Oral Presentation Session 1

1A

Malaak Moussa, PhD Student
Wake Forest University Health Sciences
Mentor: Paul Laurienti and Linda Porrino
Broad Abstract Category: Consequences of Alcohol Consumption in Humans
Keywords: Moderate alcohol, Older adults, Human, Brain, fMRI networks

MODERATE ALCOHOL CONSUMPTION IN OLDER AGE: EFFECTS ON WORKING-MEMORY AND FUNCTIONAL BRAIN NETWORK CONNECTIVITY

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BACKGROUND: Alcohol use and normal aging negatively affect several cognitive functions. Here, we tested for differences between low and moderate drinkers of older age in working-memory task performance and evaluated underlying functional brain network connectivity. Nodes, or voxels, and their corresponding functional connections were used to represent brain networks. Specifically, these data focus on functional communities, which represent brain regions with high interconnectivity.
METHODS: Percent accuracy on the n-back task was used as a behavioral measure of working-memory. Functional magnetic resonance imaging data was modeled as a voxel-wise network and subsequently analyzed using a graph theoretic approach in both low and moderate drinkers ≥65 years old. Functional community organization was identified by finding densely connected groups of nodes that were only sparsely connected to other groups of nodes.
RESULTS: Percent accuracy on the 1-back task was significantly higher in low drinkers than in moderate drinkers. Differences in functional community organization between low and moderate drinkers were detected in the resting-state condition. The '*default mode'* community included the precuneus (PC) and medial frontal cortex (MFC) in low drinkers. In moderate drinkers, the '*default mode'* community included the PC but not the MFC. The '*limbic'* community was confined to basal ganglia brain structures, like the caudate, in low drinkers. In moderate drinkers, '*limbic'* community organization was diffuse, and included ventral portions of the frontal lobe. No differences in the organization of the '*working memory'* community, which included the dorsolateral prefrontal and parietal cortices, were found between low and moderate drinkers.
CONCLUSIONS: Moderate alcohol consumption was found to exacerbate well-established age-related declines in working-memory performance. Baseline differences in both '*default mode'* and '*limbic'* community organization between low and moderate drinkers were detected. On the other hand, no differences in '*working memory'* community organization were found. Future analyses will explore the relationship between both resting-state and 1-back functional community structure and observed group differences in performance. This work will extend research focused on identifying brain phenotypes at high risk of accelerated age-related cognitive decline due to regular moderate alcohol consumption.

Research supported by NIAAA grants T32 AA007565, F31 AA021639 and P01 AA021099.

1B

Melanie Pina, PhD Student
Oregon Health & Science University
Mentor: Christopher Cunningham
Broad Abstract Category: Animal Behavior
Keywords: ALCOHOL, ETHANOL, DOPAMINE, PLACE CONDITIONING, INBRED MICE

INVOLVEMENT OF DOPAMINE RECEPTOR SUBFAMILIES IN ETHANOL REWARD

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BACKGROUND: Studies suggest that dopamine D1- and D2-receptor subfamilies are differentially involved in the conditioned rewarding effect of ethanol and other drugs of abuse. However, the relative contributions of these receptor subfamilies to the primary rewarding effect of ethanol have not been fully described.
METHODS: Systemic administration of selective dopamine receptor antagonist drugs was used to examine the roles of D1- (SCH-23390) and D2-like (raclopride) receptors in the acquisition of an ethanol-induced conditioned place preference (CPP). All experiments used an unbiased place conditioning procedure and adult male DBA/2J mice. In experiments 1 and 2, mice were pretreated with raclopride (0-1.2 mg/kg) or SCH-23390 (0-0.3 mg/kg) prior to conditioning sessions when ethanol (2 g/kg) was paired with a distinctive tactile floor cue. Based on significant findings for SCH-23390, we then determined whether SCH-23390 (0.3 mg/kg) produced a place preference on its own (Experiment 3). To evaluate whether SCH-23390 impaired learning, we used a conditioned place aversion (CPA) paradigm and pretreated animals with SCH-23390 (0-0.3 m/kg) before conditioning sessions with LiCl (Experiment 4).
RESULTS: Whereas raclopride (0-1.2 mg/kg) did not affect acquisition, SCH-23390 (0.1-0.3 mg/kg) impaired the development of ethanol-induced CPP. SCH-23390 (0.3 mg/kg) did not produce a place preference when tested alone and SCH-23390 (0.1-0.3 mg/kg) did not perturb the acquisition of LiCl-induced CPA.
CONCLUSIONS: Our results support a role for dopamine D1-like but not D2-like receptors in the primary rewarding effect of ethanol, as indexed by CPP. Moreover, the significant impairments produced by SCH-23390 were not due to aversive properties of D1-like receptor antagonism or general impairments in associative learning.

Supported by NIAAA grants T32 AA007468 and R01 AA007702.

1C

Ami Cohen, Postdoctoral Fellow
The Scripps Research Institute
Mentor: George Koob
Broad Abstract Category: Pathology: Human / Animal
Keywords: Dependence, Nicotine, Alcohol, Rats, Vapor

NICOTINE PROMOTES ALCOHOL DRINKING AND FACILITATES THE TRANSITION TO ALCOHOL DEPENDENCE IN RATS

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BACKGROUND: Approximately 80-90% of alcohol dependent individuals are also heavy smokers, suggesting that nicotine may contribute to alcohol dependence. Nicotine has been shown to moderatly increase alcohol drinking in non-dependent rats, however, the neurobiological mechanism is unknown, and it is not know if exposure to nicotine will facilitate the transition to alcohol dependence and increase compulsive alcohol intake in alcohol dependent rats.
METHODS: Rats were injected daily with nicotine (0.8 mg/Kg; s.c.) 50 minute before measuring the motivation for alcohol using operant chambers (30 min session). Alcohol intake, breaking point and alcohol drinking despite adverse consequence (quinine) were measure before and after exposure to chronic (17 days) intermitent (14 h/day) exposure to alcohol vapor.At the end of the experimente brain mapping technique using c-fos was used to determine the neuronal network mediating the effect of nicotine on the motivation for alcohol.
RESULTS: Nicotine increased the motivation for alcohol in non-dependent rats and facilitate the transition to alcohol dependence by shortening the duration of exposure necessary to develop alcohol dependence symptoms by ~50%. In addition, nicotine increased compulsive alcohol intake measured using the quinine test. Finally, nicotine-induced increase in alcohol was associated with a specific activation of the dmPFC (but not vmPFC and OFC), nucleus accumbens core (but not shell), CeA, BNST, BLA, and pVTA (but not aVTA). Nicotin-induce increases in alcohol in non-dependent rats was associated with a recruitment of the BLA only.
CONCLUSIONS: These results demonstrate that nicotine not only increases alcohol drinking in non-dependent rats but also facilitates the transition to alcohol dependence and produces compulsive alcohol taking. We also show that nicotine-induced increases in compulsive alcohol intake is associated with the specific recruitment of an extended network including the dmPFC, NAC core, CeA, BNST and VTA.
UPDATE: Approximately 80-90% of alcohol dependent individuals are also heavy smokers, suggesting that nicotine may contribute to alcohol dependence. Nicotine has been shown to moderately increase alcohol drinking in non-dependent rats, however, the neurobiological mechanism is unknown, and it is not known if exposure to nicotine will facilitate the transition to alcohol dependence. We now report that daily nicotine administration (0.8 mg/Kg; s.c.) not only increased alcohol drinking in non-dependent rats but also facilitated the transition to alcohol dependence in rats chronically exposed to alcohol vapor (14 h/day). Specifically, nicotine significantly shortened the duration of exposure necessary to develop alcohol dependence symptoms, and increased compulsive alcohol intake as measured using the quinine test. Finally, c-fos analysis reveled that the contribution of nicotine to the development of alcohol dependence was associated with specific recruitment of an extended brain network including the dmPFC, NAC core, CeA, BNST and VTA.

Supported by NIAAA grant T32 AA0456, TRDRP 17RT-0095, NIDA DA023597 and the Pearson Center for Alcoholism and Addiction Research.

1D

Rachel Gunn, PhD Student
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Mentor: Peter Finn
Broad Abstract Category: Epidemiology
Keywords: alcohol dependence, working memory, attention, antisocial problems, decision making

THE EFFECTS OF WORKING MEMORY LOAD AND ATTENTION REFOCUSING ON DELAY DISCOUNTING RATES IN ALCOHOL DEPENDENCE WITH COMORBID ANTISOCIAL PROBLEMS.

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BACKGROUND: Research has shown that alcohol use disorders (AUDs) are associated with impulsive decision making and reduced working memory (WM) capacity; and when comorbid with high levels of antisocial behavior (AUD-HiANT) reveal higher levels of impulsive decision making. The current study investigated: (1) of the effects of a WM load on impulsive decision making (delay discounting (DD)) in those with AUDs with and without high levels of antisocial behavior (phase 1); and (2) the effects of an attention refocusing intervention designed to offset the effects of a WM load on impulsive decision making (phase 2).
METHODS: Three groups of young adults (Controls n = 223, AUD-LoANT n=310, and AUD-HiANT; n=235) were administered one of three delay discounting conditions, No WM load (n=302), WM load (n=310), and WM load with Attention refocusing (n=119).
RESULTS: Analysis of phase 1 revealed: (1) a highly significant main effect of WM load, $F(1, 606) = 34.2$, $p < .00001$. A WM load significantly increased impulsive decisions (DD rates) for all groups. And (2) a highly significant main effect of group, $F(1, 606) = 44.8$, $p < .00001$. Post hoc analyses revealed Controls had lower DD rates (less impulsive) compared with both AUD groups; and AUD-LoANT had lower DD rates than AUD-HiANT (all $ps < .01$).
Analysis of the Phase 2 effects revealed a significant main effect of refocusing, $F(1, 423) = 10.7$, $p < .001$. The attention refocusing significantly lowered DD rates (reduced impulsive decisions) compared with the load condition. However, planned comparisons revealed that this effect was only significant for the AUD-HiANT group ($p < .001$), which is likely due to the fact that the AUD-HiANT had substantially higher DD rates in the WM load condition. Planned comparisons revealed that while the three groups differed in the WM load condition ($p < .001$), there were no significant group differences in the refocusing condition.
CONCLUSIONS: These results indicate that: 1. AUDs are associated with more impulsive decision-making, which is elevated by the presence of comorbid antisocial symptoms, 2. a WM load significantly increases impulsive decision making for all individuals regardless of AUD status, and 3. An attention refocusing intervention has some effectiveness in offsetting the effects of a WM load on impulsive decision-making in those with AUD and high levels of antisocial symptoms.

Research support from NIAAA R01 AA13650. Support for Rachel Gunn from NIAAA training grant NIAAA AA07462.

1E

Ryan Vetreno, Postdoctoral Fellow
University of North Carolina at Chapel Hill
Mentor: Fulton Crews
Broad Abstract Category: Consequences of Alcohol Consumption in Humans
Keywords: binge drinking, human, innate immunity, Toll-like receptor, receptor for advanced glycation end products

PERSISTENTLY INCREASED DANGER SIGNALING IN THE ADULT PREFRONTAL CORTEX FOLLOWING ADOLESCENT INTERMITTENT ETHANOL IS ASSOCIATED WITH REVERSAL LEARNING DEFICITS

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BACKGROUND: Adolescence is a critical period of prefrontal refinement, neuroplasticity, and increased risk-taking and sensation seeking. It is also a time of alcohol experimentation and abuse that might impart long-term effects on adult neurocognitive functioning due to the heightened frontal cortical neuroplasticity associated with adolescent brain maturation. Our laboratory recently linked alcohol-induced neuroinflammation to neurodegeneration in the adult brain through the induction of TLR/HMGB1 neuroimmune signaling. Since binge drinking is common during adolescence, the persistent effect of adolescent intermittent ethanol (AIE) exposure on neuroimmune signaling was assessed in the prefrontal cortex of adolescent and adult male Wistar rats.
METHODS: To determine whether AIE persistently increases innate immune gene expression in the prefrontal cortex, male Wistar rats were exposed to AIE (5.0 g/kg, i.g., 2-day on/2-day off) from postnatal day (P)25 to P55. On P56, HMGB1/TLR/RAGE danger signaling was assessed using immunohistochemistry. In a separate group of rats, spatial and reversal learning was assessed on the Barnes maze in early adulthood (P64 to P75).
RESULTS: On P80, HMGB1/TLR/RAGE danger signaling was assessed using immunohistochemistry and RT-PCR. In addition, expression of danger signals was measured in the orbitofrontal cortex from human alcoholic post-mortem samples, and was compared to reported age of drinking onset. Adolescent binge ethanol exposure altered the developmental expression of RAGE/TLR/HMGB1 signaling markers in the young adult prefrontal cortex. This change in receptor expression was accompanied by increased expression of downstream proinflammatory cytokines and oxidases. AIE exposure induced long-term reversal learning deficits while increasing perseveration in adult rats assessed on the Barnes maze, which was associated with expression of danger signal receptors. In human alcoholics, we found significantly increased expression of RAGE/TLR/HMGB1 signal expression in the post-mortem orbitofrontal cortex, which was correlated with age of drinking onset.
CONCLUSIONS: Together, these findings provide evidence that an earlier age of drinking onset is associated with persistent expression of neuroimmune danger signaling and might contribute to adult neurocognitive dysfunction.

Research supported by NIAAA grants T32 AA007573 and F32 AA021040, and Neurobiology of Adolescent Drinking in Adulthood (NADIA [AA020023, AA020024, and AA020022]).

Oral Presentation Session 2

2A

Brianna Klein, Postdoctoral Fellow
University of Colorado Denver (AMC)
Mentor: Tatiana Kutateladze (Lab) and Paula Hoffman (Fellowship)
Broad Abstract Category: Molecular / Cell Biology, including C.N.S.
Keywords: CBP, p300, Bromodomain, Structure, Affinity

REGULATION OF CBP/P300 BY BROMODOMAIN

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BACKGROUND: Post-translational modifications of histones or epigenetic marks are involved in fundamental biological processes. Human CBP/p300 is a major acetyltransferase, acetylating chromatin and controlling transcription of genes essential for learning and memory storage. Dysfunction of CBP is associated with a number of behavioral disorders including alcohol and drug addiction and depression. Recent reports demonstrate that CBP/p300 activity can be disrupted by point mutations in the most conserved region containing bromodomain (BD) and adjacent PHD (plant homeodomain) finger. Despite high importance, very little is known about how the BD and PHD modules regulate functions of the CBP/p300 or their roles in the development of alcohol and drug dependence.
METHODS: Using nuclear magnetic resonance (NMR) spectroscopy we investigated the specificity of CBP and p300-BD binding to acetylated histones and the involvement of the PHD finger. Additionally, the apo structures of CBP-BD and p300-BD/PHD were studied by X-ray crystallography.
RESULTS: The BD and PHD finger regions in p300 and CBP have high degree of sequence similarity. Both CBP and p300-BD bind to H3K56ac, however, the adjacent PHD finger has no effect on binding of p300-BD to H3K56ac. To structurally characterize the H3K56ac interaction, we determined the crystal structure of CBP-BD at a 1.4 Å resolution and defined the H3K56ac-binding site by analyzing NMR resonance perturbations. Furthermore, diffraction quality crystals have been obtained for p300-BD/PHD and structure determination is currently underway.
CONCLUSIONS: CBP and p300 BDs are identified as core-histone binding modules by NMR. The interaction between CBP and p300-BD and H3K56ac was in the slow-to-intermediate exchange regime on the NMR time scale. This range is exhibited by other histone-binding modules, including chromodomains and PHD fingers1, suggesting that recognition of H3K56ac is physiologically relevant. Mapping of the most perturbed residues onto the surface of the CBP-BD structure revealed a well-defined groove in the ZA and BC loops where H3K56ac is bound. These experiments provide important insight into the p300/chromatin-dependent signaling pathways that may constitute new targets for therapeutic interventions.

1. Musselman CA, Lalonde ME, Côté J, Kutateladze TG. Perceiving the epigenetic landscape through histone readers. *Nat Struct Mol Biol* 2012;19(12):1218-27.

This work was supported by NIAAA grants T32 AA007464 and T32 AA007464 and an award from The American Heart Association.

2B

Sarah Prins, PhD Student
Loyola University Chicago
Mentor: Toni Pak
Broad Abstract Category: Molecular / Cell Biology, including C.N.S.
Keywords: microrna, puberty, binge, hippocampus, alcohol

PERIPUBERTAL BINGE ALCOHOL EXPOSURE ALTERS NORMAL DEVELOPMENTAL MICRORNA EXPRESSION PATTERNS

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BACKGROUND: Adolescent binge alcohol abuse may induce long-term changes in stress responses and memory formation, two functions controlled by the ventral (VH) and dorsal (DH) hippocampus. microRNAs (miRs) are small RNAs that play an important role in gene regulation and are potential mediators of long-term changes in gene expression. We have previously determined that repeated binge pattern alcohol exposure in peri-pubertal male rats altered hippocampal expression of miR-10a-5p, miR-495, miR-32, miR-103 and miR-26a. The context of these changes was not clear and we, therefore, set to determine the following objectives: 1) normal developmental expression pattern of miRs at pre-, peri-, and post-pubertal ages, 2) how alcohol alters the normal developmental expression pattern of miRs. We hypothesized that alcohol differentially modulates expression of miRs in the DH and VH in pubertal rats exposed to binge pattern alcohol and that these miRs are important for regulating hippocampus development.
METHODS: Male Wistar rats were treated with water or the following repeated binge alcohol (EtOH) paradigm via gavage beginning at PND 37 (3g/kg; 1x/day/3days EtOH, +1x/day/2days water + 1x/day/3days EtOH). Brains were sectioned at 200 mm on a freezing microtome and VD and HD were microdissected using a 0.75 mm Palkovit's brainpunch tool. Total RNA was isolated and cDNA was made using Invitrogen's NCode miRNA Frist-strand cDNA synthesis kit.
RESULTS: Overall, the DH demonstrated greater changes in miR expression with age. Specifically, 3 of the 5 miRs increased with age and 1 miR decreased with age, compared to the VH, where one miR increased and one miR decreased with age. Repeated peri-pubertal alcohol exposure was capable of recapitulating the pre-pubertal phenotype of 2 miRs while it also increased miR expression beyond adult levels for 3 miRs.
CONCLUSIONS: These data demonstrate that miRs play an important role in pubertal hippocampus development and that pubertal alcohol abuse alters the normal developmental expression pattern of miRs. Furthermore, pubertal alcohol abuse-induced changes in miRs may underlie the mechanism whereby alcohol abuse increases the risk of developing adult mood disorders and memory disturbances.

Supported by NIH R21AA018398 and NIH T32 AA013527.

2C

Benjamin Hughes, PhD Student
Medical University of South Carolina
Mentor: John Woodward
Broad Abstract Category: Pharmacology, including C.N.S.
Keywords: N-methyl-D-aspartate, Ethanol, Electrophysiology, GluN2B, Pharmacology

DECOUPLING AGONIST EFFICACY FROM ETHANOL INHIBITION OF NMDA RECEPTORS: EFFECTS OF PRE-TM4 MUTATIONS ON NMDA RECEPTOR FUNCTION AND ETHANOL SENSITIVITY

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BACKGROUND: N-methyl-D-aspartate (NMDA) receptors are a primary site of action of the commonly abused drug ethanol, though it remains unclear precisely how ethanol inhibits NMDAR function. Work by our laboratory has characterized a site in the GluN1 subunit, phenylalanine 639, where alcohol may at least partially exert its effects. Interestingly, mutation of this site to an alanine not only reduced ethanol inhibition of the receptor complex but as well produced a left-ward shift in glycine potency. On such a basis, we sought to determine if changing agonist potency necessarily resulted in altered ethanol inhibition. Specifically, we introduced a number of mutations in the Pre-TM4 region of GluN2 subunits, which has only recently been determined by our laboratory to affect agonist potency distinct from the S1/S2 ligand binding domains.
METHODS: Human embryonic kidney (HEK) cells were transfected 2:2:1 with GluN1, GluN2, and eGFP plasmids. Whole-cell electrophysiological experiments were conducted 24-48 hours after transfection, during which time concentration-response curves were established for glutamate (0.03 – 10uM), glycine (0.03 – 10uM), and ethanol (10 – 300mM). As well, current-voltage relationships were determined using a ramp protocol consisting of a jump from 0 mV holding potential to -80 mV, a 1.3s ramp to +80 mV, and a return to 0 mV.
RESULTS: Introduction of a glycine substitution at S810 or S811 in GluN2B produced a significant left-ward shift in glutamate potency, as well as producing a modest left-ward shift in glycine potency. Unexpectedly, inhibition of channel function by ethanol or magnesium was unaffected. The Pre-TM4 region has high sequence homology between the four different GluN2 subunits, with the exception of three substitutions seen in GluN2D not seen GluN2B. Mutation of N806 to isoleucine in GluN2B, as seen in GluN2D, produced a left-ward shift in glutamate sensitivity similar to that seen in GluN2D, suggesting this residue may be critical in dictating the higher glutamate potency seen in GluN2D versus the other three GluN2 subunits.
CONCLUSIONS: Results obtained demonstrate that manipulation of agonist potency via site-directed mutagenesis in the Pre-TM4 region of GluN2B did not elicit a change in ethanol sensitivity, counter to results obtained with other mutations in GluN1. It thus appears that altered agonist potency is not necessarily concomitant to ethanol inhibition or vice versa.

Research supported by NIAAA grant T32 AA007474

2D

Rafael Renteria, PhD Student
University of Texas at Austin
Mentor: Richard Morrisett
Broad Abstract Category: Physiology, including C.N.S.
Keywords: LTD, DSE, Accumbens, Endocannabinoid, Plasticity

ETHANOL ATTENUATION OF ENDOCANNABINOID SIGNALING IN THE NUCLEUS ACCUMBENS SHELL CAN BE OVERCOME BY URB597 AND AM404

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Background: Alterations in the expression of synaptic plasticity within the nucleus accumbens (NAc) appears to constitute a critical neuroadaptive response to ethanol and other drugs of abuse. We have previously reported that NMDA-receptor dependent long term depression (LTD) is markedly affected by both acute ethanol exposure as well as chronic intermittent ethanol exposure in vivo. Conversely, while endocannabinoid (eCB) mediated synaptic depression is very well-documented in the dorsal striatum, its role in the nucleus accumbens is much less well understood. The purpose of this study was to characterize the contribution of eCBs in NMDA-receptor dependent LTD in the NAc and determine the effects of ethanol on eCB signaling.
Methods: Whole cell patch clamp electrophysiology was used to measure excitatory post synaptic currents (EPSCs) in the NAc shell. Plasticity was induced by pairing 1 Hz stimulation with postsynaptic depolarization to -50 mV. Depolarization induced suppression of excitation (DSE) is an eCB dependent form of short term depression and was used as an assay of ethanol's effects on eCB signaling.
Results: As previously reported, pairing 1 Hz stimulation with postsynaptic depolarization resulted in a reliably induced form of NMDAR-dependent LTD. In the presence of AM251, a CB1 receptor antagonist, the pairing protocol resulted in NMDAR-dependent long term potentiation (LTP) that was blocked with 40 mM ethanol. Using 40 mM ethanol, the magnitude of DSE was significantly reduced. To increase eCB signaling, URB597, a fatty acid amide hydrolase inhibitor, and AM404, an anandimide reuptake inhibitor were used in the presence of 40 mM ethanol. The expression of LTD was rescued in the presence ethanol when eCB signaling was increased through a distinct mechanism requiring activation of TRPV1 receptors.
Conclusions: Our results show that the NAc is capable of expressing many different forms of plasticity that may involve interactions between different signaling systems. Future work should be directed at understanding how the various signaling systems interact and ultimately how they are affected by drugs and alcohol.

Research supported by NIAAA grants R01 AA15167, U01 AA16651 and T32 AA007471.

2E

Egle Juskeviciute, Postdoctoral Fellow
Thomas Jefferson University
Mentor: Jan Hoek

Broad Abstract Category: Molecular / Cell Biology, including C.N.S.
Keywords: Rat, partial hepatectomy, chronic ethanol treatment, miR-21, proliferation

INHIBITION OF miR-21 REVEALS A KEY microRNA REGULATORY NETWORK CONTROLLING LIVER REGENERATION IN CHRONIC ALCOHOL ADAPTED STATE

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BACKGROUND: Chronic alcohol consumption interferes with normal repair mechanisms in the liver. Our recent studies suggest that the microRNA regulatory network may contribute to the deregulation of the regenerative response in ethanol-treated animals. miR-21, which has been identified as a pro-proliferative miRNA, increases its expression during liver regeneration following partial hepatectomy (PHx). However, chronic ethanol treated animals show even stronger up-regulation of miR-21 expression than their corresponding pair-fed controls. The objective of this study was to investigate the role of miR-21 in liver regeneration.
METHODS: Following the established Lieber-DeCarli protocol, rats were fed a liquid diet containing 36% of total calories derived from ethanol; for pair-fed controls ethanol calories were replaced by carbohydrates. After 5 weeks on the diet, rats were subjected to 70% PHx and liver samples were collected at 24 and 48h after the surgery. miR-21was inhibited using a locked oligonucleotide antisense to miR-21 (AM21). The effects of AM21 treatments on the expression levels of cell cycle related genes and potential mir-21targets in the regenerating rat liver were analyzed using high-throughput qPCR. Digital assay platform was used to study the expression levels of miRNAs in the regenerating liver.
RESULTS: AM21 treatment suppressed detectable levels of miR-21 by >97% in the regenerating rat liver. Inhibition of miR-21 resulted in up-regulation of expression of validated miR-21 targets such as RhoB, E2f1, Il6ra, Nfib and Tgfbr2. AM21 treatment did not interfere with cell cycle progression in the control rat livers. On the contrary, inhibition of miR-21 recovered cell proliferation in chronic ethanol fed animals to the levels of untreated pair-fed controls. Of the 420 miRNAs measured, a total of 128 miRNAs were expressed in the rat liver. miR-93 and miR-19b were up-regulated after PHx similarly to miR-21, but AM21 treatment did not affect their expression. Several miRNAs were down-regulated after PHx, including miR-146a, miR-150, and miR-139-5p, and in AM21 treated samples this down-regulation was less pronounced.
CONCLUSIONS: Our results suggest that miR-21 functions as part of an interacting miRNA network regulating regenerative response after PHx. Our data on miRNA expression profiles in liver regeneration also implicate a role for non-parenchymal cells in shaping the dynamics of these regulatory networks.

This work is supported by NIAAA grants R01 AA018873, K05 AA017261, and T32 AA07463.

Oral Presentation Session 3

3A

Jennifer E. Merrill, Postdoctoral Fellow
Center for Alcohol and Addiction Studies, Brown University
Mentor: Kate Carey
Broad Abstract Category: Determinants of Alcohol Consumption in Humans
Keywords: alcohol use, alcohol consequences, college students, subjective evaluations, hierarchical linear modeling

AVERSIVENESS OF RECENT CONSEQUENCES PREDICTS FUTURE DRINKING BEHAVIOR AMONG COLLEGE UNDERCLASSMEN

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BACKGROUND: Social learning theory (SLT) suggests drinking behavior is learned in part through direct reinforcement, but that cognitions are among the most proximal predictors of alcohol use behavior. The cognitive evaluation of alcohol-related consequences varies among drinkers and may be related to later consumption. The present study extends prior research by examining whether consequence evaluations predict subsequent alcohol use and consequences in college underclassmen, at a time when alcohol-related learning processes are most likely to take place.
METHODS: Participants (N=679) completed bi-weekly web-based surveys through freshmen and sophomore year on alcohol use, consequences, and consequence evaluations. Hierarchical linear modeling was used to test the hypothesis that negative evaluations would predict alcohol use and consequences at bi-weekly intervals. We also conducted an exploratory test of whether the effect of evaluations on subsequent drinking behavior differed by gender or class year.
RESULTS: The most common negative consequences were blacking out and getting sick. The most negatively evaluated consequences were disappointing close others and driving after drinking, while the least negatively evaluated consequences were those that were least common – getting into a physical fight and accidentally hurting someone else. Higher deviations on a given week above one's own average negative evaluation score across weeks resulted in lower alcohol use at the next assessment, supporting our hypothesis. The effect of negative evaluations on subsequent drinking behavior did not differ by gender or class year. More negative evaluations also predicted downward change in alcohol consequences, but only during freshmen year. The effects of negative evaluations on alcohol use and consequences were observed in the context of controlling several between- and within-person variables, including experience of positive consequences.
CONCLUSIONS: Findings are consistent with SLT and provide support for the role of negative consequence evaluations in the naturalistic adjustments college students make to their drinking behavior. Future research should examine whether the cultivation of such negative evaluations within the context of brief motivational interventions results in intervention-related change.

Research supported by NIAAA grants R01 AA013970 and T32 AA007459.

3B

Magdalena Kulesza, Postdoctoral Fellow
University of Washington
Mentor: Mary Larimer
Broad Abstract Category: Determinants of Alcohol Consumption in Humans
Keywords: college students, at risk for AUD/SUD, stigma, alcohol severity

STIGMA AS A PREDICTOR OF ALCOHOL USE AMONG AT-RISK COLLEGE STUDENT SAMPLE

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BACKGROUND: Among adults, alcohol/drug use is subject to harsh moral judgments and this stigma affects employment, physical and mental health. The literature on the impact of alcohol/drug use stigma among college students is scarce. So far, we know that stigma may be positively related to alcohol/drug use severity. However, these are cross sectional findings, and researchers focused on "stigma proness," which is a less precise method of assessing stigma related to alcohol/drug use. Although preliminary evidence suggests that stigma may be positively related to drug/alcohol use frequency and problems, no such data has been reported for college students. Given the negative impact of alcohol use among college students, it is important to investigate whether stigma may be related to alcohol use, severity and problems.
METHODS: We present baseline and 3-month follow-up (f/u) data from a sample (n=49) of college students participating in a study on the efficacy of brief intervention for at risk college students with comorbid SUDs and gambling problems. Participants were predominantly Caucasian (53%), male (21%), and 20.1 (SD= 1.4) years old. On average, they consumed 17.8 (SD=15.5) drinks per week in a 3 month period prior to study enrollment.
RESULTS: Regression analyses were performed to evaluate if baseline stigma would predict alcohol use related variables. In all analyses, we controlled for depression, and for both randomization assignment and baseline alcohol consumption for 3-month f/u analyses. Stigma was a significant positive predictor of alcohol-related problems and number of alcohol dependence criteria endorsed at baseline. After controlling for baseline, at 3-month f/u, stigma was a significant positive predictor of alcohol severity as assessed by the ASSIST. Stigma was not a significant predictor of alcohol use frequency/quantity at either baseline or f/u.
CONCLUSIONS: Our preliminary results are consistent with prior cross sectional findings suggesting that stigma is significantly related to alcohol problems and severity. We extended these findings by showing a prospective relationship between stigma and alcohol use severity. These results are preliminary and demonstrate the need to further investigate these constructs and relationships. Also, more research is warranted to determine if similarly to adult samples, stigma has a detrimental impact on physical/mental health and treatment seeking of college students engaged in risky drinking.

Research supported by NIAAA grants T32 AA007455 and NIDA R01 DA025051.

3C

Ross O'Hara, Postdoctoral Fellow
University of Connecticut Health Center
Mentor: Howard Tennen
Broad Abstract Category: Determinants of Alcohol Consumption in Humans
Keywords: Drinking motives, African-American, College students, Daily diary, Gender differences

DRINKING TO COPE AMONG AFRICAN-AMERICAN COLLEGE STUDENTS

O'Hara RE, Boynton MH, Scott D, Williams C, Armeli S, Tennen H, Covault J.
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BACKGROUND: Most prior research on drinking to cope among college students has measured drinking motives at the global level, which ignores potential effects of within-person variation in coping motives on alcohol use. In addition, most studies primarily examined students of European descent, and the etiology of alcohol use and drinking to cope is markedly different among African Americans. To address these issues, we studied the influence of episode-specific coping motives on alcohol use among 462 African-American college students (59% female) at a Historically Black University.
METHODS: At baseline, we measured students' global coping, enhancement, and social motives for drinking. Students then completed a 30-day diary during which they reported each day how many standard alcoholic drinks they consumed the previous night. If participants drank, they also reported their motives for doing so on that occasion. Using multilevel modeling, we examined the between- and within-person effects of episode-specific coping motives on number of drinks consumed and the odds of heavy drinking (defined as 4+ drinks for women/5+ drinks for men) during a drinking episode. We also compared the predictive validity of episode-specific versus global coping motives for both outcomes.
RESULTS: Male and female students consumed significantly more drinks when reporting higher mean episode-specific coping motives (between-person effect), controlling for episode-specific enhancement and social motives. Male students also drank more on drinking days when reporting episode-specific coping motives higher than their own average (within-person effect), whereas women drank less and were less likely to drink heavily on such days. Finally, global coping motives failed to predict either drinking outcome when competing with episode-specific coping measures.
CONCLUSIONS: Our results indicate that African-American college students' drinking is influenced by coping motives. Both men and women drank more when reporting higher mean coping motives, but only men showed significant and positive within-person coping effects. Although students still drank primarily for enhancement and social reasons, the addition of coping, especially for men, represents a maladaptive and possibly dangerous drinking motive. Furthermore, global coping motives failed to predict alcohol use in the presence of episode-specific measures, suggesting that assessing coping at the within-person level may be important to understanding the drinking-to-cope process.

Research supported by NIAAA grants R21 AA017584, P20 AA014643, T32 AA007290, and P60 AA03510, and NCRC grants M01 RR10284 and UL1 RR031975.

3D

Melissa Munn-Chernoff, Postdoctoral Fellow
Washington University School of Medicine
Mentor: Andrew Heath
Broad Abstract Category: Epidemiology
Keywords: twins, females, early substance use, bulimia, genetics

BULIMIC BEHAVIORS AND EARLY SUBSTANCE USE: FINDINGS FROM A COTWIN-CONTROL STUDY

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BACKGROUND: Bulimic behaviors (i.e., compensatory behaviors- such as self-induced vomiting and laxative misuse- and binge eating) and substance use frequently co-occur; however, the mechanisms underlying this association are poorly understood. This study evaluated the association between bulimic behaviors and early substance use, after controlling for the effects of familial risk factors.
METHODS: Participants included 3540 young adult women from the Missouri Adolescent Female Twin Study. A telephone adaptation of the Semi-Structured Assessment for the Genetics of Alcoholism interview assessed DSM-IV bulimic behaviors, substance use, and other psychological behaviors. Lifetime bulimic behaviors were examined in twin pairs concordant and discordant for early substance use (or early sex, which was reported as having the first consensual sex before age 15). Logistic regressions were adjusted for the non-independence in the twin data, zygosity, age, body mass index, early menarche (onset before age 12), and other early risky behaviors in all models.
RESULTS: Women who reported early use of alcohol, nicotine, or cannabis, as well as early sex, had higher odds of engaging in bulimic behaviors compared with those who did not report early use of these substances or early sex. Discordant twin analyses indicated that the early alcohol using twin was more likely to report bulimic behaviors than her cotwin who did not use alcohol before age 15 (adjusted OR = 1.62, 95% confidence interval = 1.05-2.50). Among twins who regularly used alcohol before age 16, the risk for bulimic behaviors was greater among dizygotic twin pairs (4.17, 1.52-11.45) than monozygotic twin pairs (1.06, 0.42-2.66). No significant differences between twins emerged for early nicotine use, early cannabis use, or early sex in the discordant twin analyses.
CONCLUSIONS: Findings suggest that alcohol use before age 15 may be a causal mechanism for the development of bulimic behaviors and regular drinking before age 16 may contribute to bulimic behaviors via shared genetic factors. These results indicate an important association underlying comorbid bulimic behaviors and alcohol use that is not shared with other substance use or early sex.

Research supported by NIAAA T32 AA07580, R01 AA09022, R37 AA07728, P60 AA011998, K05 AA017688, R01 AA017915, NIDA K08 DA019951 and NICHD 21 HD49022.

3E

Camillia Lui, Postdoctoral Fellow
Alcohol Research Group & UC Berkeley School of Public Health
Mentor: Nina Mulia
Broad Abstract Category: Epidemiology
Keywords: Social Status, Transition to Adulthood, Race/Ethnicity, Health Disparities

LIFE-COURSE SOCIAL STATUS, RACE/ETHNICITY AND ALCOHOL BEHAVIORS DURING THE TRANSITION TO ADULTHOOD

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BACKGROUND: The relationship between social status and alcohol behaviors during the transition to adulthood has varied across race/ethnicity. A limitation of prior research is the use of single time point measures of social status that are assumed to be equivalent across racial/ethnic groups. Life-course social status (LSS) is a more informative measure, as it can capture the ebb and flow of advantages or disadvantages from adolescence into adulthood. This study examines LSS within racial/ethnic groups, and its effects on heavy episodic drinking (HED) among White, Black, and Latino adults.
METHODS: Using 3 data waves from the National Longitudinal Study of Adolescent Health, LSS measures were captured in adolescence, young adulthood, and adulthood (to age 31). Through latent class analysis (LCA), LSS was operationalized as two constructs: economic capital (i.e., income, home ownership) and human capital (i.e., education, work). For HED, adult respondents were asked past year frequency of 4/5+ drinks in an occasion. HED was recoded to no past year use, drank but no weekly HED, and weekly HED. Models were stratified by race/ethnicity: Whites (n=5,248), Blacks (n=1,875), and Latinos (1,268). Analyses were conducted in Mplus (for LCA) and in Stata (for multinomial regression).
RESULTS: Weekly HED varied across Whites (14%), Blacks (7%), and Latinos (11%). For Whites, LCA models identified 4 economic capital groups (persistently advantaged, upward, downward, and persistently disadvantaged) and 5 human capital groups (persistently low, upward via work, upward via school, downward via work, and persistently high). Among current drinkers, HED was lowest among upwardly mobile Whites and highest among persistently low and downwardly mobile Whites for both LSS domains. Blacks and Latinos showed qualitatively similar LSS groups as Whites except there were no downward groups in either domain. HED was highest among persistently low and upwardly mobile Blacks in both domains. Results were not significant for Latinos.
CONCLUSIONS: These results highlight racial/ethnic disparities in life-course economic capital and human capital during the transition to adulthood. While persistently disadvantaged and downward trajectories are indicative of riskier alcohol behaviors for Whites, the economically disadvantaged and upward trajectories are indicative of riskier behaviors for Blacks. Future research should examine the mechanisms by which LSS influences HED within racial/ethnic groups.

Research supported by NIAAA grant T32 AA007240 and NIDA grant T32 DA007272.

3F

Mandy Owens, PhD Student
University of New Mexico
Mentor: Barbara McCrady
Broad Abstract Category: Treatment / Recovery
Keywords: criminal justice, incarceration, relapse, social networks, social support

CHANGES IN SOCIAL NETWORKS PREDICT SUBSTANCE USE OF ADULT MALE PROBATIONERS RECENTLY RELEASED FROM JAIL

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BACKGROUND: Evidence has shown social support to be a factor in individuals' alcohol and drug relapses. The purposes of the current study are to describe the social networks of adult male probationers recently released from jail, and examine how social networks relate to substance use.
METHODS: Fifty adult males were recruited from a Southwest Probation and Parole office and completed a single assessment session. Mean age was 40.8 (SD=12.4); 56% were Hispanic, 16% were White, 20% were African American, and 8% were other; 42% did not have a formal degree; 66% were unemployed. Measures included the Important People Interview, which assessed social networks during the 30 days prior to incarceration (T1), 30 days post-incarceration (T2), and from 31 days post-incarceration to the day prior to the interview (T3); and the Form-90, which assessed substance use for T1, T2, and T3. We examined descriptive information about participants' social networks (social network size, and percent of social network members that were heavy drinkers, heavy drug users, and users of any kind), and used hierarchical linear modeling (HLM) and paired t tests to determine if social networks changed across time. Regression models were used to test the relationships between changes in social networks and percent days abstinent from alcohol and drugs (PDA).
RESULTS: Findings highlighted the severity of this population, including the over-representation of minorities, the high rates of unemployment, and the low educational level. HLM and t tests revealed that social networks changed significantly across time, with most changes occurring between T1 and T2 or T1 and T3. Changes from T1 to T2 in the percentage of network members who were heavy drug users ($B=-.458$, $p<.01$) and percentage of network members that were users of any kind ($B=-.531$, $p<.01$) significantly predicted T2 PDA (controlling for T1 PDA), such that a greater reduction in the percentages of network members who were heavy drug users or users of any kind was related to more abstinence. The reciprocal also was true; changes in PDA from T1 to T2 significantly predicted T2 percentage of network members who were heavy drugs users ($B=-.251$, $p<.01$) and percentage of network members who were users of any kind ($B=-.326$, $p<.01$).
CONCLUSIONS: Results suggest that substance using social network members are an important factor in alcohol or drug relapse for adult male probationers recently released from jail.

Research supported by NIAAA grant T32 AA018108.

Oral Presentation Session 4

4A

Niloofar Bavarian, Postdoctoral Fellow
University of California, Berkeley
Mentor: Robert Saltz
Broad Abstract Category: Prevention
Keywords: Adolescents; substance use prevention; mediation

REDUCING ADOLESCENT ALCOHOL USE BY IMPROVING PEER AFFILIATION: RESULTS FROM A RANDOMIZED TRIAL OF A SOCIAL-EMOTIONAL CHARACTER DEVELOPMENT PROGRAM

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BACKGROUND: Adolescent substance use remains a significant public health problem associated with negative outcomes such as future problematic use, early sexual initiation, and school drop-out. During the adolescent years, association with deviant peers is a strong predictor of substance use. As such, programs that can positively impact one's peer affiliations should, theoretically, have an impact on adolescents' use of alcohol and other substances. Accordingly, the purpose of this study was to determine whether a school-based social-emotional and character development program (SECD) impacted adolescents' substance use behaviors by creating relative improvements in peer affiliation.

METHODS: The cluster-randomized control trial of Positive Action (PA) in Chicago Public Schools (a low income, urban setting) ran from fall 2004 through spring 2010 and followed a dynamic cohort of 1,170 students in 14 schools from the start of grade 3 through the end of grade 8. Across all eight waves, students self-reported on their number of deviant friends (i.e., friends who bully others, fight others, make fun of others, and do bad things). At endpoint, students self-reported on their frequency of drinking, being drunk, and use of additional substances (i.e., cigarettes, marijuana, and more serious drugs). We used intent-to-treat longitudinal mediation analyses to test the direct and mediated (through changes in number of deviant friends) effects on overall substance use. Supplemental analysis tested for the mediated effects specifically on a composite measure of alcohol-related behaviors.

RESULTS: Significant program effects across time were observed for the hypothesized mediator (i.e., number of deviant friends), the composite measure for substance use, and the composite measure related to drinking and drunkenness. In the primary analyses, the effect of PA on overall substance use was fully mediated by changes (i.e., relative reductions) in affiliation with deviant friends. In the supplemental analyses, the effect of PA on alcohol-related behaviors was partially mediated by relative reductions in deviant friend affiliation.

CONCLUSIONS: A universal, school-based, program that fostered social-emotional and character development had an impact on substance use overall and alcohol-related behaviors specifically, with effects mediated by relative reductions in affiliation with deviant friends. Strengths, limitations, and future research directions will be discussed.

Project funded by IES grants R305L030072, R305L030004 and R305A080253; Preparation of this manuscript supported by NIAAA T32 AA014125.

4B

Patrick Carter, Postdoctoral Fellow
University of Michigan
Mentor: Rebecca Cunningham
Broad Abstract Category: Prevention
Keywords: Alcohol-involved Motor Vehicle Crash, Injury Prevention, Alcohol Interlocks, Alcohol-impaired Driving

ALCOHOL IGNITION INTERLOCK INSTALLATION IN NEW VEHICLES AS A PRIMARY PREVENTION MEASURE TO DECREASE ALCOHOL INVOLVED CRASH FATALITIES AND NON-FATAL INJURIES

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University of Michigan Transportation Research Institute (UMTRI)
Departments of Emergency Medicine, University of Michigan School of Medicine
Department of Psychiatry, University of Michigan School of Medicine

BACKGROUND: Alcohol-impaired drivers are responsible for one-third of annual motor vehicle crash (MVC) fatalities and $51 billion in economic costs per year. Alcohol ignition interlock devices (AIID), currently utilized to prevent convicted DUI offenders from drink driving, are under study by federal regulators as a potential primary prevention tool among the general population to decrease alcohol-impaired driving and alcohol related traffic fatalities. This analysis models the number of alcohol-involved fatalities and non-fatal injuries prevented, as well as the associated MVC-related cost savings when AIID are installed in all new US vehicles.
METHODS: The Fatality Analysis Reporting System (FARS) and National Automotive Sampling System's General Estimates System (NASS-GES) were used to identify fatal/non-fatal injuries from 2006-2010 associated with drinking drivers of non-bus passenger vehicles. Data were adjusted to account for crashes that would have occurred independent of alcohol consumption. The estimated impact of AIID installation for the first year was derived using the number of preventable alcohol-related injuries associated with vehicles <1 y/o. The estimate was repeated for each subsequent year to estimate the cumulative effect over a 15-year implementation period. Existing estimates of crash-induced injury costs were applied to estimate the cumulative economic savings associated with the policy.
RESULTS: Installation of AIID in all new vehicles would prevent 83% of all crash fatalities and 84-88% of non-fatal injuries attributed to alcohol over a 15-year implementation period, totaling 44,403 alcohol related MVC crash fatalities and 1.42 million non-fatal injuries prevented. The greatest impact was noted among recently legal drinking drivers age 21-29 years old. AIID installation in all new vehicles would save an estimated $286 billion in unintentional injury costs over 15 years. Injury cost-savings outweighs the estimated device cost ($200-400/per vehicle) after approximately 4 years.
CONCLUSIONS: Alcohol interlock device installation in all new vehicles is likely to be a cost-effective, primary prevention policy that substantially reduces alcohol-involved crash fatalities and injuries, especially among young drivers. Results have implications for expansion of the current AIID program and future implementation of new in-vehicle detection technologies to prevent alcohol-impaired driving.

Research Support Provided by NIAAA T32 AA007477.
Updated Title: MODELING THE INJURY PREVENTION IMPACT OF MANDATORY ALCOHOL IGNITION INTERLOCK INSTALLATION IN ALL NEW U.S. VEHICLES

4C

Rachel Sayko Adams, Postdoctoral Fellow
Brandeis University
Mentor: Mary Jo Larson and Constance M. Horgan
Broad Abstract Category: Health Services
Keywords: binge drinking; alcohol-related consequences, traumatic brain injury; military personnel; posttraumatic stress disorder

EXAMINING UNHEALTHY ALCOHOL USE AND ITS CONSEQUENCES AFTER COMBAT-ACQUIRED TRAUMATIC BRAIN INJURY

Adams RS, Larson MJ, Corrigan JD, Horgan CM, Ritter GA, Bray RM, and Williams TV.
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BACKGROUND: Studies suggest that drinking after a traumatic brain injury (TBI) may be problematic. Research on unhealthy alcohol consumption after combat-acquired TBI is in its infancy despite high rates of both binge drinking and TBI among active duty military personnel. The purpose of this study is to determine if combat-acquired TBI is an independent risk factor for two alcohol outcomes (frequent binge drinking and alcohol-related consequences), and whether its effect is almost entirely through posttraumatic stress disorder (PTSD).
METHODS: This study analyzes the 2008 Department of Defense Survey of Health Related Behaviors, an anonymous, worldwide survey completed by 28,546 active duty military personnel with a 70.6% response rate. The selected study sample is personnel who returned from a combat deployment in the past 12 months (N = 7,155). Data are weighted to account for the complex sampling design. Dependent variables are 1) frequent binge drinking - 5+ drinks on the same occasion, at least once per week, in the past month (4+ for women), and 2) negative drinking-related consequences measured by 22 social, medical, and military-specific consequences. TBI is measured by a hierarchical variable that captures severity. Multivariate models adjust for demographics, lifetime combat exposure, and a positive screen of PTSD.
RESULTS: One-fourth of active duty military personnel who returned from a combat deployment are frequent binge drinkers and 13.9% experienced a TBI during their last deployment. In logistic regression models, personnel with TBI had 1.67 the odds of frequent binge drinking in the past month compared to those without TBI (95% CI, 1.00-2.79). Negative binomial regression models found that personnel who experienced a TBI with a loss of consciousness of more than 20 minutes were estimated to have 3.91 times (95% CI, 1.98-7.73) the number of drinking-related consequences as those without a TBI, even when controlling for frequent binge drinking, suggesting that the higher rate of consequences among those with TBI was not even partially explained by increased frequent binge drinking among this group.
CONCLUSIONS: This study contributes to emerging understanding of the relationship between experiencing a TBI and post-deployment drinking and its consequences, and suggests that the presence of TBI should prompt targeted alcohol assessment and brief counseling after the injury and into the post-deployment months.

Research supported by NIAAA grants F31 AA021030 and T32 AA007567.

4D

Sophie Teng, PhD Student
Louisiana State University Health Sciences Center
Mentor: Patricia Molina
Broad Abstract Category: Physiology, including C.N.S.
Keywords: Alcohol, Brain, Injury, Inflammation, Neurobehavior

ACUTE ALCOHOL INTOXICATION PROLONGS NEUROINFLAMMATION WITHOUT EXACERBATING NEUROBEHAVIORAL DYSFUNCTION FOLLOWING TRAUMATIC BRAIN INJURY

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BACKGROUND: Approximately 1.7 million people sustain a traumatic brain injury (TBI) annually, which constitutes a third (30.5%) of all injury-related deaths in the U.S. Acute alcohol intoxication (AAI) contributes to 36% to 51% of TBI incidents. Although high blood alcohol concentrations (BAC) have been demonstrated to increase the risk of injury, conflicting reports from animal and clinical studies have failed to establish whether AAI significantly impacts outcomes from TBI. The aim of this study was to determine whether AAI at the time of TBI aggravates the early neurobehavioral and neuroinflammatory sequelae.
METHODS: Male Sprague-Dawley rats were surgically instrumented with gastric and vascular catheters prior to fitting with a female Luer-lock over a 5 mm left lateral craniotomy. After a 3 day recovery, animals received a primed (2.5 g/kg) 15 h constant (300 mg/kg/h) intragastric alcohol infusion achieving BAC of 266±10 mg/dl. Time-matched controls received an isocaloric/isovolumic dextrose infusion. TBI was induced by lateral fluid percussion (~1.4J, ~30 ms) 30 minutes following discontinuation of the infusion.
RESULTS: TBI induced apnea duration (26.5+8 s), delay in righting reflex (522+83 s), and neurobehavioral dysfunction at 6 h and 24 h post TBI. AAI at the time of injury increased the delay in righting reflex (716+118) but did not significantly exacerbate the apnea duration (15.3+5.3) or neurobehavioral outcomes within the initial 24 h following TBI. TBI resulted in a localized inflammatory response as reflected by increased IL-6 mRNA expression (15-fold; $p<0.05$) at 6 h and myeloperoxidase (MPO) activity (10-fold; $p<0.05$) at 24 h post-TBI in the ipsilateral cortex of dextrose treated animals. AAI did not exacerbate MPO activity or IL-1, IL-6, TNFα, and MCP-1 mRNA expression at 6 h post TBI; however, AAI markedly accentuated neuroinflammation at 24 h post-TBI as reflected by significantly ($P<0.05$) higher IL-1, IL-6, TNFα, and MCP-1 mRNA expression as compared to the dextrose-treated animals.
CONCLUSIONS: These results show dissociation between neuroinflammation and clinical neurobehavioral measures within 24 h following TBI in AAI. The clinical implications of enhanced neuroinflammation on long term recovery in the AAI TBI victim warrant further investigation.

Research supported by DOD-W81XWH-11-2-0011 and NIAAA-AA7577.

4E

Jennifer Cadigan, PhD Student
University of Missouri
Mentor: Matthew Martens
Broad Abstract Category: Treatment / Recovery
Keywords: meta-analysis, personalized feedback, intervention, alcohol

PERSONALIZED FEEDBACK: A META-ANALYSIS OF IN-PERSON AND COMPUTER-BASED INTERVENTIONS

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BACKGROUND: Personalized Feedback Interventions (PFIs) are brief alcohol interventions that include personalized feedback about one's alcohol-use and related-problems and have been shown to be efficacious in reducing use and consequences (e.g.,Carey et al., 2012). Although exact components of feedback can vary among interventions, they typically include social norms feedback, BAC on various drinking occasions, and alcohol-related consequences. PFIs have been delivered both in-person and via computer (Walters & Neighbors, 2005). In a meta-analysis, Carey et al. (2012) found face-to-face interventions were efficacious in reducing alcohol use and problems when directly compared to computer-based interventions. Carey and colleagues found intervention content to differ across groups as some computer-delivered interventions provided harm-reduction approaches and not personalized feedback. The purpose of the present study was to conduct a meta-analysis of randomized controlled trials directly comparing in-person versus computer-based PFIs.
METHODS:. Seventeen intervention comparisons were identified: in-person (N = 1324, 72% white) and computer-based (N = 1289, 71% white). Analyses from two independent coders yielded a 98% agreement among raters, kappa = .945, ICC = .995.
RESULTS: We examined weighted mean effect sizes between intervention conditions for alcohol use and problems outcomes. At short follow-up (< 4 months), there were no differences between in-person and computer-based PFI, although effect sizes favored the computer-based conditions. Homogeneity analyses indicated effects for drinks per week, binge episodes and composite alcohol consumption were heterogeneous. At long follow-up (>4 months), there was a significant difference between in-person and computer-based PFI ($p < .05$) on the drinks per week outcome, as the effect size favored the in-person condition. On all other outcomes, there were no differences between in-person and computer-based PFI, although effect sizes favored the in-person conditions. Homogeneity analyses indicated effects for composite alcohol consumption were heterogeneous.
CONCLUSIONS: Additional analyses of moderation will be explored. These preliminary findings suggest PFIs with no in-person contact may be as efficacious as in-person PFIs at reducing alcohol-related problems and drinks per week at a short follow up. However, in-person PFIs may be favorable at longer outcomes.

Research supported by NIAAA grant T32 AA13526.

Oral Presentation Session 5

5A

Minhnoi Wroble Biglan, Postdoctoral Fellow
University of Pittsburgh
Mentor: Nancy Day
Broad Abstract Category: Epidemiology
Keywords: Prenatal alcohol use, Pregnancy, Age-related alcohol use changes, Women's health, Racial differences

RACIAL DIFFERENCES IN WOMEN'S ALCOHOL CONSUMPTION FROM PREGNANCY THROUGH 22 YEARS POSTPARTUM

Wroble Biglan MC, Cornelius MD, Kim KL, Day NL.
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BACKGROUND: Alcohol use and abuse remain one of the largest threats to public health in the western world, increasing risk for morbidity and mortality among individual. Little research has focused on whether change in use patterns of alcohol during pregnancy may be used to predict women's later substance use disorders. The current study examines whether psychological health and changes in alcohol use during pregnancy may predict risk of substance use disorders in women in their 40's and 50's.
METHODS: Women were recruited from a prenatal clinic by the 4th month of pregnancy and were followed for 23 years. Depression, hostility, anxiety, and substance use (quantity and frequency) were measured at the end of the 2nd and 3rd trimesters, and at 3, 6, 10, 14, 16, and 22 years postpartum, with a resulting cohort of 763 participants.
RESULTS: Alcohol use did not differ between African American and Caucasian women at the first assessment. Patterns of alcohol use emerged across pregnancy and the postnatal period. African American women consumed more alcohol during the 2nd and 3rd trimesters of pregnancy than Caucasian women. Among women who consumed 2+ alcoholic drinks per day during pregnancy, racial differences emerged. African American women continued to consume alcohol at a similar or greater rate as during pregnancy, however Caucasian women were no longer consuming alcohol 22 years postpartum. Psychosocial and socioeconomic factors may help to elucidate these racial differences in consumption over time.
CONCLUSIONS: Changes in alcohol use across pregnancy predict later substance use among women. These changes differed by race. As pregnancy is a time of much physician-patient interaction, changes in alcohol and drug consumption during pregnancy, even if not sustained after delivery, may help to identify women at greatest risk for substance use disorders throughout adulthood and greatest risk for disease development at midlife.

Research was funded by NIAAA T32 AA007453 (PI: M Cornelius), NIDA R01 DA03874 (PI: N Day) and NIAAA AA06390 (PI: N Day).

5B

Brian Coffman, PhD Student
University of New Mexico Health Sciences Center
Mentor: Julia Stephen
Broad Abstract Category: Fetal Alcohol Syndrome / Development
Keywords: FASD, inhibition, impulsivity, working memory, fMRI

CONGENITAL DISINHIBITION: RESPONSE INHIBITION, IMPULSIVE BEHAVIOR, AND RISKY DECISION-MAKING IN ADOLESCENTS WITH FETAL ALCOHOL SPECTRUM DISORDERS

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The Mind Research Network and Lovelace Respiratory Research Institute, Albuquerque, New Mexico, 87106.

BACKGROUND: Fetal Alcohol Spectrum Disorder (FASD) is a prevalent and preventable epidemic that results in moderate to severe physiological, cognitive, and social disabilities, including impulsive behavior and decision-making. This study examined three different types of behavioral inhibition/impulsivity as assessed by behavioral measures and functional Magnetic Resonance Imaging (fMRI) in adolescents with and without FASD.
METHODS: Adolescents (ages 12 to 21 years) with FASD (n=20) and age-matched healthy controls (HC; n=21) were assessed using the Random Sustained Attention to Response Task ($SART_{Random}$) and the CANTAB neuropsychological test battery (gambling [CGT] and spatial working memory [SWM]). Participants performed the $SART_{Random}$ task during fMRI (3T).
RESULTS: Groups were matched on age and gender. FASD scored significantly higher than HC on neuropsychological measures of impulsivity and risky decision-making in the CGT; however, groups did not differ on measures of basic response inhibition during the $SART_{Random}$. Additionally, impulsivity and risk adjustment index scores from the CGT were significantly correlated with each other and with measures of working memory obtained in the SWM task (strategy and between-errors) for HC. Within FASD, however, there was a significant correlation between risky decisions and risk adjustment index that was not found for HC. Finally, HC participants showed greater fMRI activation in visual areas compared to FASD during response inhibition in the $SART_{Random}$.
CONCLUSIONS: Our results demonstrate specific behavioral deficits in impulsivity and risky decision making in FASD, with no difference in basic response inhibition. These higher forms of inhibition could be relevant to secondary deficits in FASD, such as higher incarceration and drug use rates reported for this population. The correlation between motor inhibition, impulsivity, risk adjustment, and working memory in HC, but not in FASD, also suggests lower cognitive control of high-level inhibitory processing in FASD.

Supported by NIAAA grants P20 AA017068, 5P20 RR021938, T32 AA014127 and ARRA supplement 3P20AA017068-03S1.

5C

Leila Glass, PhD Student
Center for Behavioral Teratology - San Diego State University
Mentor: Sarah Mattson
Broad Abstract Category: Fetal Alcohol Syndrome / Development
Keywords: Reading, FASD, Prenatal Alcohol Exposure, Academic Achievement, Learning Disorders

READING DYSFUNCTION IN CHILDREN WITH PRENATAL ALCOHOL EXPOSURE: COMPARISON OF THREE DEFINITIONS

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BACKGROUND: The adverse effects of prenatal alcohol exposure on neuropsychological functioning are well documented. However the secondary disability of academic dysfunction is not fully understood, particularly in the reading domain. The current study examined the presence and prevalence of reading dysfunction (RD) in exposed children and the appropriateness of multiple RD definitions.
METHODS: 237 children (8-16y) were tested with the WISC-IV, WRAT-3, and CBCL. Two groups were tested: children with prenatal alcohol exposure (AE, n=122) and non-exposed children (CON, n=115). Follow-up analyses were conducted with an IQ-matched (p=.107) subsample (N=157; AE, n=78; CON, n=79). Group differences on RD were tested using ANOVA. Three definitions of RD were compared: 1) discrepancy model, (IQ – WRAT-3 Reading) 2) low achievement (bottom 25th percentile defined by the WRAT-3 norms, control, and total samples for whole and matched analyses) and 3) cut-point of 1.5SD below the mean of the normative sample. Chi-square and 2-tailed z-tests were used to compare prevalence of RD. Regressions determined which RD definitions predicted CBCL School Problems.
RESULTS: AE performed significantly worse ($p<.001$) than CON on Reading, even when matched on IQ ($p=.019$). The discrepancy model failed to predict reading problems in either analysis. In the whole sample analysis, all other definitions of RD found higher prevalence rates ($p<.001$) of AE (22.1-64.6%) compared to CON (7.0-24.3%). In the matched analyses, low achievement definitions (bottom 25th for WRAT norms, control, and total matched sample) also found significantly higher prevalence rates ($p<.038$) of RD in AE (32.1-43.6%) compared to CON (17.7-24.1%). Using non-discrepancy definitions, AE had higher prevalence of RD for the whole (AE: 44.25%, CON: 14.58%; $z=5.17$, $p<.001$) and the matched (AE: 33.67%, CON: 18.45%, $z=2.19$, $p=.029$) analyses. For both analyses, all non-discrepancy definitions of RD significantly predicted School Problems ($p<.001$).
CONCLUSIONS: Exposed children have significantly lower reading performance and higher rates of RD compared to controls, above and beyond the effect of IQ. These data support discontinuing the use of the discrepancy definition in this population and reinforce the use of low achievement definitions, which predict school problems. Future research should aim to understand the mechanisms of these impairments.

Research supported by NIAAA grants T32 AA013525, R01 AA10417, R01 AA019605, and F31 AA022261.

5D

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Broad Abstract Category: Lifespan / Development - Human
Keywords: Aggression, Cognitive Biases, Parents, Alcohol Problems, Early Childhood

THE INFLUENCE OF PARENT ALCOHOL PROBLEMS AND ANGER ON EARLY CHILDHOOD AGGRESSION

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BACKGROUND: Parent alcohol problems are well-established risk factors for the development of externalizing problems for children, but less is known about aggression especially in early childhood. Physical aggression at kindergarten age may be particularly problematic given normative declines in the preschool years and its potential to affect social interactions and learning. Children's social cognitive biases such as hostile attribution biases (HAB; i.e., over-attributing hostile intent) and response decision (i.e., aggressive social responses) may be mechanisms for continued aggression beyond preschool. The present study examines parents' alcohol problems and anger in early childhood (12 months of child age) and child social cognition in Kindergarten as predictors of child aggression in Kindergarten.
METHODS: Participants were 171 families from a community sample of children of fathers with alcohol problems and a demographically similar control group from an ongoing longitudinal study at both 12 months of child age and upon entry to kindergarten.
RESULTS: We examined a regression model predicting father-reported child aggression in Kindergarten. Child gender was entered at step 1, parents' self-reported anger at 12 months of child age were entered at step 2, social cognition measures in Kindergarten were entered at step 3, and parents' alcohol abuse and dependence symptoms over the first year of the child's life were entered in step 4. Gender (i.e., male; β=-.15, $p<.05$) predicted aggression [$F(1, 169)=4.07$, $p<.05$] at the first step. In the second step, gender as well as mother (β=.26, $p<.001$) and father (β=.21, $p<.01$) anger predicted aggression [$\Delta F(2, 167)=10.73$, $p<.001$]. In the third step, response decision tended to predict (β=.14, $p=.05$), but the overall change in the model was not significant [$\Delta F(2, 165)=2.88$, $p=.059$]. In the final step, father alcohol problems (β=.24, $p<.01$), male gender, and parent anger predicted above and beyond mother alcohol problems, HAB, and response decision [$\Delta F(2, 163)=5.58$, $p<.01$].
CONCLUSIONS: Father's alcohol problems in the child's first year of life, male gender, and mother's and father's anger when their child was 12 months old appear to play an important role in the child's level of aggression at Kindergarten. This adds to the literature by examining the role of parent alcohol problems on children's aggression during Kindergarten as well as the impact of the child's aggressive cognitive biases and parent anger.

Research supported by NIAAA grants R01 AA010042 and T32 AA007583.

5E

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Broad Abstract Category: Lifespan / Development - Human
Keywords: impulsivity, ventral striatum, reward, fMRI, family history

RELATIONSHIPS BETWEEN COMPULSIVITY, REWARD SENSITIVITY, RISK-TAKING AND FAMILY HISTORY OF ALCOHOLISM DURING AN INTERACTIVE COMPETITIVE fMRI TASK

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BACKGROUND: Individuals with a positive family history for alcoholism (FHP) have shown differences from family-history-negative (FHN) individuals in the neural correlates of reward processing. FHP versus FHN individuals have demonstrated relatively diminished ventral striatal activation during anticipation of monetary rewards, and the degree of ventral striatal activation has demonstrated an inverse correlation with impulsivity measures in people with alcohol dependence. Rewards in socially interactive contexts relate importantly to addictive propensities, yet have not been examined with respect to how their neural underpinnings relate to impulsivity-related measures.
METHODS: Forty FHP and 29 FHN subjects without histories of Axis I disorders completed a socially interactive fMRI Domino task and completed self-report and behavioral impulsivity-related assessments.
RESULTS: FHP versus FHN individuals showed higher scores ($p=.004$) on an impulsivity-related factor relating to compulsivity (Padua Inventory) and reward/punishment sensitivity (Sensitivity to Punishment/Sensitivity to Reward Questionnaire). Multiple regression analysis within a reward-related network revealed a correlation between risk-taking (involving the Balloon Analog Risk Task (BART)) and right ventral striatum activation under reward > punishment contrast ($p<0.05$ FWE corrected).
CONCLUSIONS: Behavioral risk-taking scores may be more closely associated with neural correlates of reward responsiveness under socially interactive contexts than do FH status or impulsivity-related self-report measures. These findings suggest that risk-taking assessments be examined further in socially interactive settings relevant to addictive behaviors.

Research supported by NIAAA grants T32 AA015496, P50 AA012870 (Project #4), and R01 AA016599.