marijuana gambled more frequently, $t(813)=2.66$ $p=.008$, lost greater amounts of money, $t(815)=3.08$, $p=.002$, and experienced nearly twice as many gambling consequences as those who only used alcohol, $t(615)=1.997$, $p=.046$. No significant differences were found among those who used alcohol and cocaine versus those who only used alcohol. Although a greater percentage of individuals in this sample reported using marijuana compared to cocaine prior to or while gambling in the past 3 months, this difference was not significant. Moreover, the majority reported co-occurring alcohol use as well.
Although cross-sectional data is a limitation, findings suggest the combination of alcohol and marijuana use may uniquely promote gambling behavior and contribute to greater related consequences, which has implications for interventions targeting these behaviors.

8. TREATMENT/RECOVERY

1127

THE IMPACT OF THE FIRST YEAR OF AA MEMBERSHIP ON SPIRITUALITY/RELIGIOUSNESS, DRINKING BEHAVIORS, AND DRINKING CONSEQUENCES

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Aims: Qualitative, cross-sectional, longitudinal, and meta-analytic studies have described the relationship between AA and drinking. Because AA membership cannot be manipulated, most studies have employed naturalistic designs. This has been a limitation as individuals join at different times. Our study followed alcoholics from before joining AA, through the event of their joining and afterwards to examine associated changes, asking 1) are there changes in spiritual/religious, clinical, and drinking variables after joining, and 2) if so, what pattern do they take?
Methods: This study is based on a subset of the Life Transitions Study, a three-year longitudinal survey of 364 alcohol-dependent individuals, who were and were not in treatment. Respondents were asked, ''Do you consider yourself to be a member of AA?'' Those who answered ''No'' at one wave and then ''Yes'' at the next two consecutive waves were included in the current analysis. A total of 62 participants demonstrated this pattern of responding ''No,'' then ''Yes'' and ''Yes'' at any point over 6 waves. Their data were shifted to align all ''No'' waves. A repeated measures ANCOVA analyzed changes subsequent to joining AA in spiritual/religious, clinical, and drinking variables.
Results: Percent Days Abstinent significantly increased, while percent Heavy Drinking Days and negative consequences of alcohol use decreased, indicating linear improvement over the first year of membership. From the initial ''No'' response to ''Yes'' at 6-months, Daily Spiritual Experiences and Positive Religious Coping both increased significantly but then stabilized suggesting no further change in the second half of the first year of joining AA. No significant changes were found in other spiritual/religious variables or psychological symptoms.
Conclusions: These results suggest that becoming a member of AA provides benefits for recovering alcoholics within the first six months and first year. Joining AA helps members decrease drinking and the negative consequences of drinking, but also seems to encourage a stronger and more positive relationship with God or a higher power. While some effects occur within the first six months, drinking outcomes continue to improve throughout the first year suggesting that clinicians encourage sustained membership for some time in order for clients to reap the full benefits of membership.

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FURTHER EVIDENCE FOR THE ROLE OF ABSTINENCE SELF-EFFICACY AS A MECHANISM ACCOUNTING FOR 12-STEP RELATED BENEFIT: GRADIENT EFFECT TESTS

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Kazdin (2007) specified six necessary conditions for the identification of a causal mechanism. Several of these conditions have been considered in prior investigations of abstinence-self-efficacy as a mediator of AA-related benefit, e.g., consistency, plausibility, and specificity (e.g., Connors et al., 2001; Moos & Moos, 2004). This study investigated a rarely considered causal condition, potential gradient effects, between varying intensities of AA attendance and later changes in self-efficacy, defined as the confidence to remain abstinent when experiencing negative affect, physical distress, and social cues for drinking (AASE; DiClemente et al., 1994). This study also examined gradient effects between changes in AASE scores and later alcohol use. Early AA affiliates were recruited from outpatient treatment (n = 185) and community-based AA (n = 68). In this single-group longitudinal study, participants were interviewed at intake and in three-month increments for 24-months (R01AA014197, Tonigan). Follow-up rates were 85%, 85%, 75%, and 81% for the 3, 6, 9, and 12-month interviews, and reconstruction of missed data at a later interview increased these rates. Using GLM, clear ascending gradient effects were observed between low-medium-high 12-step attendees (months 0–3) on all three AASE scales (month 6), such that higher rates of 12-step attendance were predictive of larger increases in later AASE scores. These effects persisted after controlling for baseline values of AASE scores, problem recognition, and proportion of formal treatment days (months 0–6). Likewise, significant ascending gradient effects were found between low-to-high changes in AASE scores at six-months and proportion of alcohol abstinent days (PDA) collected at nine-months. For example, for low-medium-high changes in abstinence self-efficacy in the context of social cues for drinking, PDA at nine-months was .65, .78, and .89, respectively ($d = 1.29$, $p < .001$). These effects persisted after controlling for baseline values of PDA, proportion of formal treatment days (months 0–6), and problem recognition. This study offers substantial evidence that 12-step attendance mobilizes later increased abstinence self-efficacy, as measured by the AASE. While potential self-selection biases preclude firm conclusions about the actions of 12-step programs, statistical control for concurrent treatment and readiness for change render this rival explanation unlikely.

1129

EMERGING ADULTS AND ALCOHOLICS ANONYMOUS: ATTENDANCE, INVOLVEMENT, AND RECOVERY-RELATED BENEFITS IN THE YEAR FOLLOWING RESIDENTIAL TREATMENT

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Background: Participation in mutual-help groups, such as Alcoholics Anonymous (AA) and Narcotics Anonymous (NA), during and following treatment has been found to confer recovery-related benefits among adults and adolescents, but little is known about emerging adults. This transitional life-stage is distinctive for its greater distress, higher density of psychopathology, and poorer treatment and continuing care compliance. Greater knowledge would inform the utility of treatment referrals to 12-step mutual-help organizations for this age-group.
Methods: Emerging adults (N=303; aged 18–24yrs; 26% female; 95% White; 51% comorbid [SCID-derived] axis I disorders) enrolled in a naturalistic study of residential treatment effectiveness were assessed at intake and 1, 3, 6, and 12 months later using standardized validated measures assessing AA/NA attendance and involvement (sponsorship), and outcome (Percent Days Abstinent [PDA]).
Results: The proportion attending AA/NA prior to treatment (38%) rose sharply at 1m after treatment (91%) and remained high at 3- (85%), 6- (75%), and 12-month (71%) follow-ups. The proportion reporting having an AA/NA sponsor prior to treatment (14%) also rose substantially in the first month following discharge (42%) and remained high at 3- (51%), 6- (43%) and 12-month (38%) follow-ups. Controlling for baseline PDA, more frequent AA/NA attendance was strongly and consistently associated with greater PDA across follow-ups (ps <.0002 - <.0001). Regarding AA/NA involvement, having an AA/NA sponsor was also related to better outcomes and appeared to partially mediate the effect of attendance on outcome.
Conclusions: Findings suggest emerging adults treated in 12-step oriented residential treatment attend AA/NA at high rates and many become engaged in the fellowship through obtaining an AA/NA sponsor. Such participation is associated with substantially improved alcohol/drug outcomes. These ubiquitous community resources appear to provide a supportive recovery context for this high-risk population at a developmental stage in which non-using/sober peers are scarce.

1130

THE DIFFERENTIAL EFFECT OF ALCOHOLICS ANONYMOUS (AA) AND DRINKING ON DIMENSIONS OF SPRITUALITY

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Recovery from alcohol use disorders has been associated with increases in spirituality; however, the cause of such increases is unclear. Involvement in AA has been shown to have a positive impact on the spirituality of AA members. However, a decrease in drinking alone may engender many bio-psycho-social benefits among alcoholics, including spiritual change. This study compares the independent effects of decreased drinking and increased AA involvement on multiple dimensions of spirituality to determine their differential impact.
Methods: A 3-year panel study recruited 364 SCID-diagnosed alcoholics from treatment and non-treatment sources. Increases in AA involvement (AAI) and decreases in drinks per drinking day (DDD) between baseline and six months were examined as predictors of changes in 7 dimensions of spirituality at one year: daily spiritual experiences, private religious practices, purpose in life, negative and positive religious coping, and forgiveness of self and others. Multiple regression was used for all analyses. Changes in AA and drinking were explored simultaneously in each model, which also controlled for baseline AA, drinking, spirituality, and demographic and clinical characteristics.
Results: DDD decreased significantly from baseline to the 6 month follow up (from 9.1 to 3.9 drinks, $p < .001$). Contrary to expectations, there was no change in AAI from baseline to 6 months. Controlling for AAI, decreases in drinking independently predicted increases in purpose in life and forgiveness of self. Controlling for changes in drinking, AA independently predicted increases in private religious practices, positive religious coping, daily spiritual experiences, and forgiveness of others. Neither AA nor drinking had an effect on negative religious coping.
Conclusions: Changes in AAI, but not in drinking, predicted more frequent spiritual practices, increased daily spiritual experiences, more positive religious coping, and higher forgiveness of others. However, decreases in drinking predicted higher self-forgiveness and increases in purpose in life, controlling for AAI. This suggests that individuals with alcohol dependence experience some spiritual improvement simply by decreasing or stopping drinking. Other forms of spiritual change seem to be sparked by the AA experience.
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A LONGITUDINAL COMPARISON OF URBAN NATIVE AMERICAN AND NON-HISPANIC WHITE 12-STEP ATTENDANCE AND SUBSTANCE USE

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This study investigated the acceptability and effectiveness of 12-step programs for urban Native Americans (NA). The study had three aims: (1) compare 12-step attendance and engagement trajectories of NA and Non-Hispanic White (NHW) adults over nine-months, (2) compare patterns of 12-step disaffiliation of the NA and NHW adults, and (3) assess if participant racial status (NA vs. NHW) moderated the lagged relationship between 12-step attendance and reductions in substance use. The sample (N = 196) was formed by merging data from two prospective longitudinal studies investigating common and 12-step specific behavior change mechanisms (R21AA016974; R01AA014197) in community-based 12-step programs. Baseline differences in substance use and help-seeking between NA (n = 66) and NHW (n = 133) adults were modest although, as a group, NA participants reported higher alcohol dependence relative to the NHW participants. Using HLM, no between-group differences were found in trajectories of 12-step attendance and engagement in prescribed 12-step practices from baseline to nine-months, with most participants attending one 12-step meeting about every 4–5 days. A random-coefficient regression model was done to see if rates of 12-step attrition differed between NA and NHW adults. Findings showed that NHW ($b = .59$) were significantly more likely to discontinue 12-step attendance over time relative to the NA participants ($b = .05$), $t (529) = -2.19$, $p < .029$. Finally, we found that racial status did not moderate the positive effect of 12-step attendance on later increases in abstinence (PDA: $b = .09$, $t (526) = 2.13$, $p < .034$). In contrast, racial status did moderate the effectiveness of 12-step attendance to reduce later drinking intensity, (DPDD: $t (524) = 2.79$, $p < .006$). For the NHW participants, 12-step attendance was predictive of decreased DPDD, ($b = -4.76$), but among NA participants 12-step attendance was predictive of later increases in drinking intensity, ($b = 2.81$). Findings indicated that urban NA attended 12-step programs as readily as NHW adults and that, as a group, urban NA adults reported significantly lower 12-step drop out rates. While 12-step attendance was equally beneficial to NA and NHW participants in increasing abstinence future research is required to understand how, and to what extent, racial status moderates drinking intensity.

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MEASURING TWELVE-STEP PROGRAM AFFILIATION

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Research into the mechanisms of action of twelve-step programs have led to an evolution in the assessment of twelve-step program participation from a simple count of the number of the meetings an individual attends to multi-item scales assessing a variety of twelve-step behaviors and experiences. One such scale is the 14-item Twelve-Step Participation Questionnaire (TSPQ; Tonigan, Miller, & Connors, 1997).The present study examined the psychometric properties of the TSPQ in a sample of 184 substance dependent individuals consecutively admitted to a sober house. We sought to understand the factor structure, reliability, and validity of the TSPQ as information concerning its properties have yet to appear in the peer-reviewed literature. Principal components analysis revealed a nine item, two factor scale. Factor 1 (alpha = .85) consisted of five items that reflected active twelve-step identification (e.g., considering oneself a member, having a sponsor, calling other members for help), while Factor 2 (alpha = .78) consisted of four items reflecting a passive orientation (e.g., meeting attendance, reading literature). Scores on both factors were correlated with measures of lifetime substance use, negative consequences due to substance use, and motivation to change, with Factor 1 showing stronger correlations with these constructs. Future TSPQ validity research should examine the relationship of the active and passive factors to engagement in treatment and relapse.

1133

SOCIAL SUPPORT AND THE IMPACT OF SELF-HELP GROUPS ON SIGNIFICANT OTHERS OF PROBLEM DRINKERS

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Social support is a concept that is the basis for programs such as Alcoholics Anonymous (AA) and other outpatient, as well as inpatient treatment programs for alcohol abuse. Literature indicates that social support, particularly from spouses or loved ones actively involved in the treatment process, is an essential component to long term recovery from problem drinking. Affiliated with AA, Al-Anon Family Group (AAFG) is a self-help program based on this principle of social support that emphasizes the importance of family involvement for the drinkers' abstinence, and also provides significant others (SO's) of problem drinkers a forum to obtain information, resources, and support to cope with a problem drinker in their life. Studies using data collected from AAFG members have been limited and the few that have been conducted have not focused on of the impact of AAFG membership on the health outcomes of the SO's. The current study examined the relationship between SO's health problems and treatment-seeking behavior after attending AAFG. Moreover, we hypothesized that the current drinking status of the problem drinker (yes/no) would moderate the relationship between the SO's perception of current mental health and impact of AAFG membership on life, controlling for membership length. Specifically, those reporting more negative mental health and the problem drinker still drinking would show the greatest risk for experiencing negative feelings about the impact of AAFG membership. Results indicated that the interaction between SO's perception of current mental health and current drinking status of problem drinker was not significant. However, the number of continuous years of membership in AAFG and SO's current mental health status was significantly related to the positive impact of AAFG membership (β = .003, p<.01 and β= .126, p<.01, respectively). Further analyses showed that AAFG members that had personal sponsors sought additional treatment, counseling, or therapy after attending meetings less often than those without sponsors, irrespective of the drinker's status. These findings suggest that regardless of the problem drinker's current drinking status, being involved in AAFG has a positive impact on SO's perception of mental health and feelings about the group, which may be as a result of improved coping skills. Treatment programs should emphasize the benefits and positive health outcomes for SO's involved in the treatment process and self-help groups.

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CHANGES IN 12-STEP-SPECIFIC SPIRITUAL PRACTICES AND ABSTINENCE OUTCOMES: A PROSPECTIVE LAGGED ANALYSIS

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Spiritual practices and beliefs are central to the Alcoholics Anonymous (AA) program. Indeed, the seminal text of AA, the "Big Book", states that "alcoholic[s]…suffer from an illness which only a spiritual experience will conquer" (AA, 2008, p. 44). To date, six studies have confirmed that increased spirituality mediates the association between AA participation and abstinence (cf. Kelly, Stout, & Magill et al., 2011). However, the measure of spirituality used in all but one of these studies, the Religious Background and Behaviors questionnaire (RBB; Connors, Tonigan, & Miller, 1996), is a composite measure that combines religious and spiritual practices, and many of these practices are not prescribed in the core AA literature, e.g., attending religious services. The purpose of the current study was to determine whether *12-step-specific* spiritual beliefs and practices would mediate the abstinence outcomes of 12-step attendees. Participants were 129 individuals recruited from community-based 12-step groups, outpatient treatment programs, and via flyer advertisements. Spiritual beliefs and practices were measured using a subscale of the General AA Tools of Recovery Questionnaire (GAATOR; Montgomery, Tonigan, & Miller, 1991) that captured the extent to which participants endorsed spiritual precepts outlined in the 12 steps. This subscale was validated using factor analysis in a previous study (Greenfield & Tonigan, under review). The *Form 90* interview (Miller, 1996) was used to measure participants' 12-step attendance, proportion of days abstinent from alcohol (PDA), and drinks per drinking day (DPDD). To determine whether GAATOR scores in months 4 – 6 mediated the association between 12-step attendance in months 0 – 3 and drinking outcomes in months 7 – 9, we used a product of coefficients approach with bootstrapping (cf. Preacher & Hayes, 2008) and an intent-to-treat design. Results showed that, controlling for baseline PDA and baseline GAATOR scores, the mediating effect of GAATOR was significant. Higher 12-step attendance predicted greater 12-step-specific spiritual practices and beliefs, which predicted a higher PDA. These findings suggest that 12-step-specific spiritual practices and beliefs are key ingredients in the 12-step approach to recovery. They further indicate that clinicians may maximize the abstinence outcomes of clients they refer to 12-step programs by encouraging them to practice the spiritual steps of these programs.

1135

ROMANCE IN MEETINGS: HOW INTIMATE RELATIONSHIPS WORK FOR THE RECOVERY OF ALCOHOLICS

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This study examines the role of love or intimate relationships in the recovery process for Japanese alcoholics and aims to identify what kind of intimate relationships are accepted in Japanese Alcoholics Anonymous (AA). Looking at previous literatures, when researchers undertook research, especially about such sensitive topics as "sexual matters", they chose ethnographic research. I therefore participated an AA meeting in a residential district in Tokyo from 2010 to 2011 using ethnographic methods and attempted unobtrusive observation to understand AA culture and members' attitude toward intimate relationships. I kept field notes after meetings and analyzed them, and also used booklets published by AA as research material. First, all members reported that AA in Japan prohibits having intimate relationships among members. An intimate relationship, which may lead to a relapse, is worse than a simple sexual adventure. Second, although members know intimate relationships are taboo, many members find their future partner in AA. Practically, AA members think that a member who has stopped drinking for more than 3 years and has attended meetings regularly, is allowed to have intimate relationships. Third, marriage is one of the most accepted forms of having intimate relationships among members. Fourth, the role of sponsor is very important. In general, sharing experiences about intimate relationships is important to maintain intimate relationships and maintain abstinence. Research findings reveal that intimate relationships in AA meetings is a sensitive topic and highlights the double standard on sexual intimacy between members in AA culture; that is, on one hand "Love is taboo", but on the other "Love is overlooked" if it satisfies some conditions, for example long term abstinence and/or having a good sponsor. Members understand that it is dangerous to have intimate relationships with others because of the danger of relapse. However, if an intimate relationship between members coincides with long term abstinence and the support of a good sponsor, then it may assist in achieving good results in recovery from alcoholism.

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MUTUAL-HELP PARTICIPATION AND 1-YEAR OUTCOMES IN VETERANS DUALLY DIAGNOSED WITH BIPOLAR OR UNIPOLAR DEPRESSION

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The goal of this study was to determine the extent to which use of 12-step mutual-help groups (MHGs) by patients dually diagnosed with substance use and either bipolar disorder or major depressive disorder was associated with substance use and depression outcomes. Patients entering treatment were followed at 6 months and 1 year. Diagnostic groups were based on standardized clinical interviews. We conducted logistic regressions at each follow-up to predict past 30-day abstinence from alcohol and/or drugs from (1) involvement in mutual-help groups (a count of 14 practices, such as reading 12-step literature, socializing with group peers), (2) need fulfillment in groups (6 summed items with higher scores indicating more fulfillment), and (3) psychiatric diagnosis (BD, n=48; or MDD, n=32). We also conducted regressions to predict past 30-day depressive symptoms from the same variables.
More MHG involvement, more need fulfillment in MHGs, and having a major depression rather than a bipolar diagnosis significantly predicted a higher likelihood of abstinence from both alcohol and drugs at the 6-month and 1-year follow-ups. More specifically, at each follow-up, patients with bipolar disorder were significantly less likely to be abstinent from drugs than patients with major depression, but groups did not differ on abstinence from alcohol. Patients with bipolar disorder improved less on depressive symptoms at each follow-up than did patients with major depression. Supplementary analyses found that patients with bipolar disorder were less likely than patients with major depression to report having participated in MHGs at each follow-up; however, within the bipolar, but not within the major depression, group, need fulfillment in MHGs predicted a significant reduction in depressive symptoms. These results suggest that involvement and need fulfillment in 12-step mutual-help groups may be associated with increased abstinence from alcohol in patients with bipolar disorder, similar to that in patients with major depressive disorder, but not with abstinence from other drugs. These results support theoretical frameworks suggesting that substance use by patients with bipolar disorder may be an attempt to alleviate depressive symptoms and are associated with faster cycling from depressive to manic episodes.

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BENEFITS OF MUTUAL-HELP GROUPS FOR DUALLY DIAGNOSED PATIENTS

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The use and benefits of substance-focused 12-step mutual-help groups such as Alcoholics Anonymous by patients with both substance use and psychiatric disorders has been a subject of debate. We examined dually diagnosed patients' participation in mutual-help groups (MHGs) and the extent to which more participation was associated with better alcohol and drug outcomes up to 2 years post-treatment.

The sample was 304 dually diagnosed patients entering outpatient mental health treatment who were assessed at treatment entry and 6 months, 1 year, and 2 years post-treatment for MHG attendance and involvement (engagement in 12-step practices, e.g. obtaining a sponsor), need fulfillment from MHGs, and alcohol and drug use outcomes (using the Addiction Severity Index). At baseline, 11.1% of participants had alcohol use disorders only, 23.3% had drug use disorders only, and 65.5% had both alcohol and drug use disorders. Participants reported high rates of MHG attendance at each follow-up: about three-quarters had attended at least one meeting at 6 months, and about two-thirds had attended at least one meeting at 1 and 2 years since the previous follow-up assessment. At each follow-up, patients who had attended at least one MHG meeting during the follow-up period were significantly more likely to report past 30-day abstinence from both alcohol and drugs than were non-attendees. For example, at 2 years, 71.3% of patients who had attended a MHG meeting were abstinent, versus 53.8% of those who had not (AOR = 1.89, 95% CI = 1.06–3.37). In addition, attending a greater number of MHG meetings during the initial follow-up period was associated with better alcohol and drug abstinence rates at 6 months (AOR=1.02, CI=1.01–1.03) and 2 years (AOR=1.02, CI=1.01–1.03).

Higher levels of overall MHG involvement were associated with higher rates of abstinence from both alcohol and drugs at all follow-ups; in particular, aspects of involvement that predicted abstinence were having a sponsor and having a home group. Patients who worked more of the 12 steps by the 1-year follow-up were more likely to be abstinent at 1 year, and more need fulfillment from MHGs was related to better abstinence rates at 2 years.

Our results indicate that dually diagnosed patients participate in MHGs at high rates and gain positive alcohol and drug outcomes from participation. Because these patients participate in and benefit from MHGs, treatment providers should facilitate their connections to local groups.

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12-STEP INVOLVEMENT AND ABSTINENCE OUTCOMES FOR THOSE WITH PSYCHOACTIVE SUBSTANCE AND PSYCHIACTRIC COMORBIDITY

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Purpose: Research has shown that those with co-occurring psychiatric and substance use disorders are less likely to stay clean and sober after treatment compared to those without co-occurring psychiatric disorders. Also, empirical evidence from heterogeneous populations shows that involvement in 12-step groups (e.g. meeting attendance, sponsorship, service and having a home group), significantly increases the odds of post treatment abstinence outcomes. This analysis examined whether psychiatric severity was associated with 12-step affiliation and whether 12-step affiliation at six months post baseline was associated with 12-month post baseline outcomes.

Methods: A quasi-experimental, longitudinal California treatment sample (N=508 baseline) was analyzed. Aggregated and stratified data (Baseline ASI Psychiatric severity scores of no, < median and > median) were used.

Results: Using logistic regression, aggregated outcomes showed no association between baseline ASI psychiatric severity and six month 12-step outcomes. Stratified analysis for the no psychiatric severity group (N=82) showed no relationship between multiple 12-step involvement measures at six months (overall involvement using the AAI, past 30 day meeting attendance, having a sponsor, having a home group and doing service) and 12 month abstinence outcomes. There were significant and positive relationships between these same 12-step involvement measures at six months and 12 month abstinence outcomes for those in the low psychiatric group (N=128) and the high psychiatric group (N=114).

Conclusion: Twelve-step involvement is an important predictor of abstinence outcomes for those with psychiatric severity. Further, clinicians should consider 12-step involvement for their comorbid psychiatric and substance using clients to increase odds of abstinence outcomes.

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GOALS FOR INITIATING PARTICIPATION IN AL-ANON FAMILY GROUPS: IMPLICATIONS FOR IMPROVING FACILITATION

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Alcohol use disorders often negatively affect the personal functioning of the drinker's family members. Al-Anon Family Groups, a 12-step recovery program, is a common source of support for individuals who have problem drinkers in their lives. Despite Al-Anon's widespread use, there is a lack of research documenting the goals of new members. We describe the characteristics of Al-Anon newcomers and examine their goals of attending Al-Anon meetings. We recruited 272 newcomers (having attended 6 or fewer meetings) from 182 Al-Anon Family Groups in the U.S. to complete a paper-based survey. The newcomers' mean age was 46.4 years (SD = 13.7); 83.5% were female, 93.4% were white, and half (50%) were married. Measures included the newcomer's 1) goals of participation in Al-Anon for one's self, and 2) goals of participation for the Al-Anon trigger (the main problem drinker in the newcomer's life). When asked their reasons for attending Al-Anon meetings, the majority of newcomers had the following goals for themselves: gaining a better overall quality of life (94.9%), learning how to handle the problems that they have due to their Al-Anon trigger (93%), finding better ways to relax (90.8%), having a better relationship with their Al-Anon trigger (87.5%), and reducing anger (82.7%) and depression/moodiness (72.4%). About one-half (48.2 %) had the goal of stopping or reducing their receipt of verbal and/or physical abuse. Less common goals included having a better financial (41.2%), work or school (33.5%), home/neighborhood (33.1%), and legal (10.7%) situation.

The majority of the triggers were male (69.5%), with a mean age of 44.2 years (SD = 15.2). When asked their reasons for initially attending Al-Anon meetings, the majority had the following goals for their Al-Anon trigger: having a better relationship with the respondent (83.3%), a better overall quality of life (78.7%), less stress, tension, or anxiety (72.1%), and reduced drinking (56.3%).

Results suggest that most people initially attend Al-Anon meetings with the understanding that the program is a resource to help the self, rather than to better control the drinker's behaviors. Our findings may help Al-Anon groups better meet the needs of new members and sustain their participation. Professional treatment providers may be more likely to recommend Al-Anon to their clients with research documenting the goals of its members.

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RECOVERY-RELATED PREDICTORS OF PSYCHOLOGICAL WELL-BEING AMONG NARCOTICS ANONYMOUS MEMBERS

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Although much empirical work has examined the salutary impact of 12-step involvement on substance-related outcomes, far less is known about how 12-step involvement might impact other meaningful psychosocial outcomes. The current study examined correlates of six facets of psychological well-being (e.g., purpose in life) among Narcotics Anonymous (NA) members. NA is an international 12-step organization modeled after Alcoholics Anonymous. Members often report problematic use of alcohol and other drugs. We examined whether duration of abstinence and prescribed 12-step practices (e.g., 12-step work) predicted psychological well-being, over and above demographics and other covariates (e.g., neuroticism). NA members (N = 134) from over 25 US states completed an online survey assessing a broad array of recovery practices and psychosocial outcomes. Participants were required to have at least one year of continuous abstinence, which ranged from 1 to 33 years (M = 11.94, SD = 8.03). Six hierarchical regression models were estimated—one for each facet of psychological well-being. Age and sex were entered on the first predictor block; other covariates (e.g., neuroticism) were entered on the second predictor block; and twelve recovery-related predictors (e.g., time in recovery, 12-step work) were entered on the third block. The six models accounted for between 35% (autonomy) and 60% (environmental mastery) of outcome variance (M = 48, SD = 8). The set of recovery-related predictors accounted for significant incremental variance in purpose in life (17%), personal growth (14%), and positive relations with others (13%). The strongest individual predictor across all models was neuroticism, which was consistently associated with lower levels of psychological well-being. Time in recovery was positively associated with purpose in life, autonomy, and positive relations with others. Comfort at one's home group was positively associated with self acceptance, purpose in life, personal growth, and positive relations with others. Interestingly, time in recovery emerged as a more relevant developmental marker for psychological well-being than chronological age. In addition to stable personal characteristics (neuroticism) and time in recovery, other recovery experiences (e.g., comfort at hone's home group) were associated with psychological well-being. Although accruing time in recovery cannot be hastened, finding the right home group can occur relatively early on in recovery.

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MEMANTINE EFFECTS ON NEURAL COMPLEXITY OF EVENT-RELATED POTENTIAL (ERP) IN SUBJECTS WITH AND WITHOUT FAMILY HISTORIES OF ALCOHOLISM

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Objective: Family history of alcoholism is hypothesized to be associated with disturbed glutamatergic/dopamine interactions and abnormal inhibitory rhythms. We investigated effects of memantine on the Fractal Dimension (FD) of ERPs associated with P300 in adults with and without familial alcoholism. Based on central nervous system hyperexcitiability model for alcoholism risk and the hypothesis that P300 corresponds to the termination of the decision making process reflecting inhibitory mechanisms, we expected to detect abnormal baseline FD in family history positive subjects that was normalized by memantine.
Methods: We assessed 22 family history positive (FHP; i.e. with alcohol dependence in father plus other close relatives)) and 20 demographically-matched family history negative (FHN; no alcoholic relatives) non-alcoholic individuals. Subjects were administered placebo or 40mg of memantine under double blind crossover conditions on 2 separate occasions. EEG data were collected from 8 midline electrodes during an auditory ''oddball'' task. Higuchi's FD was computed for each trial for target stimuli and area under the mean FD curve between 300–600ms was used as dependent measure. Repeated measures ANOVAs were performed for FD to assess main effect of drug and group X drug interaction.
Results: Main effect of drug was insignificant ($p<0.73$). Interaction of group X drug was significant ($p<0.05$), while group X drug X sex displayed a trend ($p<0.08$). Mean FD was significantly higher in FHP individuals relative to FHN at baseline ($p<0.03$); after memantine this group difference diminished ($p<0.8$).
Conclusion: High FD in FHP at baseline may indicate an unsynchronized neuronal interaction resulting in disorderly state of neural oscillations underlying the P300 response. As predicted, after memantine FD increased for FHN subjects and decreased for FHP, equalizing values between groups, thus FHPs tend to resemble FHN after memantine. Results suggest that FHP individuals may have altered NMDA receptor function compared to FHN. Abnormal baseline FD in FHP may result from an excitation-inhibition imbalance associated with altered glutamatergic levels.

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MAGNESIUM & ACAMPROSATE FOR THE TREATMENT OF ALCOHOL WITHDRAWAL

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Background: Magnesium (Mg) deficiency is common for alcoholics. Earlier research suggests that Mg treatment may help to decrease the risk of delirium tremens (DT) and withdrawal symptoms among alcoholics but the evidence is still controversial. The purpose of this study is to investigate how the magnesium affects withdrawal and DT of alcoholics.
Method: A retrospective study was done by reviewing medical records of patients diagnosed as alcohol dependence according to DSM-¥[3] diagnostic criteria between March 1st, 2007 and December 31st, 2008 at the Inchon christian Hospital. According to use of Mg, it was made into two groups by thirty one people and thirty four people. And through the chart review, sociodemographic data was included. At baseline(1st), 2nd, 3rd and 4thweek after admission, we examined complete blood count, liver function test, total dose of benzodiazepines of every week, occurrence and duration of DT, Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar).
Result: 1) To compare the two groups, there was no difference of demographic data. 2) Mg treatment groups showed lower total dose of benzodiazepines used during 1st week after admission than control groups. 3) Mg treatment groups showed lower DT frequency & duration
even though does not show a significant difference. 4) Mg treatment group showed more rapid decrease in total CIWA-Ar score but a significant difference begin to show at 4th week compared to control group. 5) But, among subtest of CIWA-Ar, sweating and anxiety score began to show a significant difference at 3rd week.
Conclusion: This study showed that magnesium could be one of the effective and beneficial treatment options of alcoholic withdrawal symptoms by reducing and stabilizing hyperexcitotoxicity of the glutamate system.

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MEC1005MYLAMINE FOR THE TREATMENT OF PATIENTS WITH DEPRESSION AND ALCOHOL DEPENDENCE

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Depression with co-morbid alcohol dependence is very prevalent and it is very costly to treat. The co occurrence of the two disorders leads to greater severity and worse long-term outcome. Although a number of treatment strategies have been implemented for depressed patients with alcohol dependence the controversy concerning best treatment options for those patients persists. It has been hypothesized that medications that block presynaptic nAChR may be effective in the treatment of alcoholism and depression. Mecamylamine (Inversine ®) is a noncompetitive, high affinity nAChR antagonist with low selectivity for the alpha-7 receptor.
The objective of this study was to evaluate the efficacy of adjunct mecamylamine (MEC, 10 mg/day) versus placebo in reducing depressive and alcohol symptoms in patients with depression and co-morbid alcohol dependence.
Twenty-one smokers (n=11) and non-smokers (n=10) with a current diagnosis of depression *and* alcohol dependence were recruited for this 12-week treatment study. Eleven participants were randomized to mecamylamine and ten to placebo. Participants were included in the study if: they met current DSM-IV criteria for Major Depression and Alcohol Dependence and were on a stable SSRI dose for 2 weeks. All participants came weekly to take their medications and complete weekly assessments that evaluated depressive symptoms and alcohol consumption.
The results indicated a significant medication by smoking status interaction for all drinking measures. Non-smokers who were treated with mecamylamine had significantly lower number of drinking days, heavy drinking days, percent number of drinking days and percent heavy drinking days than non smokers taking placebo. Also, there was a trend towards a significant 3-way interaction (medication X smoking status X time) on the 17-item HAMD scale. Again, non-smokers benefited more from mecamylamine when compared to placebo while there was no change in HAMD scores over time for smokers either on mecamylamine or placebo.
The results from this study show that mecamylamine seems to be effective in reducing alcohol consumption in these dually diagnosed patients. The study also suggests that mecamylamine when used in conjunction with an antidepressant can be effective in further reducing depressive symptoms. The results also suggest that smoking moderates the efficacy of mecamylamine.

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MIRTAZAPINE PILOT TRIAL IN COMORBID MDD-AUD

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Previous trials of various antidepressants have produced disappointing results for treating comorbid disorders. The authors recently conducted a first open label trial of the pharmacologically unique (non-SSRI, non-tricyclic) antidepressant mirtazapine (15 mg for two weeks, then 30 mg for 6 weeks) among adults with major depressive disorder (MDD) and alcohol dependence (AD) to determine whether it decreases the drinking and the depressive symptoms of that population. All subjects also received motivational enhancement therapy during the 8-week study. Data was collected weekly for the first 4 weeks and biweekly for the second 4 weeks. The 12 subjects included 5 women and 7 men. All subjects provided data at all data collection times throughout the study. No serious adverse events were noted. Depressive symptoms sharply from 31.8 to 8.3 on the BDI ($p<.001$) and drinking decreased from 33.9 to 13.3 drinks per week on the TLFB ($p<0.003$) during the study. Sleep symptoms (HDRS) also decreased significantly during the course of the study. None of the subjects were employed full time at the start of the study, but 9 of the 12 (75%) were employed full time at the end of the study. These findings suggests safety and within-group efficacy for mirtazapine for treating both the depressive symptoms and the excessive drinking of this comorbid population. A double-blind placebo-controlled trial of mirtazapine appears to be warranted.
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EFFECTS OF ZONISAMIDE TREATMENT ON SHORT-TERM REMISSION FROM ALCOHOL DEPENDENCE

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Purpose: In a 12-week randomized trial of subjects with current DSM-IV alcohol dependence whose goal was to cut down or stop drinking, treatment with zonisamide, an anticonvulsant with multiple neuronal mechanisms and neuroprotective effects, was associated with a greater reduction in heavy drinking days per week, drinks per week, and craving over time than placebo treatment. In a secondary analysis of those data, we examined whether, at the end of treatment, zonisamide affected 1) the rate of remission from alcohol dependence and 2) the percentage of subjects with no heavy drinking days (PSNHDD).
Methods: 40 alcohol dependent subjects were randomized to receive treatment with zonisamide or placebo, titrated over 8 weeks to a target dosage of 500mg daily, and continued at that dosage for 4 weeks. Most subjects' goal was to reduce drinking (~65%) rather than to become abstinent (only ~35% had abstinence as a goal). Subjects also received 6 brief CBT sessions. We compared the groups on their 30-day prevalence of alcohol dependence and on PSNHDD during the last 4 weeks of treatment.
Results: Four subjects (10%) failed to complete the treatment (3 in the zonisamide group, 1 in the placebo group). Comparisons on outcomes of interest were made on subjects that completed the study. At the end of treatment, a significantly greater number of zonisamide-treated subjects (94%, 16 of 17 subjects) than placebo subjects (58%, 11 of 19 subjects) no longer met criteria for alcohol dependence [p = 0.02, (Fisher's exact test)]. There was no significant between-group difference on PSNHDD.
Conclusions: Zonisamide, by reducing heavy drinking, appears to aid in remission from alcohol dependence; however, greater attrition in the zonisamide group confounds the conclusion about this outcome. Thus, further study of zonisamide for alcohol dependence treatment is warranted. A larger study, with longer exposure to the target dosage of medication is needed to more thoroughly examine the effects of zonisamide on remission rates and PSNHDD.

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CLINICAL TRIAL OF ESCITALOPRAM FOR ALCOHOLISM COMORBID WITH AFFECTIVE DISORDERS

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Aim: To study efficacy of one of the most selective SSRI - escitalopram for treatment of alcoholics with co-morbid affective disorders (mild to moderate depression).
Methods: 60 recently detoxified patients with alcohol dependence and mild to moderate depression had been randomized to one of two treatment groups. Patients of the first group were treated with escitalopram (10mg/day) for 3 months while patients of the 2nd one received identically looking placebo. All the study subjects were scheduled to come to the clinic on the weekly basis for psychiatric evaluation (severity of depression and anxiety, and craving for alcohol), control of alcohol use and compliance with the study medications (by riboflavin marker in urine). The study design was double blind.
Results: Escitalopram was significantly superior to placebo in treating depression, anxiety, and craving for alcohol. In particular, depression measured with Montgomery-Ashberg scale and anxiety measured with Hamilton scale reduced significantly faster and greater in escitalopram group compared to placebo group. Craving for alcohol reduced faster and deeper in escitalopram group in comparison to baseline according to all three carving scales (Obsessive-Compulsive Drinking scale, Penn Alcohol Craving scale, and Visual Analog Scale of Craving for alcohol) with the limited number of differences between groups. Also, escitalopram was superior to placebo in preventing relapse to heavy drinking: The number of those who completed treatment was significantly higher in escitalopram group while the number of drinking days – significantly lower. Kaplan-Meier survival functions also demonstrated significantly better retention in treatment in escitalopram group compared to placebo group. However, the mean period of abstinence (time to first drink) did not differ significantly between the study groups. Overall treatment effect measured with Clinical Global Impression scale was significantly better and Global Assessment of Functioning scale score improved significantly higher in escitalopram group. The number of side effects was higher in escitalopram group, however, all adverse events were mild and there were no serious adverse events in either one of two groups.
Conclusion: Escitalopram is effective medication for alcohol dependence with co-morbid affective disorders.

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D-CYCLOSERINE AND EXTINCTION TO ALCOHOL CUES IN TREATMENT-SEEKING AUD+ ADULTS: PRELIMINARY FINDINGS

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D-Cycloserine (DCS) is a partial glutamate agonist that has been found to enhance exposure therapy for anxiety disorders by augmenting the extinction of conditioned fear. Moreover, there is preliminary clinical evidence that DCS facilitates extinction to tobacco cues and preclinical evidence DCS attenuates alcohol-seeking behavior. The current study investigates whether DCS facilitates extinction of cue-elicited alcohol craving in treatment-seeking individuals with alcohol use disorders (AUDs). Participants were enrolled in an evidence-based AUD treatment within which two experimental extinction periods were included to investigate DCS effects (DCS-50 mg or matched placebo in advance of the extinction sessions, which were approximately one week apart). Eligibility criteria included AUD+ status, absence of other current comorbid Axis I psychopathology, and evidence of initial alcohol cue reactivity, (i.e., increase in subjective craving when exposed to alcohol cues relative to neutral cues). To date, 22 participants have been enrolled in the study, undergone randomization, and received at least one DCS dose. Blinded analyses suggest that all the manipulations are operating as expected. At the first extinction session, omnibus within-subjects ANOVAs revealed a significant overall effect of time ($F=2.25$, $p < .05$) and follow-up comparisons revealed increases in craving in response to alcohol cues compared to neutral cues ($p = .06$) and subsequently significant decreases (ps <.001–.08), reflecting extinction. At the second extinction session ($n = 16$), no omnibus time effect was present ($F=1.50$, $p = .16$), but follow-up tests revealed a significant effect of cues ($p < .05$) and no subsequent attenuation based on exposure (all ps >.50). Examining cue reactivity between the two sessions, there was evidence of significantly lower craving during the second session, following both exposure to neutral and alcohol cues (ps<.002), reflecting an extension of extinction from the first to the second session. These findings suggest that the study is meeting the boundary conditions of the design for testing the effects of DCS on extinction to alcohol cues. Recruitment is ongoing and findings in the larger sample and by medication status will be presented. Significant augmentation of extinction effects by DCS would suggest it may be useful for treating AUDs and that further clinical investigations are warranted.

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TOLERABILITY OF D-CYCLOSERINE IN TREATMENT-SEEKING AUD+ ADULTS: PRELIMINARY FINDINGS

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D-Cycloserine (DCS) is an NMDA agonist that has demonstrated effectiveness in augmenting exposure therapy in the extinction of conditioned fear and facilitated extinction of alcohol-seeking behavior in rats, suggesting it has promise in treating alcohol use disorders (AUDs). The current study examined the associated side effects of 50 mg DCS vs. placebo in an ongoing study of DCS's effects on cue-elicited craving. Participants were AUD+ adults who were receiving evidence-based treatment within which two experimental extinction periods were included to investigate DCS effects. The experimental protocol included two acute administrations of either DCS or placebo, approximately one week apart, and several other study visits. Using the SAFTEE, the following side effects were assessed: 1) Drowsiness; 2) Dizziness; 3) Headache; 4) Slurred speech; 5) Tingling in hands or feet; 6) Mental confusion; 7) Irritability; 8) Anxiety; 9) Skin rash; and 10) Aggression. Side effects were assessed on the days of the acute administrations and over the intervening periods between sessions (i.e., acute and protracted effects; total of five assessments). Medication status currently remains blinded, but frequencies of side effects were examined for all participants to ascertain overall levels. Sample sizes ranged from 12–22 based on number of sessions attended. Following the first acute dose, only drowsiness (18%; 4 of 22) and dizziness (4%; 1 of 22) were reported. During the intervening period before the next session, participants reported drowsiness, headache, tingling, confusion, irritability, anxiety, and rash (6%-22%; 1–4 of 18). At the beginning of the second DCS administration, drowsiness, headache, tingling, irritability, anxiety, and rash were reported since the last assessment (6–13%; 1–2 of 16). Following the second acute dose, only drowsiness was reported (7%; 1 of 14). At the assessment of protracted effects, drowsiness, headache, and irritability were reported (all 8%; 1 of 12). Although the medication blind prevents clear conclusions, the profile of side effects in general was most notable following the intervening period after the first administration and, in general, was relatively mild. Recruitment is ongoing and results with the complete sample and by medication status will be presented. A modest side-effect profile reflecting high tolerability would support further study of DCS as an AUD pharmacotherapy.

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PLACEBO GROUP IMPROVEMENT IN TRIALS OF PHARMACOTHERAPIES FOR ALCOHOL USE DISORDERS: A MULTIVARIATE META-ANALYSIS EXAMINING CHANGE OVER TIME

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Objective: Placebo group improvement in pharmacotherapy trials has been increasing over time across several pharmacological treatment areas. However, it is unknown to what degree, if any, that this increasing improvement has occurred in pharmacotherapy trials for alcohol use disorders or what factors may account for placebo group improvement and, if present, increasing placebo group improvement over time. This meta-analysis of 47 alcohol pharmacotherapy trials (1) tested for placebo group improvement in pharmacotherapy trials for alcohol use disorders and (2) examined several potential moderators of placebo group improvement and changes in placebo group improvement over time.
Method: Random effects univariate and multivariate analyses were conducted that involved examination of several moderators of placebo group improvement. These included (a) publication year, (b) country in which the study was conducted, (c) outcome data source (subjective, moderately subjective, or objective), (d) number of administrations of the placebo, (e) overall severity of study participants, and (f) additional psychosocial treatment.
Results: Large placebo group improvements were found across the 47 studies. Publication year was found to moderate these improvements, with an increase in placebo improvement occurring over time. Outcome data source also moderated placebo group improvements and the effect size on outcome from each type of data source was significantly larger than zero.
Conclusion: Similar to previous pharmacotherapy placebo research, findings supported substantial pre- to post-test placebo group improvement, an effect that has been increasing over time. Placebo group improvement over time persisted even after controlling for several potential covariates of this relationship.

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MEDICAL MANAGEMENT USING THE NIAAA GENERIC VERSION MAY BE APPROPRIATE FOR PRIMARY CARE SETTINGS

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Purpose: With the full 'rollout' of the Parity Act and Health Care Reform, reimbursable medical treatment will become more available for problem drinkers, not just those with alcohol dependence who may require specialty care (McLellan, 2011). Consequently, there is renewed interest in finding effective medications for alcohol use disorders. Pharmacotherapy trials for alcohol dependence have been using brief, medically-based psychosocial interventions as a platform for providing medications for alcohol treatment in order to more consistently educate patients and to enhance treatment compliance. Medical Management (MM) was developed for the NIAAA-sponsored COMBINE study and is perhaps the most widely used medication management protocol for alcohol pharmacotherapy trials. Recently, a generic version of the MM manual has been made available on the NIAAA website (Medications Management Manual: Generic Version; Pettinati and Mattson, 2010). This adaptation removed specific references to the COMBINE study to facilitate the use of MM in clinical drug trials and in practice-based clinical settings. Following the COMBINE study, concerns were raised that the amount of time spent in MM initial and follow-up sessions might be too long to be incorporated into primary care and certain alcohol trials. MM initial and follow-up sessions are proposed to last from 40–60 minutes and 15–25 minutes respectively. This presentation provides information on the length of the sessions using a pre-version of the Generic MM manual in alcohol clinical trials.
Methods: The pre-version of the Generic MM manual has been in use in alcohol clinical trials at the University of Pennsylvania since the COMBINE study was completed. The sessions in these trials were audiotaped from which the length of the sessions was determined.
Results: The median length of the initial sessions was 24.5 minutes. Only 18% were greater than 30 minutes. The median length of the follow-up sessions was 13.9 minutes. Only 19% were greater than 20 minutes.
Discussion: A Medical Management protocol may be more easily applied in primary care and other settings than originally thought because with the generic version, we found the initial sessions were typically under 25 minutes and the subsequent sessions were typically under 15 minutes. The length of these sessions may be shorter than those recorded in the COMBINE study because of differences in the study specific assessments completed by the MM clinician.

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CONSUMER SATISFACTION AND EFFICACY OF THE HANGOVER CURE AFTER-EFFECT©

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Introduction: Alcohol hangover is the most commonly experienced negative consequence of heavy drinking. Currently no effective hangover cure is available. A consumer satisfaction study was conducted to examine the effectiveness on hangover of After-Effect©, a new hangover cure.
Methods: N=113 persons were invited to participate in a home-based open label study to test the effectiveness of After-Effect©. On a night when they intended to consume alcohol, three pills were taken before alcohol consumption and two pills afterwards, before going to bed. The following day, participants completed a survey on the amount of alcohol consumed, hangover symptom severity, and satisfaction of the product.
Results: N=103 participants completed the study. 88% of participants reported After-Effect© to be effective in reducing alcohol hangover. After-Effect© significantly improved overall hangover severity, and all individual hangover symptoms, except for palpitations. In addition, a significant reduction (p=0.0001) in the severity score on concentration problems was reported when using After-Effect©. No gender differences were observed, and there was no relationship with the number of alcoholic drinks that were consumed. Customers were satisfied with the package, pill size and instructions for usage, and the use of After-Effect© showed to be devoid of adverse effects.
Conclusion: Consumer satisfaction and hangover severity scores suggest that After-Effect© is effective in reducing alcohol hangover. However, controlled, double-blind clinical trials should confirm these findings.

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SOCIAL ANXIETY, DRINKING, AND DELIBERATE DRINKING TO COPE: A COMPLEX RELATIONSHIP

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Our group previously reported that successful amelioration of social anxiety with paroxetine did not automatically decrease quantity and frequency of alcohol use in socially anxious alcoholics seeking social anxiety treatment (Book et al. 2008). It did decrease intentional drinking to cope, and it uncoupled the relationship between social anxiety and alcohol use (Thomas et al. 2008). We reasoned that this uncoupling of drinking and anxiety represented a therapeutic window for an adjunctive brief alcohol intervention (BI), and we conducted a randomized clinical trial to examine whether or not adding BI to paroxetine treatment would be effective in decreasing alcohol use in this population. Participants seeking treatment for social anxiety were recruited from two metropolitan areas (Charleston SC and Minneapolis MN). Inclusion criteria included a diagnosis of social anxiety disorder by structured interview, endorsement of drinking to cope with anxiety, and hazardous alcohol use (as defined by NIAAA). All subjects were given a target dose of 60mg paroxetine for 22 weeks. At Week 6 (the time we had previously found social anxiety to be significantly reduced from baseline), subjects (N=83) were randomized to either continued paroxetine alone, or continued paroxetine plus a BI delivered by the treating psychiatrist at weeks 6, 10, 14, and 18. As expected, paroxetine significantly improved social anxiety severity from baseline to week 6. Contrary to our hypothesis, no differences were found between those who did and did not receive BI on any traditional index of quantity/frequency of alcohol use. Of importance, however, we observed that subjects in both groups reported less intentional drinking to cope, and this decrease corresponded with their decreased anxiety. Taken together, these results indicate that although neither the amelioration of anxiety severity nor the addition of BI was effective at decreasing drinking, paroxetine treatment effectively decreased social anxiety severity and also decreased coping related drinking. Since drinking to cope is a well-known risk factor for development of alcohol dependence, reducing coping-related drinking in socially anxious drinkers may prevent the escalation of drinking and subsequent alcohol dependence.

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MIRTAZAPINE FOR COLLEGE STUDENTS WITH ALCOHOL DEPENDENCE AND COMORBID MAJOR DEPRESSION: A NATURALISTIC OPEN LABEL STUDY
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Given that comorbidity between depressive disorders and alcohol dependence is common there is a great interest in discovering effective treatments for both, the mood symptoms and alcohol use in patients experiencing these problems.
Objective: The primary aim of this study was to evaluate the effectiveness and tolerability of mirtazapine (15–45 mg QHS) in conjunction with supportive psychotherapy in the treatment of college students diagnosed with alcohol dependence and major depression (ICD-9) in an open label fashion.
Subjects and Methods: The Time-Line Follow-Back Assessment, the 17-item Hamilton Depression Rating Scale, the Hamilton Anxiety Rating Scale and the Pittsburgh Sleep Quality Index were measured at baseline and at weeks 4 and 8 in a sample of college students (n=33, 57% women, age= 20.6 years ± 2.6) seeking treatment in a student's mental health clinic. ANOVA for repeated measures was used to asses change is symptom severity over time.
Results: At the end of the 8 weeks of treatment there was a significant reduction of the depressive symptoms (p=0.002) and a reduction in the number of drinks consumed per drinking occasion (p= 0.01). At the level of a non significant trend (p=0.07) there was an improvement of sleep quality but no significant changes in severity of anxiety symptoms (p=0.20). Adverse events (drowsiness, dry mouth) related to mirtazapine treatment were observed in 12% of the patients.
Conclusion: the results from this naturalistic study suggest that treatment with mirtazapine for the treatment of college students diagnosed with alcohol dependence and major depression is a useful strategy that improves mood symptoms and drinking behavior.

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DIFFERENTIAL IMPACT OF CANNABIS ABUSE ON DEPRESSION REMISSION IN COMORBID DEPRESSION AND ALCOHOLISM
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The aim of this study was to examine the impact of long standing cannabis abuse on the rate of remission from major depressive disorder among patients with major depression and comorbid alcoholism. We examined the impact of long standing cannabis abuse (defined as 10 or more years) on depression remission (defined as a clinician rating of very much improved on the Clinical Global Improvement Scale AND a mean HRSD score below 7) in a sample of 64 subjects (50% females) who completed a 24-week randomized, double-blind, placebo-controlled, parallel-group trial evaluating the efficacy of fluoxetine (dose range 20–60mg/day) ± naltrexone hydrochloride (dose 50 mg/day) in the treatment of major depression with comorbid alcoholism. Post-randomization assessments were undertaken weekly for the first 4 weeks, every two weeks for the subsequent 8 weeks, and every 4 weeks for the remaining 12 weeks of the 24-week study. The results indicated significantly lower proportion of patients with major depression and chronic cannabis abuse were rated in remission (very much improved on the CGI with a mean HRSD of 5.7 (sd 2.7)) compared to those without chronic cannabis abuse (5.8% vs.14.7%, p=0.002). The Odds Ratio for remission of the latter group was 2.79 (p-value=0.0018). Furthermore, the chronic cannabis abuse groups included more males (65.4% vs 39.5%, p=0.04), reported lower baseline depression severity (HRSD-25 mean score 19.6 (sd 4.4) vs. 22.4 (sd 5.9), P=0.045), and higher proportion of drug use days during the study (mean weakly days 0.9 (sd 1.8) vs. 0.05 (0.2), p=0.025). The two groups did not differ on average weekly alcohol drink or on average dose of fluoxetine. Long standing cannabis abuse appears to impact on depression remission. Patients in this group appear to be three times less likely to have rating of very much improved and remission of depressive symptoms. This is despite the fact that those with chronic cannabis abuse reported lower baseline depressive symptoms and had similar average dose of fluoxetine. Given the high rate of chronic cannabis abuse in major depression and other psychiatric disorders, future studies are warranted to further elucidate the role of chronic cannabis abuse as a predictor of treatment response and remission of major depressive disorder.
Source of Funding: Supported by USPHS Grants R01 AA11929and in part by R01AA015385; R01 DA019992; R01 DA-019142, R01AA13370, NIDA K02-017822, NIDA CTN; & VA MIRECC grant.

9. EPIDEMIOLOGY
a. Special Populations (children/adolescents, ethnic groups, gender) 191–208/1155–1172

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SEXUAL ORIENTATION DISCORDANCE AND HAZARDOUS DRINKING AMONG WOMEN
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Substantial evidence over the past three decades points to high rates of hazardous drinking among sexual minority women, but relatively few studies have examined potential explanations for this risk. Several recent studies posit that women who report discordance among the three major dimensions of sexual orientation (e.g., heterosexual identity but same-sex behavior or lesbian identity but opposite–sex attraction) may be at particularly high risk for hazardous drinking.
To test this hypothesis we used data from a combined sample of 953 women from a national general population sample (n=548) and a community sample of Chicago-area self-identified lesbians (n= 405). In addition, given findings suggesting that women of color are less likely than White women to identify as lesbian or bisexual, regardless of their sexual behavior or attraction we tested racial/ethnic differences in the relationship between sexual orientation discordance and hazardous drinking. Nearly one-third (32%) of the sample was discordant on sexual orientation and more than one-half (54%) of the sample reported hazardous drinking; however, 65% reported both. Rates of hazardous drinking did not differ by race/ethnicity; however, African American women were more likely to report discordant sexual orientation (42.6%) than Latina (30.4%) or White (30.5%) women (p=.007). Multiple regression analyses showed a significant association between sexual orientation discordance and hazardous drinking (β = 0.134, p = .001) for the whole sample. However, associations between sexual orientation discordance and hazardous drinking did not differ by race/ethnicity.
In this sample, only African Americans were significantly more likely to report sexual orientation discordance, compared to Whites. As anticipated, overall rates of hazardous drinking in the sample were high. Moreover, despite that sexual orientation discordance was related to hazardous drinking, this association was not moderated by race/ethnicity. Studies examining the relationship between sexual orientation discordance and hazardous drinking among adult women of color are scant; future research is needed to understand why results are mixed among the few studies available. (Supported by NIAAA/NIH Grants AA13328 and AA00266 (Hughes) and AA004610 (Wilsnack))

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ETHNIC AND RACIAL DIFFERENCES IN TRAUMA, MENTAL HEALTH, AND SUBSTANCE USE AMONG YOUNG ADULT SEXUAL MINORITY WOMEN
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Previous research suggests that sexual minorities are at greater risk for trauma exposure (Hughes et al., 2010; Roberts et al., 2010), mental health problems (Meyer, 2003; Mustanski et al., 2010), and substance use (Green & Feinstein, 2011; Hughes et al., 2010; Marshal et al., 2008). To date, few studies have examined ethnic/racial differences among sexual minorities in relation to health-related behaviors and outcomes (e.g., Andres-Hyman et al., 2004; Balsam et al., 2010). Furthermore, studies of ethnic/racial differences among young adult sexual minority women are virtually non-existent. The current study adds to the previous literature by exploring ethnic/racial differences in trauma exposure, mental health, and substance use in a national sample of young adult sexual minority women. A total of 967 self-identified lesbian and bisexual women were recruited using social networking sites to participate in a larger study on women's health behaviors. The ethnic/racial composition of the sample included 730 (76%) White, 108 (10%) African American, 91 (9%) Latina, and 38 (4%) Asian women. Results revealed significant differences between ethnic/racial groups for childhood sexual assault (p = .004) and forcible rape at any age (p = .037). However, no significant differences were found in overall lifetime trauma exposure or lifetime exposure to LGBT bias-related trauma exposure. In terms of mental health variables, Asian women had significantly lower PTSD symptoms than all other participants (p < .001). No significant group differences were found for social anxiety, general anxiety, or depression symptoms. Finally, no significant differences were found for any of the indicators of alcohol use, including peak drinking, typical number of drinks per week, drinking days per week, alcohol-related consequences, or heavy episodic drinking between groups. Results will be discussed in terms of implications for prevention and treatment of alcohol and mental health problems among diverse sexual minority women

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SELF-IDENTITIES AND RISK BEHAVIORS IN LGBT YOUNG ADULTS

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Purpose: To compare relationships among the total collection of positive and negative self-identities, four dimensions of sexual identity development, substance-related problem behaviors, and sexual risk behavior in three groups of sexual minority young adults: men, women, and transgender men and women.
Methods: Participants aged 16-24 were recruited for a study of self-identities and behavioral risk factors in sexual minority young adults. An open-ended cardsort was used to measure the number of positive and negative self-identities and a computer-assisted self interview was used to measure four dimensions of sexual identity (*uncertainty* about sexual orientation, *exploration* of sexual needs, *commitment* to a sexual minority identity, and *integration* of sexual minority identity into the self-concept), substance-related problem behaviors, and sexual risk behavior. Results: The sample includes three groups: 1) men (n=40; mean age 21.7; 75% Black, 15% White; 73% gay, 20% bisexual, and 8% prefer no labels); 2) women (n=41; mean age 20.6; 29% Black, 59% White; 29% lesbian, 20% bisexual, 34% mostly heterosexual, 5% curious, 10% prefer no labels); and 3) transgender men and women (n=30; mean age 21.1; 22 male-to-female, 11 female-to-male; Black 67%, White 20%; 26% heterosexual, 23% bisexual, 20% gay/lesbian, 3% questioning, and 17% prefer no labels). In sexual minority men, the number of negative self-identities was associated with sexual risk behavior (r=.32) and exploration of sexual needs was associated with substance-related problem behaviors (r=.27). In sexual minority women, the number of positive self-identities was associated with sexual risk behavior (r=-.27), and commitment to sexual minority identity and integration of sexual minority identity into the self-concept was associated with substance-related problem behaviors (rs -.33 and -.36). In the transgender group, the number of negative self-identities was associated with substance-related problem behaviors (r=.38).
Conclusions: Different aspects of self-identities may confer unique risk and protective influences on substance-related problem behaviors and sexual risk behaviors. Moreover, the pattern of relationships among self-identities, substance-related problem behaviors, and sexual risk behaviors differs for sexual minority men, sexual minority women, and transgender persons. Findings have important implications for prevention in this vulnerable and under-researched population.

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LIFETIME SEXUAL VICTIMIZATION RISKS AMONG SEXUAL MINORITY MEN

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Purpose of Study: To address a dearth of research regarding sexual victimization risks among sexual minority men, we examined experiences of childhood sexual abuse (CSA), adult sexual assault (ASA), and sexual re-victimization among bisexual and gay men (n = 183) and explored risk factors associated with ASA vulnerability.
Methods: Self-identified gay (n = 96) and bisexual men (n = 87), 18–35 years old, were recruited by advertisements and Respondent Driven Sampling to complete self-administered surveys.
Results: Half (51%) of men reported CSA and 67% reported ASA. Fifteen percent reported that their most serious ASA experience involved unwanted sexual touching, 16% reported sexual coercion, 35% reported attempted rape or rape. Over half (61%) of men's AUDIT scores indicated hazardous alcohol use and 14% indicated possible alcohol dependence. Bisexual men reported significantly higher alcohol severity scores, greater internalized heterosexism (IH), and higher rates of revictimization (CSA + ASA) than gay men. Hierarchical regression was used to test whether sexual identity, CSA severity, IH, lifetime number of male sexual partners, and alcohol problems were associated with ASA severity. Results indicated no significant association between bisexual identity and ASA severity. Greater CSA severity was significantly associated with greater ASA severity ($\Delta R^2 = .06$, $p < .01$). Lower IH was significantly associated with greater ASA severity ($\Delta R^2 = .04$, $p < .05$). Number of lifetime male sexual partners was not significantly associated with greater risk for severe ASA. Lastly, we found that more alcohol problems were significantly associated with greater ASA severity ($\Delta R^2 = .05$, $p < .01$). The final regression model accounted for 14% (adjusted R^2) of the variance in ASA severity.
Conclusion: Similar to patterns found among heterosexual, lesbian, and bisexual women in prior studies, we found that gay and bisexual men experienced a cycle of sexual violence that began in childhood and continued into adulthood. Rates of lifetime sexual victimization and risky alcohol use were high in this sample. Regression findings indicated that ASA severity was associated with a combination of factors, including more severe CSA experiences, lower levels of IH, and higher alcohol severity scores. Knowledge about history of sexual trauma and risky drinking is critical for the future development of effective intervention efforts to reduce ASA risks among sexual minority men.

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DISCRIMINATION, ALCOHOL USE, AND HIV RISK BEHAVIORS IN TRANSGENDER ADULTS

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There is a well-documented association between the use of alcohol and other substances and HIV risk behavior. Most work has focused on men who have sex with men (MSM) and heterosexual adults. One factor that plays a role in alcohol use is stress, including the stress induced by discrimination. Prior work has documented associations between discrimination experiences and alcohol use, but this has been primarily examined in racial minority populations and in MSM. The interrelationship between these factors has not been thoroughly investigated in transgender adults. In the present study, transgender adults (N=105) completed an anonymous survey assessing demographic characteristics, alcohol use, discrimination, and sexual behavior. Participants were also asked to indicate if they believed they had a substance use problem. Most participants (77%) reported alcohol use in the prior 3 months with a substantial number reporting daily use (19%). Most participants (74%) reported at least one discrimination experience in the prior year, including being insulted because of their gender identity (57%), losing a job because of gender identity (26%), or being assaulted because of gender identity (13%). The total number of discrimination experiences was correlated with alcohol use (*rho*=0.21, p <.05). Participants who indicated their belief that they had a substance use problem reported more discrimination experiences (M=4.0, SD=1.0) than individuals who indicated they did not have a substance use problem (M=1.95, SD=1.7), t=2.06, p <.05. Alcohol use was also associated with HIV risk behaviors, including total sex partners (*rho*=0.20, p<.05) and the use of excessive amounts of alcohol in conjunction with sexual activity (*rho*=0.42, p<.001). Results suggest that discrimination experiences in transgender adults are common and are associated with alcohol use and that alcohol use is further associated with HIV risk behavior. Addressing the broader societal issues with stigma reduction campaigns may reduce problematic alcohol use in this population. Interventions designed to reduce problematic alcohol use in transgender adults may have the additional benefit of lowering HIV risk behaviors. This research was supported by departmental support from VCU Psychology and Institute of Women's Health, and NIDA CTN grant 2U10DA013034-11

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INTIMATE PARTNER VIOLENCE AND ALCOHOL USE IN TREATMENT-MANDATED MEN AND WOMEN: DO SUBTYPES MATTER ACROSS GENDERS?

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Alcohol use closely co-occurs with intimate partner violence (IPV). Thus, there have been calls to investigate the prevalence of alcohol use among IPV offenders to determine whether alcohol content should be included in IPV treatment protocols. Additionally, while prior typologies have been established, the robustness of those typologies across genders has not yet been examined. Therefore, with a sample of court-mandated IPV men and women, this study aimed to evaluate: (1) the ability of an established triadic typology to classify IPV men and women and (2) the relationship of alcohol use to IPV categories across genders. It was anticipated that: (1) the triadic typological system would be supported across genders and (2) across genders, Generally-Violent/Antisocial (GV/A) subtypes would have the greatest, Borderline/Dysphoric (B/D) subtypes would have the middle, and Family-Only (FO) subtypes would have the lowest rates of IPV and alcohol use behaviors. Using cluster analysis, 149 men (68% Hispanic; 15% Caucasian; M age=29; M years education=13) and 131 women (54% Hispanic; 32% Caucasian; M age=28; M years education=13) mandated to IPV treatment were classified into three types (FO, B/D, and GV/A). As hypothesized, a 3-cluster solution was the best-fitting model for both genders (Men: AIC = 417.88; Women: AIC = 167.04). Consistent with IPV hypotheses, significant differences emerged on physically assaultive behaviors [Men: F (2, 146) = 65.30, p<.01; Women: F (2, 128) = 4.75, p<.05] with men showing significantly different rates of injurious behaviors [Men: F (2, 146) = 37.84, p<.01]. Across genders, the GV/A subtype committed the highest rates of physical assault (and in men, the highest rates of injury), followed by B/D and FO subtypes. Across genders, FO subtypes had the lowest rates of hazardous drinking in men [AUDIT: F (2, 146) = 7.35, p<.01] and women [AUDIT: F (2, 128) = 3.81, p<.05]. Contrary to predictions, the B/D subtype (vs. the GV/A subtype), reported the highest rates of alcohol use across genders. Although high rates of alcohol use have been established in the GV/A subtype, our findings of even higher rates in the B/D subtype suggests that alcohol intervention may be particularly important for the B/D subtypes. Ultimately, the current study provides support for the value of a triadic model of IPV across both genders, and highlights the need for alcohol treatment within IPV interventions.

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SOCIAL SUPPORT AND PARTNER AGGRESSION AMONG WOMEN WITH DUIS IN REMISSION FROM ALCOHOL USE DISORDERS

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Social networks have been found to influence recovery from alcohol use disorders (AUDs). Using a sample of women with histories of driving under the influence of alcohol (DUI), the current study characterizes recent alcohol use and examines network support and intimate partner aggression as a function of remission status. Women with recent documented histories of DUI (n=98) participated in diagnostic telephone interview and completed 2 questionnaires: the Norbeck Social Support Scale and the Conflict Tactics Scale. AUD was defined as 2 or more DSM-IV abuse or dependence symptoms (items confounded with DUI were excluded from consideration toward symptoms). Remission among women with AUD (n=85) was defined as no current symptoms and specified as abstinent (no alcohol for at least 6 months) and non-abstinent. A majority (57%) met criteria for current AUD, 29% were in non-abstinent and 14% in abstinent remission. Length of abstinence ranged from 6 months to 6 years. Women with current AUD drank greater quantities more frequently over the previous 6 months than non-abstinent remitted women. 56% drank more than 5 drinks on a typical drinking day, versus 10% of still-drinking remitted women; 41% had more than 7 drinks over the last week versus 9% of remitted women. Abstinent women had the lowest and non-abstinent remitted women had the highest levels of emotional and network support. Higher levels of network support showed a trend (p=.06) for association with non-abstinent remission. Levels of psychological and physical aggression by and towards intimate partner over the previous year decreased with remission, with current AUD having the highest and abstinent remission having the lowest scores. Lower levels of sexual coercion by a partner and psychological aggression towards a partner were associated with abstinent remission. Although limited by the small number of women in abstinent remission, results suggest that their support networks are smaller than those of remitted women who still drink. This could be an artifact of alcohol-related behaviors that may have alienated previously supportive individuals, or could reflect changes in the network with abstinence, such as dropping of former drinking friends. Lower levels of partner aggression among abstinent women suggest lifestyle changes accompanying abstinence. Future work will characterize network support as supportive or non-supportive of remission.

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INTIMATE PARTNER VIOLENCE AND ALCOHOL MISUSE: A TWO-WAY STREET?

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The aims of this study were to examine racial/ethnic differences in the trajectories of adult onset of traumatic intimate partner violence (IPV) victimization and alcohol misuse and whether childhood trauma moderated these relationships among non-Hispanic white, black, and Hispanic women in the U.S. Two waves of the National Epidemiologic Surveys on Alcohol and Related Conditions were utilized. Age of onset of traumatic IPV, binge and frequent heavy drinking, alcohol abuse, and alcohol dependence were used to conduct multiple extended Cox regression, adjusted for sociodemographics, family history of problem drinking, social networks/support, and lifetime major depression, GAD, and PTSD. In the IPV to alcohol trajectory analyses, the hazard/risk of binge drinking was greater among women with prior IPV relative to those without IPV (HR 1.61; CI 1.25, 2.09); similar findings were revealed with regard to frequent heavy drinking and alcohol abuse. The risk of alcohol dependence was also greater among women with IPV (HR 1.45, CI 1.15, 1.84); the cumulative effect of active alcohol abuse (HR 3.18, CI 2.66, 3.81) also increased the risk for alcohol dependence. IPV predicted binge and frequent heavy drinking and alcohol abuse among white and black women only; among black women, however, the risk of alcohol abuse was greater only among those without childhood trauma. IPV predicted alcohol dependence among white women only. In the alcohol to IPV trajectory analyses, the risk of IPV was significantly greater among women with compared to those without prior onset of binge (HR 1.97; CI 1.35, 2.87) and frequent heavy (HR 2.15; CI 1.44, 3.23) drinking in the total sample. The cumulative effect of active alcohol abuse (HR 1.75, CI 1.05, 2.92), but not prior history of alcohol abuse, significantly increased the risk of IPV. Alcohol dependence did not predict IPV. The findings for white women were similar to those of the total sample for binge and frequent heavy drinking. Among black women, binge and frequent heavy drinking predicted IPV only among those without childhood trauma; active alcohol abuse also predicted IPV. Among Hispanic women, a prior history of alcohol abuse predicted IPV only among those without childhood trauma. No significant findings were revealed for alcohol dependence and IPV. These findings suggest a reciprocal relationship between IPV and alcohol use, highlighting the importance of primary and secondary alcohol prevention and intervention efforts.

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ETHNICITY AND PREDICTORS OF BINGE DRINKING AND ALCOHOL USE DISORDER IN THE U.S. POPULATION: 1992 TO 2002

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Trend analyses from 1992 to 2002 show increases in U.S. rates of alcohol abuse, decreases or stability in alcohol dependence, and decreases in drinking five or more drinks in a day (i.e., binge drinking) (Grant et al., 2004; Caetano et al., 2010). This study aimed to examine the factors predicting binge drinking and alcohol use disorder (AUD) across Whites, Blacks, and Hispanics for this 10-year period.

Data were the 1991–1992 National Longitudinal Alcohol Epidemiologic Survey (NLAES) and the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Subjects were general population White, Black, and Hispanic adults (ages ≥ 18 years) living in the 48 contiguous states and the District of Columbia. A multiple-group path model was tested. The model included socio-demographic predictors of binge drinking and AUD and a direct feedback loop between binge drinking and AUD. The moderator was a combined 'ethnicity-survey year' variable with six groups: Whites-1992 (n = 30,967); Whites-2002 (n = 23,219); Blacks-1992 (n = 5,715); Blacks-2002 (n = 7,843); Hispanics-1992 (n = 2,697); and Hispanics-2002 (n = 7,835). Equality constraints and chi-square difference tests located variance on model paths across groups.

Model fit was high; CFI = .998 and RMSEA = .011. Ethnicity-year moderated all model paths with the exception of three direct paths from education, income, and AUD to binge drinking. Group differences varied depending on the path. Male gender had a stronger effect (positive) on binge in Hispanics, but a stronger effect on AUD in Blacks and Whites-1992. The negative relationships of age with binge and AUD were strongest for Whites and for Whites-1992 and Hispanics-1992, respectively. The protective effect of being married on binge was highest for Whites and then Hispanics. For Blacks, the paths from being married to binge (2002) and age to AUD (1992 and 2002) were non-significant. The effects of U.S. birthplace on binge and AUD were strongest for Blacks, but were non-significant for Whites on binge and for Hispanics-1992 on AUD. The effect of binge drinking on AUD decreased from 1992 to 2002 in all ethnic groups.

The trends described in this analysis show a complex picture of similarities and differences in the predictors of binge drinking and AUD between 1992 and 2002 and across Whites, Blacks, and Hispanics. The findings may indicate some shifts in the 'at risk' population for binge drinking and AUD.

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HEALTH-DISPARITIES RESEARCH: WHEN BLACK IS NOT COVARIATE-ADJUSTED WHITE

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Covariate adjustment for race or ethnicity, though commonly applied, depends for statistical validity upon assumptions about distributional overlap and balance that may not always hold when combining data from white non-Hispanics and one or more disadvantaged minority groups. We illustrate using data from a prospective twin cohort study of the determinants and outcomes of excessive alcohol use in young women (target sample N=2369 twin pairs identified from vital records, including 370 African-American pairs). Birth record address information was geocoded, and merged with census-tract level 1990 census data, to identify socioeconomic variables that characterized differences in birth neighborhood (strictly, census tract). Factor analysis with oblique promax rotation identified two weakly correlated factors that distinguished birth neighborhoods: the first of these distinguished neighborhoods on the basis of household wealth and educational and occupational statuses; the second primarily in terms of measures of family intactness (two parent versus parent households). Factor scores were computed, with those for the second factor highly correlated with maternal African-American ancestry (polyserial correlation 0.78). Since these analyses were conducted using population birth record data, not achieved sample data, they of course cannot be explained by sampling bias. For scores on the second factor, only a handful of African-American families were represented below the median, such that any covariate adjustment in a joint analysis of African-Americans and white non-Hispanics would involve, for the former, extrapolation into regions with essentially no data, giving a very uncertain foundation for inferences about associations with alcohol and related variables (e.g. early sexual behavior). A propensity score analysis using African American race as an outcome variable confirmed this problem in interpretation for jointly analyzed data. The current NIH policy typically requiring equal representation of minority groups in treatment trials, but not for psychosocial research, though convenient for investigators, comes at the cost of generating findings for minority groups about the etiology of alcohol problems that are either misleading (because combined with white non-Hispanics with inappropriate covariate adjustment) or too imprecise (when analyzed separately because of inadequate power).

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DETERMINANTS OF PROBLEM DRINKING AND DEPRESSION AMONG LATINO DAY LABORERS: A QUANTITATIVE STUDY

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As many as 117,600 individuals in the United States are looking for day labor every day, most of whom are of Latino origin. Latino day laborers encounter many stressors including job instability, low, unpredictable wages, unsafe work environment and abuse by their employers. Despite a number of risk factors for negative outcomes, little is known about alcohol use and depression in this population. The present study sought to address these gaps in the literature by conducting a quantitative survey of urban Latino day laborers to explore how social support and stress related to day laborer status influence physical health and in turn how physical health predicts current alcohol use and depression. Structural Equation Modeling was used to test an *a-priori* model of the relationships among these constructs. It was hypothesized that stress would be negatively related to health status while social support would have a buffering effect. In turn, health status would predict heavier alcohol use and higher levels of depression. A sample of 89 Latino, male, day laborers with an average age of 46.4 (*SD* = 11.45) were recruited from a community-based labor organization in Los Angeles and completed a series of validated measures that assessed these constructs. Results indicated that migrant stress was negatively related to health status and in turn, health status was associated with depression (*ps < .05)* but not alcohol use. These results provide further evidence that the occupational stressors inherent to being a day laborer and the social context in which they operate may have a negative impact on their health status and mental health. It is likely that the low prevalence of current alcohol use was related its non-significant relationships with other constructs. Nevertheless, these findings suggest that the stressors encountered by Latino day laborers as a result of the conditions in which they work and live may generate and maintain physical and mental health disparities in this vulnerable population. Further studies are warranted to understand effective strategies to reduce health disparities with regard to health and mental health outcomes including problem drinking.

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THE EXPOSURE TO A TRAUMATIC STRESSOR AND SUICIDE ATTEMPTS AMONG ALASKA NATIVES HOSPITALIZED FOR ALCOHOL DEPENDENCE

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The purpose of the presentation is to examine the effect of both exposure to a traumatic stressor and a diagnosis of post-traumatic stress disorder (PTSD) on suicide attempts among Alaska Native men and women hospitalized for alcohol dependence. Subjects were recruited from consecutive admissions to three inpatient public alcoholism treatment facilities serving Alaska Natives in the greater Anchorage AK metropolitan area; subjects were provided with a brief description of the study and details of their participation. Consenting included providing assurances of privacy and confidentiality concerning the data provided by each subject
Methods: Following detoxification, a complete and lifetime psychiatric history was obtained via the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA), including exposure to traumatic events and symptoms of PTSD. Questions regarding suicidal thoughts and attempts are also included in SSAGA. Computer algorithms developed by the COGA project were used to make all diagnoses (DSM-IV).
Results: The sample included 305 men and 292 women; the average age of men and women was similar (34.1 vs. 33.8 yrs.) at the time of admission. The rate of exposure to traumatic stress was 33%, and the prevalence of a DSM-IV diagnosis of PTSD was 13%. There were no significant associations between traumatic stress exposure and PTSD with either age of onset of alcohol dependence or severity of alcohol dependence symptoms. Significantly more women (72.6%) than men (62.3%) said that they had thoughts about committing suicide sometime in their life. Fifty percent of men who reported having a suicidal thought also reported an attempted suicide, while two thirds of women who had thoughts also made an attempt. More men and women who were exposed to traumatic stress compared to those not exposed reported suicide attempts. However, while a higher rate of suicide attempt was reported by men with a diagnosis of PTSD, no significant association was found among women.
Conclusion: Traumatic stress exposure and a diagnosis of PTSD appear to differentially affect suicidal behavior. The longer term effects of traumatic stress is complex and further analysis including family history, nature of trauma, comorbid disorders, etc. and suicidal behavior is suggested.

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CONCURRENT MARIJUANA AND ALCOHOL USE AMONG ASIAN AND PACIFIC ISLANDER AMERICAN YOUNG ADULTS: THE ROLE OF THE FLUSHING EFFECT

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The majority of college students who use marijuana also consume alcohol. Past research suggests that concurrent users are more likely to experience substance related problems than individuals who consume alcohol alone. Within Asian and Pacific Islander (API) communities, concurrent alcohol and marijuana use remains understudied. A biological determinant common among APIs is presence of a "flushing" response to alcohol, which is associated with decreased drinking and rates of dependence. Citing gateway theory, some researchers have speculated that flushing may also reduce likelihood of marijuana use due to decreased alcohol use. In a previous study (Wall et al., 2001), there was a trend for decreased marijuana use among Chinese, Korean, and Japanese individuals carrying ALDH2*2 allele, which often accounts for flushing response. There is also speculation that marijuana use may be a means to offset flushing and therefore consume more alcohol, but to date this has not been empirically tested. Thus, the present study examined the relationship of alcohol flushing response to marijuana use and drinking behavior.
U.S. college students with API ethnic backgrounds were recruited from undergraduate psychology courses and completed survey items on alcohol and marijuana use. The entire sample was included to calculate prevalence rates (N = 2127); only students who reported current alcohol use were included in analyses of drinking behavior (N = 1,006). Of the students who drank, 39.6% reported having a tendency to experience a flushing response to alcohol.
Prevalence of current alcohol use alone, marijuana use alone, and concurrent use was 52.2%, .6%, and 12.7%, respectively. Prevalence of marijuana use was similar for those who experienced flushing (18.1%) and those who did not (18.7%). MANOVA tests revealed a main effect where marijuana users consumed more drinks than non-users, V=.05, F(2,997)=28.90, p<.01. There was also a main effect whereby flushing led to decreased drinking, V=.02, F(2,997)=7.36, p<.01. No significant interactions were observed. Results suggest that flushing was not a protective factor for marijuana use and that marijuana use was related to increased drinking *regardless* of flushing status. Future research may clarify the extent marijuana use is intended to offset flushing, and potential health implications.

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QUALITY OF LIFE AND SOCIAL ENGAGEMENT DO NOT VARY ACROSS DRINKING PATTERNS AMONG OLDER ADULTS IN SOUTH AFRICA

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Lower quality of life and poor social engagement are often associated with heavy alcohol use relative to moderate consumption among older adults. The purpose of this study was to observe if quality of life and social engagement vary across lifetime abstainers, low risk drinkers and at risk drinkers among adults aged 50 and above in South Africa, and to determine if such variations differ between the genders. This study is a secondary analysis of data from the population-based Study on Global Ageing and Adult Health Survey (SAGE) including 3143 adults aged 50 and above in South Africa. We calculated sum scores based on the WHO Quality of Life-8 item version and queries of frequency of social activity in the past 12 months to measure quality of life and social engagement, respectively. Alcohol measures were based on self-reports of having ever consumed alcohol, and the number of drinks consumed on each day of the previous 7 days. We constructed low risk and at risk drinking categories for men and women separately based on NIAAA recommendations for adults, and used analysis of variance and multinomial regressions to observe and test associations. Overall, 1860 (59.2%) were women, 2653 (84.4%) were lifetime abstainers, 313 (10.0%) were low risk drinkers and 177 (5.6%) were at risk drinkers. The mean quality of life and social engagement scores were 27.2 (SE=0.18) and 21.1 (SE=0.19), respectively. Means of quality of life and social engagement scores did not vary significantly across the drinking patterns overall or among women in bivariate and multivariate analyses. Among women, at risk drinking was signficantly associated with having ever moved and smoking. Among men, quality of life was lowest among at risk drinkers (p=0.03), although this was not statistically significant in analysis adjusted for sociodemographics, where religion and smoking behavior were significant correlates. While quality of life and social engagement are often associated with drinking behavior in both population and clinical samples in Western settings, our findings suggest they currently do not play an independent role in influencing or being consequent to patterns of drinking among the general population of older South African men and women.

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THE EXPERIENCES OF DISCRIMINATION MEASURE IN A RURAL POPULATION: INITIAL VALIDATION AND ASSOCIATION WITH ALCOHOL USE AND HIV-RELATED RISK TAKING

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The purpose of this study was to characterize the psychometric properties of the Experiences of Discrimination Measure (EoD) in a rural population, and to begin to examine the extent to which experiences of racial discrimination may account for commonly observed rural-urban health disparities, including high prevalence of alcohol abuse and HIV-related risk taking in rural populations. Participants were 244 adult individuals (56.8%, *n*=137 female; 89.2%, *n*=214 African-American) interviewed at consumption and purchase alcohol venues in primarily non-metropolitan parishes (county equivalent) in Southeast Louisiana. Anonymous questionnaires assessed basic demographics, HIV-related risk taking, and alcohol and other substance use behaviors. Past experiences of racial discrimination were quantified using the EoD frequency and situations subscales. The EoD demonstrated good psychometric properties in the rural study population, including excellent internal consistency reliability (Cronbach's α=.86 for the frequency and α=.91 for the situations subscales) and a factor structure that was comparable to that observed in urban samples. Non-white respondents reported having experienced discrimination significantly more frequently and in significantly more settings than white participants (all p<.05). Results of multiple linear regression analyses revealed a significant association between the HIV-related risk behaviors assessed and the EoD frequency [F(10, 86)=3.42, p=.001, R^2=.29] and situations subscales [F(10, 142)=1.97, p=.04, R^2=.12], with frequency of condom use and sexual encounters in exchange for drugs, money, or gifts emerging as significant predictors (all p<.05). The EoD frequency subscale was also significantly associated with the set of substance use behaviors [F(4, 41)=3.87, p=.01, R^2=.27], with number of days drunk in the past month as the only significant predictor (p<.05). Findings suggest that the EoD is suitable for use in rural samples, and provide preliminary evidence for a positive association between past experiences of racial discrimination, problem drinking, and HIV-related risk taking in this population. The exact nature of the association between racial discrimination, substance use, and HIV-related risk behaviors, as well as the extent to which discrimination may account for urban-rural health disparities should be examined further in future research.

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A PROSPECTIVE EXAMINATION OF POSTTRAUMATIC STRESS AND ALCOHOL USE DISORDERS AMONG RETURNING VETERANS

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The traumatic effects of combat on psychological functioning have long been recognized. Operation Iraqi Freedom and Operation Enduring Freedom have amplified the need for a better understanding of the association between posttraumatic stress disorder (PTSD) and alcohol use disorders (AUD). We prospectively examined PTSD and AUD symptoms and investigated relations between combat exposure (CE) and relationship status (RS) on these outcomes. We hypothesized that CE would have a main effect on both PTSD and AUD symptoms while RS would have a main effect on AUD symptoms but not PTSD. We also examined CE X RS interactions as well as hypothesized reciprocal prospective PTSD and AUD associations. Participants (*N*=238, 92% men) were National Guard and Reserve Soldiers returning from deployment, recruited as part of a larger study. Twelve month data were available for 66.8% of the initial sample with no evidence of differential attrition according to baseline AUD, PTSD or CE. We examined both PTSD and AUD symptoms for months one, six and 12 post-deployment, derived from initial and follow-up clinical interviews. Assessments consisted of the Clinician Administered PTSD Scale (CAPS) and the Longitudinal Interval Follow-up Evaluation (LIFE). We conducted separate (RS X CE X Time) mixed-design ANOVAs on our primary measures of interest (PTSD & AUD). RS was coded as single/divorced vs. married/cohabitating and CE was categorized according to ''minimal'', ''moderate'' and ''severe'' levels. CE was significantly associated with PTSD but no other main or interaction effects emerged. To examine hypothesized reciprocal associations between PTSD and AUD we conducted cross-lagged panel path models with RS, CE and the RS X CE interaction as manifest exogenous variables. In separate models we examined alcohol abuse or dependence vs. dependence alone. CE consistently predicted Time 1 PTSD symptoms and RS predicted Time 1 alcohol dependence, but in contrast to our hypotheses no other main or interaction effects were observed including anticipated reciprocal relations between PTSD and AUD. In large part, this is due to strong (i.e., > .8) autoregressive effects across the three time points. Findings support hypothesized effects of CE on PTSD symptoms but the lack of observed hypothesized associations elsewhere suggests the need for longer measurement intervals in prospective research, as well as larger and more diverse samples. Supported by Department of Defense grant (W81XWH-06-1-0573).

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NONMEDICAL PRESCRIPTION DRUG USE AMONG COLLEGE STUDENT DRINKERS IN A RURAL REGION

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Non-medical prescription drug (NMPD) use, using a psychotherapeutic drug without a prescription or in ways for which it is not prescribed (SAMHSA, 2002), has escalated at alarming rates over the past two decades among college students (Arria et al., 2008). The rise in NMPD use is concerning given the potentially fatal outcomes of NMPD use alone (DAWN, 2007; NIDA, 2005). NMPD use is particularly dangerous for this population when considering the high rates of college student alcohol use and increased risk for co-ingestion of NMPDs with alcohol. Further, data suggest that rural adolescents are at a 26% higher risk for NMPD use than non-rural adolescents (Havens et al., 2011). Unfortunately, no known published work has examined NMPD use and its correlates among college student drinkers in a predominately rural region. Therefore, the current study is a preliminary examination of NMPD use versus non-use, hazardous drinking, depressive symptoms, posttraumatic stress symptoms, and specific types of NMPD use among college student drinkers attending a university in West Virginia, a largely rural state. Participants were 251 college students (53% women; M_{age}=20.72, *SD*=5.01, 85% Caucasian) who reported current alcohol use. Nearly 55% of the sample reported NMPD use during their lifetime. Students who reported lifetime NMPD (*n*=137; 55% women; M_{age}=20.64, *SD*=4.32; 91% Caucasian) also reported higher levels of hazardous drinking than students who reported no NMPD use (*n*=114; 49% women; M_{age}=20.81, *SD*=5.76; 79% Caucasian) (*p*<.001). Additionally, these students reported more depressive symptoms (*p*=.001) and posttraumatic stress (*p*=.003) symptoms than non-users. Responses to an item asking about which prescription drugs were used indicated that about 60% of NMPD users reported opioid misuse (*n*=82), 39% reported anxiolytic medication misuse (*n*=54), and 24% reported misusing stimulant medications for Attention Deficit/Hyperactivity Disorder (*n*=33). A large proportion of students (*n*=52; 38%) reported nonmedical use of two or more of these prescription drugs. The rates of NMPD use in this sample exceeded state and national averages, suggesting that college student drinkers in a rural region could be a high-risk population for NMPD use. Furthermore, the higher rates of depressive and posttraumatic stress symptoms among college students reporting NMPD use deserves further research as these co-occurring symptoms could result in heightened vulnerability to negative outcomes.

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PRESCRIPTION DRUG MISUSE AMONG COLLEGE STUDENT DRINKERS: A RISK FACTOR FOR HIGHER LEVELS OF HAZARDOUS DRINKING?

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The incidence and prevalence of prescription drug misuse (PDM; i.e., using a prescription drug without a legitimate prescription or taking a prescription drug in ways not prescribed by a physician) by college students has increased rapidly over the past several years (Hamilton, 2009). Additionally, individuals reporting both PDM and alcohol use may be at a higher risk for negative consequences compared to those who exclusively use alcohol (Hermos et al., 2009). Mixing prescription drugs and alcohol has been shown to have many negative consequences, most notably, death. According to the Drug Abuse Warning Network, 66% of PDM-related emergency department visits and deaths involved the co-ingestion of multiple drugs and alcohol was the most common drug used in combination with prescription drugs (SAMHSA, 2006). Currently, much of the literature investigating PDM in college student populations tends to focus on the correlates of one particular drug type for PDM (e.g., painkillers), rather than examining each of the four types of commonly misused prescription drugs (i.e., tranquilizers, painkillers, stimulants, and sedatives) concurrently to determine specific relations between types of PDM and hazardous drinking. The present study is a preliminary examination of each of the four types of PDM and hazardous drinking among 297 college students (56% male; M_{age}=19.53, *SD*=1.82, 84% Caucasian) attending a mid-southern university who reported current alcohol use. From this sample, 38 students reported current (e.g., past 6 months) tranquilizer use (57.9% male, 84.2% Caucasian), 103 painkiller use (50.3% female, 83.7% Caucasian), 57 stimulant use (64.9% Male, 94.7% Caucasian), and 28 sedative use (57.1% female, 92.9% Caucasian). There was a trend for stimulant users to be men and Caucasian (*p*s.≤06). Students who reported any type of PDM in the past 6 months (*n*=125; 54.4% male; M_{age}=19.35) also reported higher levels of hazardous drinking compared to students who reported no current PDM (*n*=160; 55.6% male; M_{age}=19.69;*p*<.01); the same pattern was found when examining drug types individually (*p*s<.01). Findings suggest that college students engaging in PDM may be at a particularly increased risk for engaging in higher levels of hazardous alcohol use compared to non-prescription drug using students, regardless of drug type. In light of the current findings, research focusing on specifically on the co-ingestion of PDM and alcohol among college students is warranted.