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Broad Abstract Category: Physiology, including C.N.S.
Keywords: VTA, stress, plasticity, Kappa Opioid Receptor, Glucocorticoid

A ROLE FOR GLUCOCORTICOID AND KAPPA OPIOID RECEPTORS IN LONG-LASTING EFFECTS OF STRESS ON VTA INHIBITORY SYNAPTIC PLASTICITY

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BACKGROUND: Stress can be an important precipitating factor that drives escalation or relapse of alcohol-seeking behavior, and dopaminergic neurons in the ventral tegmental area (VTA) of the brain are important targets of alcohol and stress. We previously identified a long-term potentiation of GABAergic synapses onto these neurons (LTPGABA). Nitric oxide release by the dopaminergic neuron activates guanylate cyclase in the presynaptic terminal of GABAergic inputs, resulting in accumulation of cGMP, activation of PKG, and increased release of GABA. Multiple drugs of abuse and stress block or inhibit LTPGABA (Nugent et al, Nature, 2007; Niehaus et al, Eur J Neurosci 2010, Guan and Ye, Neuropsychopharm. 2010), suggesting that this is a common mechanism that may play a role in addiction and stress-related diseases. The loss of LTPGABA after stress or alcohol is expected to increase dopamine cell firing. Our recent work shows that the block of LTPGABA by stress is dependent on glucocorticoid (GR, Niehaus et al 2010) and kappa opioid receptors (KOR, Graziane et al, Neuron, 2013). This study addresses how long the block of LTPGABA lasts after stress, and the role of GRs and KORs in maintaining the block.
METHODS: Sprague-Dawley rats were subjected to a five minute cold-water swim stress. Midbrain slices were acutely prepared 1-10 days following stress, and whole-cell patch clamp recordings of IPSCs were performed from VTA dopamine neurons. LTPGABA was induced by bath application of the nitric oxide donor SNAP. RU486 (40 mg/kg) or norBNI (10 mg/kg) were used to block GR and KORs, respectively, and were administered via i.p. injection at varying time points after stress.
RESULTS: LTPGABA remains blocked for at least five days and returns to normal levels by ten days after stress. Thus, stress causes long-lasting, but not permanent, alterations in plasticity of GABAergic synapses in the VTA. RU486 rescues LTPGABA when administered one hour after stress, but has no effect when administered 24 hours after stress.
CONCLUSIONS: Our results show that a single exposure to acute stress can cause days-long changes in the reward circuitry. These data suggest that loss of LTPGABA may be a mechanism by which acute stress can cause lasting changes in behavior. Our studies reveal roles for GR and KORs as mediators of the lasting effects of stress on plasticity. This may provide targets for reversing neuroadaptations that could underlie stress-induced alcohol seeking behavior.

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Broad Abstract Category: Health Services
Keywords: Alcohol, Human Immunodeficiency Virus (HIV), HIV Testing, Women, Behavioral Health

ALCOHOL USE AND HIV TESTING IN A NATIONAL SAMPLE OF WOMEN

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BACKGROUND: In recent years, the HIV/AIDS epidemic continues to increasingly and disproportionately affect racial and ethnic minority groups and women in the United States. Prevention research suggests that reduced alcohol use and increased HIV testing are associated with lower incidence of HIV transmission among high-risk populations. However, there are limited empirical studies of the association between alcohol use and HIV testing among minority groups and women.
METHODS: Secondary data analyses of the 2009 National Health Interview Survey (NHIS) were performed among adult women (N=15,233). Multivariate logistic regression techniques were used to model likelihood of HIV testing controlling for individual, interpersonal, organizational, and community level factors. Interactions of alcohol use with other micro and macro characteristics were also examined. Original and imputed data samples were analyzed for this study to test robustness of the results.
RESULTS: Level of alcohol use was significantly associated with testing for HIV. Among the youngest group of women, heavy drinkers (OR = 0.063, $p < 0.01$) and moderate drinkers (OR=0.169, $p < 0.01$) were much less likely to report ever testing for HIV. Interactions between age and heavy drinking and age and moderate drinking moderated these results among older women. The odds ratios for ever having HIV testing increased by 1.052 per year among heavy alcohol users and 1.027 among moderate drinkers ($p < 0.01$). In addition, the analysis found a significant interaction between race and moderate drinking. The odds ratios for Black/African American who drink moderately was more than double what would otherwise be modeled (OR=2.305, $p < 0.01$).
CONCLUSIONS: Findings add to the limited literature on the association between alcohol use and HIV related behaviors among women. Given the rising incidence of HIV among women, this study highlights the importance of HIV testing, particularly among high risk populations. Public health policymakers should consider targeting resources for more comprehensive HIV prevention efforts with alcohol-using women. Alcohol related HIV prevention and outreach efforts need to expand to better serve women who may not be traditionally targeted.

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Broad Abstract Category: Animal Behavior
Keywords: ethanol, self-administration, hypocretin/orexin, alcohol-dependence, stress

HYPOCRETIN-1 AND -2 RECEPTOR ANTAGONISM REDUCES ETHANOL INTAKE IN DEPENDENT RATS

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BACKGROUND: Alcoholism is associated with increased stress sensitivity and negative emotional states, including dysphoria, anxiety, and depression that emerge during withdrawal. Hypocretin/orexin (HCRT) is a neuropeptide that has recently been associated with both stress and drug seeking behavior. However, the role of HCRT on escalated alcohol self-administration during alcohol dependence has yet to be examined. Thus, this study investigated the degree to which HCRT-receptor antagonism attenuates alcohol intake in both dependent and non-dependent rats.
METHODS: Wistar rats were trained to self-administer ethanol (10% w/v) until stable responding was maintained. Animals were then split into two groups: one group was made dependent by chronic, intermittent alcohol vapor exposure (i.e. dependent); the control group was not exposed to alcohol vapor (i.e. non-dependent). Upon stable post-vapor responding, rats were systemically given an injection of the HCRT-1R antagonist SB-408124 (0, 7.5, 15, 30 mg/kg) or the HCRT-2R antagonist NBI-80713 (0, 3, 10, 30 mg/kg) in a latin-square design and tested for alcohol self-administration.
RESULTS: Our results show that antagonism of either HCRT-1R or HCRT-2R elicited a dose-dependent reduction in ethanol self-administration in dependent rats, but not in non-dependent rats.
CONCLUSIONS: We show that both HCRT-1 and -2 receptor signaling is involved in escalated alcohol self-administration during alcohol dependence, further demonstrating a role for stress-related peptide signaling in the transformation to ethanol dependence. Moreover, these results support HCRT receptor antagonism as a potential pharmacological target for the treatment of alcohol dependence.

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Broad Abstract Category: Animal Behavior
Keywords: prairie vole; naltrexone; social influences; affiliation; isolation

IMPACT OF SOCIAL CONTEXT ON PHARMACOLOGICAL INTERVENTION OF ALCOHOL CONSUMPTION IN TWO SOCIAL RODENT SPECIES

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BACKGROUND: Naltrexone, a mu-opioid receptor antagonist, is used as a medication most commonly prescribed to alcoholics to decrease alcohol consumption. However, it is ineffective in many patients. One possible reason for the ineffectiveness of naltrexone is influences of the social partners of treated patients. Here we tested this possibility using two rodent models: promiscuous C57BL/6J mice and monogamous prairie voles. Both C57BL/6J mice and prairie voles are highly social and self-administer similar, physiologically relevant, doses of ethanol, but show contrasting influences of social environment on ethanol drinking: C57BL/6J mice drink more in isolation and prairie voles drink more when housed with a social partner.
METHODS: In separate studies for each species, male and female mice and prairie voles were randomly assigned to isolation or same-sex social housing. A wire screen that allowed social interaction served to separate the social housed pairs so that individual drinking values could be obtained. Alcohol (10% v/v) and water consumption were measured twice daily (at 4 hours and 24 hours each day) for eight days in a two-bottle choice test. The first four days provided a measure of undisturbed baseline consumption. During days 5-8, one animal of each pair and each singly housed animal was given daily intraperitoneal injections of either saline or 6 mg/kg naltrexone.
RESULTS: Naltrexone did not significantly reduce ethanol intake or preference in isolated or socially-housed mice. Unexpectedly, naltrexone increased drinking in socially-housed mice 4 hours after injection ($p=0.05$); this difference was gone by the 24- hour reading ($p=0.46$). There was no naltrexone effect on alcohol intake in isolated mice, nor any effect on alcohol preference in mice. In voles, naltrexone reduced average daily ethanol intake ($p=0.06$) and preference ($p=0.05$) in isolated animals at 24 hours, but not 4 hours post-injection. In contrast, naltrexone treatment did not reduce ethanol drinking in socially housed voles.
CONCLUSIONS: Our results demonstrate that the social environment has a significant impact on the effectiveness of pharmacological intervention for excessive alcohol consumption. These preliminary findings also suggest that the effects of naltrexone on alcohol drinking are species-specific. Further investigation in prairie voles can provide important translational insight into the neurobiological underpinnings of this interaction.

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Broad Abstract Category: Consequences of of Alcohol Consumption in Humans
Keywords: Intimate partner conflict, heavy episodic drinking, anger, self-control, actor-partner interdependence model

DAILY ASSOCIATIONS AMONG HEAVY EPISODIC DRINKING, SELF-CONTROL, AND RELATIONSHIP FUNCTIONING: AN EXAMINATION OF ACTOR AND PARTNER EFFECTS.

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BACKGROUND: An emerging literature suggests that temporary deficits in the ability to inhibit impulsive urges may be proximally associated with conflict within the context of intimate partnerships. This study examined the experience of disinhibitory influences, including alcohol use and the depletion of self control, in the prediction of relationship conflict and anger experience within a community sample of couples.
METHODS: Daily diary data collected from 118 heterosexual couples were analyzed using parallel multi-level Actor Partner Interdependence Models to assess the effects of heavy episodic drinking and depletion of self-control across partners on outcomes of participant-reported daily verbal conflict with and anger toward an intimate partner.
RESULTS: Heavy episodic drinking among actors predicted greater daily conflict and failed to interact with either actor or partner depletion. A significant 3-way interaction between gender, actor depletion, and partner depletion was detected in models predicting conflict. Specifically, the relationship between actor depletion and conflict was stronger on days of high partner depletion, particularly among males. Significant 2-way interactions in the prediction of partner-specific anger indicated that males felt greater anger toward partners than females, particularly on days of high partner depletion, and that the relationship between actor depletion and anger was stronger on days of high, rather than low, partner depletion.
CONCLUSIONS: Consistent with previous studies of proximal disinhibition, greater relationship conflict was reported on days of heavy drinking and high self-control demands among actors. The current study also demonstrated that disinhibitory partner effects similarly influenced actor-reported relationship functioning and that dual disinhibition, in the form of cross-partner effects, further contributed to the prediction of conflict and anger experience within couples. The current results indicate that the effects of partner-reported self-control depletion may be particularly strong among males and suggest that treatment methods to prevent the escalation of partner conflict, or to reduce the frequency and severity of more aggressive conflict, may benefit from self-control strength training as well as the inclusion of interventions at the level of the dyad.

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Broad Abstract Category: Quantitative / Computer Methods
Keywords: Computation, High-throughput, Model, Cytokine, Regeneration

CELLULAR NETWORK MODEL IMPLICATES THE BALANCE OF INFLAMMATORY CYTOKINES AS A KEY CONTRIBUTOR TO LIVER REGENERATION DEFICIT IN CHRONIC ALCOHOL ADAPTION

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BACKGROUND: Chronic alcohol consumption has been shown to cause deficient liver regeneration, a process mediated by intercellular signaling between hepatocytes and non-parenchymal cells. This study uses a combination of in vivo experiments to measure high-throughput gene and protein expression levels and in silico cellular interaction network models, to identify key factors and system properties which could explain this deficit.
METHODS: A cellular network model was constructed involving multiple resident cell types and intercellular signals that show dynamic changes as early as the first 6 hours of liver regeneration. Model parameters were estimated based on time-series, high-throughput protein measurements taken from wild type mice during the priming phase of regeneration following partial hepatecomy and from published data describing regeneration profiles.
RESULTS: Because chronic alcohol consumption alters the cytokine microenvironment in the liver, we tested how altering the balance of pro- and anti-inflammatory cytokines affects regeneration. The model predicts that altering this balance will cause a delay in the initiation of regeneration but will have no effect on total liver mass by approximately 60 h. We tested these predictions using cytokine profiles and liver regeneration data from Adiponectin knockout (Adn KO) mice, which have a chronically less active immune system than wild type mice. During the priming phase following partial hepatectomy, Adn KO mice show a shift in the balance of inflammatory factors, leading to lower levels of STAT3 phosphorylation (a key regeneration checkpoint) and a delay in the initiation of regeneration. Consistent with simulation predictions, in vivo experiments demonstrate that there is no change in final weight of the Adn KO mouse livers compared to wild type controls.
CONCLUSIONS: This study shows that the balance of pro- and anti-inflammatory cytokines plays a key role in the initiation of liver regeneration. However, our modeling studies predict that alcohol's de-regulation of the cytokine microenvironment does not fully explain the complete suppression of regeneration following chronic alcohol adaption. We further predict that chronic alcohol consumption must also strengthen anti-proliferative signals in the liver. Future work will focus on identifying and modeling the intracellular processes driving pro- and anti-proliferative signaling in the multiple cell types resident in the liver.

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Broad Abstract Category: Genetics
Keywords: gene x environment, adolescence, GABRA2, externalizing behavior, parental monitoring

DIFFERENTIAL SUSCEPTIBILITY TO ADOLESCENT ALCOHOL USE PATHWAYS: EXAMINING THE INTERPLAY BETWEEN GABRA2 AND PARENTAL MONITORING

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BACKGROUND: Elevated and persistent levels of externalizing behavior in adolescence predict alcohol abuse. As such, understanding factors differentiating transient from persistent externalizing trajectories may identify adolescents most at risk. Although, parental monitoring is protective of externalizing behaviors, youth vary in the degree to which this influence has an effect. Research suggests that those with the minor allele homozygote (GG) of GABRA2 are more likely to develop alcohol dependence and more susceptible to adverse contexts. This study's aim was to examine GABRA2, parental monitoring, their interaction on externalizing trajectories, and subsequent rates of substance abuse symptomatology.
METHODS: Prospective analyses were conducted on 504 adolescents from the Michigan Longitudinal Study (71% male). Parental monitoring, externalizing behavior, and adulthood number of binge drinking days and substance-related problems were examined. A subsample was genotyped to assess GABRA2 x parental monitoring interactions. Growth mixture models were conducted to better characterize the heterogeneity of course for externalizing behavior.
RESULTS: A three-class solution was estimated: a low (76.6%), a declining (9.8%), and an increasing pattern (13.5%) in externalizing behaviors. Adolescents in the increasing class had a higher mean of binge drinking and substance-related problems. Parental monitoring, not genotype, had a direct effect on class membership. A-carriers were largely unaffected by parental monitoring, while those with the susceptibility genotype (GG) were affected. At low levels of monitoring, those with the GG genotype had a high probability of belonging to the increasing class and a low probability of belonging to the decreasing and low classes; whereas at high levels of monitoring they had a high probability of belonging to the decreasing compared to the increasing class.
CONCLUSIONS: Understanding factors that identify those adolescents who successfully transition into adulthood and those experiencing sustained problems leading to substance abuse are critical. Parental monitoring and GABRA2 differentially predict trajectories of externalizing behaviors related to the development of problematic substance use. This study offers evidence that traditional conceptualizations of GABRA2 variants as purely risk factors may be misguided. Indeed, individuals with the GG genotype may be more susceptible to both adverse and adaptive environments.

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Broad Abstract Category: Animal Behavior
Keywords: Rostromedial tegmental nucleus (RMTg), Conditioned taste aversion (CTA), Consumption, Lesion, Tail of the VTA (tVTA)

THE ROLE OF THE ROSTROMEDIAL TEGMENTAL NUCLEUS IN ALCOHOL CONSUMPTION

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BACKGROUND: While it is well known that the rewarding properties of a drug critically contribute to its addictive properties, there is increasing appreciation that aversive properties of the drug also play an important role in the addictive process. Current theories suggest that a competitive balance between a drug's rewarding and aversive properties exist, and that this balance may change as drug use progresses from recreational use to addiction. While the rewarding properties of alcohol have been extensively investigated, little is known about the contribution of alcohol's aversive properties on its addictive potential. Interestingly, the rostromedial tegmental nucleus (RMTg) was recently identified as a region of the brain that encodes aversive stimuli and is involved in modulating the behavioral response to those stimuli.
METHODS: As an initial investigation into the role of the RMTg in alcohol addiction, we bilaterally lesioned the RMTg using stereotaxic injections of ibotenic acid in adult male Long-Evans rats. Following recovery, lesioned (n=6) and control (n=6) rats voluntarily self-administered 20% ethanol for three consecutive weeks using an intermittent access, two-bottle choice training procedure. In a follow-up experiment using a separate group of lesioned (n=5) and control (n=3) rats, the magnitude of ethanol-induced conditioned taste aversion (CTA) was measured using 0.1% saccharin as the conditioned stimulus (CS) and 1.5 g/kg i.p. ethanol as the unconditioned stimulus (US).
RESULTS: RMTg lesioned rats exhibited significantly greater ethanol intake than control rats during the two-bottle choice procedure ($p \leq 0.05$). This effect was specific to ethanol since no significant differences in total fluid or water intake were observed between groups. RMTg lesioned rats also exhibited greater saccharin consumption following US-CS pairing compared to controls ($p \leq 0.05$) indicative of a resistance to ethanol-induced CTA.
CONCLUSIONS: These results demonstrate that lesions of the RMTg increase ethanol intake and that this effect may be due to a reduction in the processing of ethanol's aversive properties. Additional work is currently underway to increase sample size and identify the specific neurocircuitry involved in RMTg-mediated signaling of the aversive properties of ethanol.

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Broad Abstract Category: Quantitative / Computer METHODS
Keywords: Clustering, Latent Variable Analysis, Alcohol Use Disorders, Factor Analysis, Latent Class Analysis

EXAMINING THE LATENT SPACE OF ALCOHOL USE DISORDERS: A COMPARISON USING NESARC AND NLAES

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BACKGROUND: Determining the latent space of alcohol use disorders (AUDs) is an important consideration when making recommendations for future editions of diagnostic manuals. McDonald (1967) showed a mathematical equivalence between a factor model with K-1 factors (continuous latent variables) and a latent class model with K classes (discrete latent variables). This led many researchers to believe the distinction between latent classes and dimensions to be an arbitrary one (see Molenaar & Von Eye, 1994). However, when the goal of a statistical analysis is to classify individuals into meaningfully different groups, choosing whether the latent space of a model consists of continuous factors or discrete classes is essential. The present research is interested in examining the nature of the latent space of alcohol use disorders by comparing results from latent variable analysis assuming (1) categorical latent variables, (2) dimensional latent variables, and (3) a combination of categorical and dimensional. In addition to determining the nature of the latent space, whether this can be replicated across data sets and techniques can attest to the robustness of the true latent structure.
METHODS: To examine the latent space of alcohol use disorders, data from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) and National Longitudinal Alcohol Epidemiologic Survey (NLAES) were used and the fit of a variety of latent space compositions were compared. The following types of latent spaces were examined: (1) latent classes (with latent class analysis, LCA), (2) latent dimensions (with factor analysis, FA), (3) a combination of classes and dimensions (with latent class factor analysis, LCFA). The replicability of the nature of the latent space is examined by comparing the best fitting model between the two data sets. To determine whether the classification of individuals into groups can be replicated across techniques, the results of the best fitting model for a LCA were compared with the best results of a K-means cluster analysis and evaluated for solution agreement.
RESULTS: Consistent with previous research, results suggest that the latent structure of the data is comprised of a combination of classes and dimensions. The best fitting solutions between the two data sets agreed fairly well (assessed via the Akaike Information Criterion, AIC), as well as the classification of individuals between model-based and non-model-based clustering techniques (assessed via the Hubert-Arabie Adjusted Rand Index, ARI, Hubert & Arabie, 1985).
CONCLUSIONS: Due to the strong agreement between model-based and non-model-based clustering techniques, the latent structure of alcohol use disorders appears to be robust to changes in technique. Results also suggest the latent space replicates well between data sets.

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Broad Abstract Category: Pharmacology, including C.N.S.
Keywords: Dorsal Raphe, Excitatory transmission, Inhibitory transmission, acute ethanol, chronic ethanol

ACUTE AND CHRONIC ETHANOL HAVE BIDIRECTIONAL EFFECTS ON SYNAPTIC TRANSMISISON IN THE DORSAL RAPHE

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BACKGROUND: Drinking to relieve anxiety during ethanol withdrawal is proposed to be a primary factor in the persistence of alcoholism. The dorsal raphe (DR) is a serotonin-rich structure that has been widely implicated in stress and anxiety responses, and behavioral data has demonstrated that this region is involved in anxiety following ethanol withdrawal. The effect of acute and chronic ethanol exposure on neurons of the DR was assessed using whole-cell slice electrophysiology.
METHODS: Male DBA/2J mice were exposed to 16-h of ethanol (CIE) or air (AE) vapor on 5 consecutive days. Brain slices containing the DR were prepared 24-h or 7 days after the final exposure, and electrophysiological recordings of inhibitory and excitatory transmission were performed.
RESULTS: Results revealed a significant reduction in the frequency of spontaneous inhibitory post-synaptic currents (sIPSCs) 24-h post-ethanol, suggesting a lack of GABAergic inhibition of DR neurons. This effect was network-dependent and specific to GABA, as no changes in miniature IPSCs (mIPSCs), spontaneous or miniature excitatory post-synaptic currents (sEPSCs, mEPSCs) were observed at this timepoint. Conversely, significant enhancements in the amplitude of sEPSCs and the frequency of mEPSCs were observed 7 days post-ethanol, suggesting long-term enhancements in network-dependent and independent glutamatergic excitation of DR neurons following CIE. Together, these data suggest a shift towards net excitation of DR neurons following chronic ethanol exposure. Because acute ethanol alters GABA transmission in other brain regions, we assessed the effects of *ex vivo* ethanol (50 mM) on mIPSCs in the DR of naïve DBA, AE and CIE mice 24-h post-ethanol. Bath application of ethanol modestly enhanced the amplitude of mIPSCs in cells from naïve, AE and CIE mice but significantly enhanced the frequency of mIPSCs only in cells from CIE mice, suggesting that DR neurons are more sensitive to the inhibitory effects of acute ethanol following CIE.
CONCLUSIONS: Based on these findings, we hypothesize that net excitation of DR neurons following chronic ethanol exposure contributes to enhanced anxiety during ethanol withdrawal and that increased sensitivity of DR neurons to subsequent ethanol exposure may mediate acute ethanol's ability to relieve anxiety during ethanol withdrawal.

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Broad Abstract Category: Animal Behavior
Keywords: Adolescent, alcohol, operant, self-administration, relapse

OPERANT ETHANOL SELF-ADMINISTRATION IN ADOLESCENT AND ADULT MALE LONG-EVANS RATS

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BACKGROUND: Alcohol is the most widely abused drug during adolescence. Rates of heavy consumption and binge drinking exceed any other time in life, and early-onset alcohol abuse might predict long-term alcohol dependence. Surprisingly, a paucity of alcohol research exists in adolescents using operant models. Thus, we characterized operant ethanol self-administration behavior in adolescent vs. adult rats using a limited access model that separates the appetitive and consummatory phases of drinking behavior, a progressive ratio (PR) test of the motivation to self-administer, and a test of reinstatement of behavior after abstinence.
METHODS: Adolescent (postnatal day (P) 29 at start of training) and adult male Long-Evans rats were first trained to self-administer 10% sucrose (10S) in an appetitive/consummatory operant model. After training on 10S (adolescents at P36), the drinking solution was switched to 10% ethanol plus 10% sucrose (10E10S) and operant ethanol self-administration continued for 2 weeks. Next, rats were tested on a fixed ratio 2 (FR2; 4 days) schedule of reinforcement, then one session using a PR schedule of reinforcement. Lastly, rats were tested for reinstatement of behavior under extinction conditions after 13 days of abstinence. Control rats only drank 10S throughout the experiment.
RESULTS: The amount of ethanol consumed was not different between adolescents and adults. Ethanol intake increased during acquisition, reaching stable maintenance levels of 1.0 g/kg in 20 min. Adolescents did display deficits in appetitive behavior compared to adults, independent of drinking solution. Blood ethanol concentration (BEC; 30 min after drinking initiation) correlated to amount of ethanol consumed in adults, while the majority of the adolescents sampled did not exhibit detectable BEC. No age differences occurred in ethanol intake under FR2 or PR schedules of reinforcement, although 10S groups reached higher breakpoints vs. 10S10E groups. No age difference occurred in the amount of sucrose consumed in control rats. Ethanol-seeking behavior also did not differ by age-at-onset.
CONCLUSIONS: We establish a relevant, voluntary, behavioral model of ethanol self-administration in adolescent vs. adult rats. Future experiments using this model will be able to directly compare the effects of age-at-onset of ethanol self-administration, thereby increasing our understanding of the neurobiological consequences of alcohol use during the critical period of adolescence.

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Broad Abstract Category: Treatment / Recovery
Keywords: Treatment attendance; Substance Use Disorders; Depression; Trauma; Co-occurring disorders

PREDICTORS OF TREATMENT ATTENDANCE AMONG VETERANS RECEIVING TREATMENT FOR CO-OCCURRING SUBSTANCE DEPENDENCE, DEPRESSION, AND TRAUMA

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BACKGROUND: Treatment attendance is associated with positive treatment outcomes; however, treatment for alcohol and substance dependence is associated with high rates of attrition. Research has broadly categorized retention predictors into treatment, demographic, and motivational characteristics.
METHODS: We evaluated predictors of attendance in a sample with co-occurring alcohol or substance dependence, depression, and trauma exposure participating in a randomized clinical trial. Of the participants with intake diagnostic data (N = 128), 28% met criteria for alcohol dependence only, 2% met criteria for substance dependence only, and 70% met criteria for both alcohol and substance dependence. All participants (89% male, mean 47 years of age) received Integrated Cognitive Behavioral Therapy (ICBT) for co-occurring depression and addiction in Phase I and were randomized to receive either a continuation of ICBT or Cognitive Processing Therapy (CPT) for PTSD during Phase II. Phase I included twice weekly group sessions for 12 weeks and Phase II included once weekly individual sessions for 12 weeks. We examined predictors for Phase I (mean = 14.1 sessions) and Phase II (mean = 6.4 sessions) attendance.
RESULTS: Phase II group assignment (ICBT vs. CPT) was not related to attendance. More years of education predicted Phase I and II attendance (ps < .05). Women attended significantly more Phase I sessions than men (p = .02). There were no statistically significant findings for ethnicity or diagnosis (alcohol dependence vs. substance dependence vs. alcohol and substance dependence). For perceived need for treatment and motivational factors, chronic housing difficulties was associated with poorer attendance (p = .03). We also examined intake levels of depression (Beck Depression Inventory), PTSD symptoms (PTSD Checklist), and mood regulation (Negative Mood Regulation Scale). None of these were predictive of attendance.
CONCLUSIONS: In summary, patient demographics were associated with treatment retention and may be useful indicators for clinicians about patients who are at-risk of treatment drop out. Similar attendance in the CPT and ICBT groups suggests that after a period of abstinence, focus on trauma does not lead to increased treatment drop-out among individuals with co-occurring depression, addiction, and history of trauma.

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Broad Abstract Category: Molecular / Cell Biology, including C.N.S.
Keywords: Alcohol, Burn Injury, Mesenchymal Stem Cells, Macrophages, Inflammation

BINGE ETHANOL EXPOSURE ALTERS INFLAMMATORY RESPONSES AND THE RATIO OF LUNG MESENCHYMAL STEM CELLS AND M2 MACROPHAGES IN THE LUNGS OF BURN INJURED MICE

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BACKGROUND: Clinical evidence reveals that alcohol is involved in about half of all burn injuries that require hospitalization. Consuming alcohol prior to burn injury results in higher morbidity and mortality rates, as well as increased risk of pulmonary complications and lung failure relative to burn injury alone. Our work has demonstrated that in a mouse model of binge ethanol and burn injury there is significant, prolonged pulmonary inflammation, including amplified interleukin-6 (IL-6) levels, relative to either insult alone. The phenotypic switch of alveolar macrophages from a pro-inflammatory, IL-6 secreting M1 profile, to an anti-inflammatory, interleukin-10 (IL-10) secreting M2 profile, is important in resolving inflammation. Recent studies have shown this transformation can be influenced by mediators secreted by mesenchymal stem cells (MSCs). Additionally, both lung MSCs and alveolar macrophages have been shown to reside in the distal airways of the lung, suggesting locally secreted factors by MSCs can drive M2 polarization.
METHODS: Experiments were performed to determine the frequency of lung MSCs and M2 macrophages, as well as pro- and anti-inflammatory cytokines levels in the lung after binge ethanol and burn injury. Eight week-old C57BL/6 male mice were subjected to episodic binge alcohol exposure (3 days of ethanol, 4 days off, and 3 days of ethanol). Thirty minutes following the final ethanol exposure, mice were anesthetized and given a 15% total body surface area dorsal scald injury.
RESULTS: At 24 hours after burn, flow cytometry showed Sca-1+CD45-CD31-EpCAM- lung MSCs from combined injured mice were decreased by 56% compared to sham groups ($p<0.05$) and by 45% compared to burn injury alone ($p<0.05$). F4/80+CD206+ M2 macrophages from combined injured mice were decreased by approximately 70% compared to sham groups ($p<0.05$) and 61% compared to burn injury. Additionally, in combined injured mice, there was a 69% increase in IL-6 levels ($p<0.05$) and a 57% decrease in IL-10 levels, compared to burn injury alone.
CONCLUSIONS: These data suggest that interaction between lung MSCs and macrophages may be important in post-burn resolution of pulmonary inflammation and that ethanol exposure decreases that association resulting in prolonged inflammation.

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Broad Abstract Category: Fetal Alcohol Syndrome / Development
Keywords: Fetal alcohol syndrome, microglia, cytokines

REPEATED ALCOHOL EXPOSURE DURING THE 3RD TRIMESTER-EQUIVALENT ALTERS INFLAMMATORY SIGNALING PATHWAYS IN THE RAT DENTATE GYRUS.

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BACKGROUND: Due to its isolation by the blood-brain-barrier, the central nervous system relies on its own highly specialized immune system. During development, the neuroimmune system has been shown to play an important role in synaptic pruning and wiring of neuronal circuits. Studies have linked alterations in the neuroimmune system to the pathophysiology of fetal alcohol spectrum disorder (FASD). Additionally, activation of the neuroimmune system during development has been shown to cause deficits in memory only unmasked by exposure to bacterial lipopolysaccharide (LPS) in adulthood (Bilbo et al., Behav. Neurosci. 119: 293-301, 2005). This study aimed to determine basal changes in the neuroimmune system after postnatal alcohol exposure (PAE), and to assess the effect of PAE on activation of the neuroimmune system in response to LPS.
METHODS: Rat pups were exposed to alcohol vapor from postnatal day (PD) 2 until PD 16 for four hours daily. On PD 17, animals received either an injection of saline or LPS (50 µg/kg). After 2 hours, whole dentate gyri from male rats were dissected and used for either protein analysis (western blotting and/or ELISA) or mRNA collection.
RESULTS: The average blood ethanol concentrations on PD 6 was 154 mg/dL ± 38 (n = 4 litters). PAE significantly increased mRNA levels for the pro-inflammatory chemokine, Ccl5 (1.41 fold, $p = 0.017$, $n = 4$) and a significantly decreased levels for the anti-inflammatory cytokine Il11 (-1.61 fold, $p = 0.016$, $n = 4$). Additionally, Il-11 protein levels were found to be decreased in PAE groups (68.7%, $p= 0.047$, $n = 4$). Preliminary results from LPS injected animals revealed that while LPS injections caused levels of Il-1β and CCL2 to increase by approximately 16-fold and 33-fold respectively ($n = 2$), this effect was blunted in dentate gyri of PAE rats.
CONCLUSIONS: PAE had a pro-inflammatory effect in the rat dentate gyrus, under basal conditions. Unexpectedly, PAE blunted the neuroimmune response to LPS challenge. This could be a consequence of PAE-induced alterations of microglia, which have been demonstrated in other studies. Given the important role of the neuroimmune system during development, changes in or a loss of immune cells at this time could have deleterious consequences for the maturing brain and potentially contribute to deficits seen in FASDs.

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Broad Abstract Category: Animal Behavior
Keywords: Alcohol consumption, rodent model, pharmacology, motor ataxia, tolerance

CROSSED HIGH ALCOHOL PREFERRING (CHAP) MICE EXHIBIT STIMULATION AND ATAXIA DURING EARLY ETHANOL ACCESS, AND DEVELOP FUNCTIONAL TOLERANCE DURING FREE-CHOICE ETHANOL ACCESS

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BACKGROUND: Reminiscent of human alcoholics, cHAP mice, selectively bred from a cross of HAP1xHAP2 lines, achieve high (~250 mg/dl) blood ethanol concentrations (BECs) during chronic, free-choice ethanol access, making them a valuable model for studying the development of and consequences of chronic, excessive-like intake.
METHODS: Using homecage locomotor monitors, we evaluated whether alcohol drinking altered locomotor activity, both initially and following chronic drinking experience. We also assessed if ataxia resulted from voluntarily consumed alcohol during the first 12 hours of access, and investigated whether tolerance develops to ethanol-induced ataxia following longer access durations. In each experiment, Ethanol mice had access to 10% ethanol and water, while Water mice had water-only access. In experiment 1, locomotor activity was recorded during the first day of ethanol access and during the last day of a 3-week access period. In experiment 2, once Ethanol mice reached an intake rate of >1.5 g/kg/h, it (and a Water mouse) was tested for footslips on a balance beam and blood-sampled to assess BEC. In experiment 3, after 3 days, 2 weeks, or 3 weeks of ethanol access, mice were tested for ataxia following a 1.75 g/kg ethanol injection, and blood-sampled to assess BEC.
RESULTS: In experiment 1, ethanol consumption increased locomotion, but only during the light part of the cycle (ps < .005), and only during initial access, not after chronic access. This may demonstrate adaptation to alcohol's stimulant actions with chronic drinking experience. In experiment 2, 10 of 12 Ethanol mice met the intake rate criterion, yielding an average BEC of 103 mg/dl, sufficient to induce ataxia ($p < .05$). In experiment 3, mice that had been drinking for 2 and 3 weeks showed tolerance to ethanol's ataxic effects (ps < .05).
CONCLUSIONS: Together, these studies demonstrate that cHAP mice show stimulation and drink to intoxication during acute ethanol access, and develop functional tolerance to the ataxic effects of ethanol following 2 or 3 weeks of ethanol access. Our findings may be important because cHAP mice encounter ethanol levels analogous to the degree of exposure seen in chronic, excessive human consumption, suggesting that they are a translational model for studying the vulnerability for and consequences of excessive ethanol consumption.

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Broad Abstract Category: Determinants of Alcohol Consumption in Humans
Keywords: Women, Sexual Minority, Emerging adulthood, Alcohol, Social relationships

PARENTS AND PARTNERS BOTH INCREASE AND DECREASE DRINKING AMONG SEXUAL MINORITY WOMEN IN EMERGING ADULTHOOD

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BACKGROUND: Alcohol use risks are higher among emerging adult (EA; ages 18-25) sexual minority women (SMW) than among heterosexuals, but explanations for this disparity are needed. Relationships are likely to influence drinking, but are understudied among EA SMW. We address this scientific gap by examining whether family support and communication reduces drinking among EA SMW, and whether family rejection due to sexual orientation increases drinking. We also examine the relative influence of living with and drinking with parents and partners.
METHODS: Participants were recruited national via social networking websites and completed online surveys between 2010 and 2011. Participants: Women (N = 1089; 40% lesbian & 58% bisexual). The mean age was 20.9 years (SD= 2.1). The three most frequently endorsed racial backgrounds were white (54.2%), multiple backgrounds (16.6%), and African American (9.6%); 10.2% endorsed a Hispanic or Latino ethnicity. Analyses: We tested negative binomial regression models of weekly drinking quantity including age, family support, family communication, family rejection, drinking with parents, dates, and partners, living with parents and living with committed partners as predictors.
RESULTS: One unit increases in family communication and practical family support reduced weekly drinking quantity by 15% and 18% respectively. Family rejection and living with parents did not influence drinking. One unit increases in drinking with dating partners, committed partners, and parents increased weekly drinking 19%, 15%, and 22% respectively. Among participants with committed partners, living together reduced drinking by 39%.
CONCLUSIONS: Relationships can both increase and decrease drinking. Family support and communication, and committed cohabitating partnerships, were each associated with reduced drinking among SMW, but more frequent drinking within these primary relationships also increased overall drinking quantity. Living with a committed partner reduced weekly drinking quantity the most, whereas drinking with parents was associated with the highest increase in weekly drinking quantity. Given the consistency with findings regarding relational risk and protective factors among heterosexual EA, these models indicate that more research is needed to explain drinking disparities between SMW and heterosexual EAs.

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Broad Abstract Category: Determinants of Alcohol Consumption in Humans
Keywords: Protective Behavioral Strategies; Drinking Control Strategies; Self-Control; Alcohol-Related Problems; College Students

USE OF ALCOHOL PROTECTIVE BEHAVIORAL STRATEGIES AMONG COLLEGE STUDENTS: A CRITICAL REVIEW

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BACKGROUND: Protective behavioral strategies (PBS) are specific behaviors one can utilize to minimize the harmful consequences of alcohol use. Recently, there has been an increasing amount of interest in PBS use among college students, especially as an intervention target. The purpose of the present critical review of the PBS literature was to 1) review inconsistencies in the measurement of PBS to make measurement recommendations, 2) summarize the nomological network of PBS, 3) weigh the evidence of PBS use as a mechanism of changing alcohol use, and 4) identify important knowledge gaps in the literature to make recommendations for future research.
METHODS: 62 published reports were identified that fit the inclusion criteria: 1) used a multi-item measure of PBS, 2) used a college student sample, and 3) reported a quantitative relationship between PBS and at least one other variable.
RESULTS: Collapsing across several different variants of many of the PBS scales, at least 11 distinct PBS measures were found, but only 2 were found with good psychometric properties that have been replicated. Several antecedents to use of PBS were examined ranging from specific beliefs regarding PBS use (descriptive norms, self-efficacy) to trait variables (conscientiousness, impulsivity-like traits). However, most of these were only examined in single studies; potential moderators have similarly suffered from a lack of replication. When interventions have been shown to successfully modify PBS use, PBS use has been found to be a significant mediator of intervention effects. The failure in some studies for PBS use to predict prospectively leads to some questions regarding its relationship to alcohol outcomes. As research addressing the time course and stability of PBS use is absent from the literature, it is difficult to make informed decisions regarding when PBS use should be measured when being tested as a mediator of an intervention.
CONCLUSIONS: Of all 62 published reports reviewed, 80% reported only cross-sectional data, only 2 attempted to minimize potential recall biases associated with retrospective assessment of PBS use, and only 2 used an approach that allowed the examination of both within-subject and between-subject effects. In terms of the gaps in the literature, there is a dearth of longitudinal studies, especially intensive longitudinal studies, which are integral to identifying more specifically how, when, and for whom use of PBS can be protective.

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Broad Abstract Category: Prevention
Keywords: HIV/AIDS, providers, knowledge, adherence, intervention

KNOWLEDGE REGARDING EFFECTS OF ALCOHOL USE IN HIV POSITIVE OUTPATIENTS AND CARE PROVIDERS

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BACKGROUND: The prevalence of heavy alcohol consumption in persons living with HIV/AIDS (PLWHA) is higher than that of the HIV negative population. Chronic alcohol use in PLWHA is associated with multiple negative biomedical and psychosocial consequences. Findings from our preclinical studies have demonstrated that chronic alcohol consumption accelerates disease progression by increasing viral set point, accelerating progression to end-stage, and accentuating muscle wasting. In PLWHA, heavy alcohol use is also associated with poorer ART adherence and effectiveness, reduced cognitive function, and increased likelihood of engaging in unprotected sex. Despite the harmful consequences of heavy alcohol use in PLWHA, no published studies have examined patient or care provider knowledge regarding these topics. The present study examined awareness of these relationships in an urban HIV outpatient setting.
METHODS: HIV positive outpatients (N=18) and HIV psychosocial care providers (N=15) completed an anonymous survey assessing knowledge related to the impact of alcohol use on HIV disease progression. Participant knowledge was subsequently re-assessed following an hour-long educational program in which pre-clinical and clinically relevant research findings regarding alcohol use in PLWHA were presented. The average age of participants was 43 years (SD=12 years) and 52% identified as male.
RESULTS: Prior to the educational program, respondents demonstrated the greatest knowledge of the increased likelihood for PLWHA who drink alcohol to engage in unprotected sex, miss medications, and feel depressed. Moderate knowledge was demonstrated regarding the impact of alcohol on immune function, nutrition, and medication effectiveness in PLWHA. Less than half of respondents correctly identified that PLWHA are more likely to engage in heavy alcohol use than those who are HIV negative. During the post-program assessment, only psychosocial care providers demonstrated a significant increase in knowledge ($p = .000$); whereas differences in PLWHA were not significant ($p = .749$).
CONCLUSIONS: PLWHA and psychosocial care providers demonstrated modest knowledge regarding the effects of alcohol use on HIV positive patients. In particular, respondents were unaware that heavy alcohol use is higher in PLWHA than in the HIV negative population. Preliminary evidence also suggests that care providers who attend an educational presentation related to alcohol use in PLWHA will experience improvements in this important knowledge base. Further research should investigate the lack of change in knowledge of PLWHA with possible modifications to promote learning and retention. Given the significant negative impact that heavy alcohol use can have on PLWHA, it will be important in future training and intervention settings to increase awareness by effectively educating both PLWHA and their care providers.

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Broad Abstract Category: Determinants of Alcohol Consumption in Humans
Keywords: alcohol expectancies, subjective response to alcohol, alcohol administration

DO ALCOHOL EXPECTANCIES ACCURATELY REFLECT SUBJECTIVE RESPONSE? A NOVEL ASSESSMENT PACKAGE SHOWS THAT INACCURATE BELIEFS PREDICT DRINKING AND PROBLEMS

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BACKGROUND: Social Learning Theory posits that alcohol expectancies (AEs) and subjective response to the acute effects of alcohol (SR) are reciprocally related predictors of drinking, and that understanding their interrelationship is critical to the development of a comprehensive model of alcohol use. However, the absence of a measurement tool permitting direct comparisons of AEs and SR has resulted in a paucity of research on the subject. Morean, Corbin, and Treat (2012; in press) recently developed a psychometrically sound assessment package for measuring AEs and SR, which permits for the first time direct evaluations of the relationship between AEs and SR. We expected AEs and SR to be related yet distinct constructs. Further, we expected that discrepancies between AEs and SR (e.g., underestimating intoxication) would relate to heavy drinking and other negative consequences.
METHODS: We administered the Anticipated Effects of Alcohol Scale (AEAS) and the Subjective Effects of Alcohol Scale (SEAS) to 215 participants who completed a placebo-controlled alcohol administration study in a simulated bar laboratory. The AEAS and SEAS assess 13 overlapping effects that comprise four subscales: high arousal positive (e.g., funny), high arousal negative (e.g., aggressive), low arousal positive (e.g., calm), and low arousal negative (e.g., woozy). Participants reported AEs based on the NIAAA binge drinking criteria (4/5 drinks in 2 hours for women/men), which approximated the target peak breath alcohol level within the alcohol administration study (.08 g%). AEs and SR were assessed for both the ascending and descending limb of the blood alcohol curve.
RESULTS: Multivariate GLM analyses revealed that AEs accounted for an average of 27% of the variance in SR, suggesting that AEs and SR are overlapping yet distinct construct. With respect to accuracy, AEs generally represented modest to moderate overestimates of SR (average Cohen's d = .59 in placebo; .42 in alcohol). However, inaccurate expectations in the form of both overestimates and underestimates were associated with alcohol outcomes. For example, expecting stronger high arousal negative effects and weaker low arousal negative effects than actually were experienced was associated with binge drinking and alcohol-related problems.
CONCLUSIONS: The current study suggests that addressing discrepancies between AEs and SR may have important implications for prevention and treatment efforts.

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Broad Abstract Category: Prevention
Keywords: Acculturation, acculturation-based conflict, acculturation gaps, underage drinking, immigrant families, Actor-Partner Interdependence Model (APIM)

EXPLORING ACCULTURATION-BASED CONFLICT AS A RISK FACTOR FOR ADOLESCENT ALCOHOL USE AMONG IMMIGRANT FAMILIES USING THE ACTOR-PARTNER INTERDEPENDENCE MODEL (APIM)

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BACKGROUND: Acculturation is a complex and dynamic process central to the immigrants' experience that can develop resilience or create struggles related to their health. One such challenge is acculturation-based conflict, which represents parent-child clashes over differences in behaviors and values due to the faster assimilation of adolescents to mainstream culture. This paper focuses on assessing acculturation-based conflict as a possible risk factor for alcohol use among Chinese American adolescents. Secondly, it explores the mechanisms by which differing rates of acculturation between parent and child along traditional versus
Western-based values and behaviors lead to this type of conflict through using the Actor-Partner Interdependence Model (APIM) (Kenny, 1996; Kenny & Cook, 1999).This new approach to examining the relationship between parent-child acculturation rates and acculturation-based conflict analyzes dyadic data while accounting for the interpersonal nature of parent-child dynamics.
METHODS: Parent -child dyads (n=191), drawn from students in 6th- 8th grades and their parents from three elementary schools in Chicago's Chinatown, completed self-administered questionnaires. Acculturation-based conflict was measured by Intergenerational Congruence in Immigrant Families (ICIF) –Parent Scale and Child Scale with parents and children respectively. The Kviz-Choi Acculturation Scale measured Chinese-oriented versus American-oriented behaviors; and the Measurement of Horizontal & Vertical Individualism & Collectivism scale assessed fidelity to individualistic (Western) and collectivistic (Eastern) values. Accordingly, there were four dimensions of acculturation (acculturation to American-oriented behaviors, enculturation to Chinese-oriented behaviors, individualistic values orientation, and collectivistic values orientation) to consider in understanding perceived conflict within parent-child dyads among Chinese American families. Risk for alcohol use was measured by a composite of items such as attitudes toward alcohol, age of initiation, alcohol use in the past month, and intentions to use in the next year.
RESULTS: Logistic regression analyses found that greater child perceived levels of acculturation-based conflict increased the likelihood for alcohol use among adolescents (OR: 2.09; 95% C.I.: 1.16, 3.75; $p < 0.05$), while controlling for demographic variables. We used APIM models to assess each of the four dimensions of acculturation on acculturation-based conflict. Findings indicate that child's acculturation toward American-oriented behaviors was positively associated with his/her own perceived level of conflict ($\beta=0.28$, $p<0.05$), while his/her enculturation toward Chinese-oriented behaviors was related to lesser perceived levels of conflict ($\beta=-0.36$, $p<0.05$). Secondly, parents and children exerted significant effects on their corresponding family members' perceptions. Adolescents perceived higher levels of acculturated-based conflict the more their parents were Chinese-oriented in their behaviors (0.42, $p<0.05$), and lesser degrees of conflict the more their parents were acculturated to American society ($\beta=-0.62$, $p<0.001$). Thirdly, results suggest that the more similar parents and children are regarding their acculturation levels, the lesser the degree of conflict was perceived by either family member. These relationships applied not only to parent-child similarities in their adoption of Western culture from the larger American society, but also to their adherence to or preservation of Chinese culture.
CONCLUSIONS: Acculturation-based conflict appears to increase risk for underage drinking. Secondly, APIM should be utilized for its strength in measuring interdependence in relationships, and applied to continue to explore how acculturation and its related challenges play out in interpersonal parent-child dynamics among immigrant families. Results highlight the need to further explore acculturation-based conflict on adolescent alcohol use and the mechanisms by which it develops for culturally sensitive prevention strategies for this population.

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Broad Abstract Category: Epidemiology
Keywords: Alcohol trends, total consumption, Ghana, emerging economies

AN INCREASE IN THE TOTAL CONSUMPTION OF ALCOHOL OVER A FIVE-YEAR PERIOD IN GHANA

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BACKGROUND: Observing changes in the total consumption of alcohol in emerging economies is important for understanding the impact of economic growth on alcohol use and for informing public health priorities. This study aimed to measure changes in the total consumption of alcohol in Ghana over a five-year period and to identify factors associated with levels of total consumption.
METHODS: This is a secondary analysis of publicly available, nationally representative cohort data from the World Health Survey conducted in 2004 and the Survey on Global Ageing and Adult Health conducted in 2009 in Ghana. We measured total consumption based on self-reports on the number of standard drinks consumed each day over the 7 days prior to interview, and constructed categorical variables for current drinkers (any drink in last 7 days), high consumers (15+ drinks per week) and risky single occasion drinkers (5+ on one day). We used multivariate regression models to identify factors independently associated with total consumption.
RESULTS: A total of 549 people were in the sample, where 49% were women and age ranged from 18 to 95 years. The proportion of current drinkers remained stable between 2004 and 2009, at 26% and 27%, respectively. Risky single occasion drinkers were uncommon at both time points, comprising less than 2% of the total sample. Among current drinkers, the proportion of high consumers increased from 9% to 22%, and the mean total consumption increased from 8 drinks per week to 12 drinks ($p=0.03$). Total consumption in 2009 was associated with being male ($p=0.000$) and a smoker ($p=0.001$) in 2004. These preliminary results will be expanded on with analysis investigating the potential mediating effect of socioeconomic status on drinking trends, and differences by gender.
CONCLUSIONS: The increase in the total weekly consumption of alcohol and the proportion of high consumers among current drinkers suggests alcohol use should be a public health priority, and may be related to the economic growth currently underway in Ghana. Being a male smoker may represent a group at particular risk for increased alcohol use in Ghana, and should be further investigated as a potential target for interventions. Broad alcohol regulations targeting the entire population may be useful in curbing an increase in total consumption, and continued monitoring of developing alcohol trends should be pursued.

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Broad Abstract Category: Animal Behavior, Genetics
Keywords: ethanol self-administration, nicotine, conditioned place preference, receptor function

THE NACHR A5 SUBUNIT POLYMORPHISM CHRNA5 D398N CHANGES BOTH CONDITIONED PLACE PREFERENCE DEVEOPMENT AND RECEPTOR FUNCTION BUT NOT ETHANOL CONSUMPTION

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BACKGROUND: In recent years a strong association between genetic polymorphisms and nicotine dependence has emerged, specifically in the nicotinic receptor gene cluster α5-α3-β4. The single nucleotide polymorphism (SNP) rs16969968 in the α5 nicotinic acetylcholine receptor (nAChR) subunit gene (CHRNA5 D398N - 'risk allele') is associated with several smoking-related behaviors.
METHODS: Knock-in mice (C57BL/6 background) possessing the equivalent of the D398N SNP were used to investigate the effects of this genetic variant. Nicotine-induced conditioned place preference (CPP) (nicotine dose 0.3mg/kg s.c.) was tested with mice of all three genotypes (D397 - wild-type; Het - heterozygous; N397 - homozygous). The unbiased CPP paradigm, paired saline and nicotine injections with distinct visual and tactile cues. During the drug-free posttest the mice had access to both sides of the chamber and time spent on each side was recorded. To investigate the functional effect of this mutation on nAChRs, nicotine-stimulated dopamine (DA) release was measured from crude synaptosomal preparation of striatal tissue of all 3 genotypes and [^{3}H]-DA release was measured. The drinking in the dark (DID) paradigm was used to test ethanol consumption across genotypes. Ethanol consumption during the four hour period on the fourth day was analyzed.
RESULTS: Analysis of the CPP data revealed a significant increase in time spent on the nicotine-paired side of the chamber in the N397 (risk variant) mice compared to the wild-type D397 group. We have previously shown that the N397 animals will voluntarily consume more nicotine than the D397 mice and this confirms that the knock-in mice find nicotine more reinforcing than do the wild-type mice. Measurement of [^{3}H]-DA release from striatum showed no significant differences in EC_{50} however, there was a significant difference in maximal DA release between groups, with the wild-type D397 mice exhibiting a 20% higher maximal response than the N397 animals. This result confirms previously published *in vitro* data showing reduced function of the risk variant with no effect of the polymorphism on the EC_{50}value. No significant differences were seen in ethanol consumption on the final day between genotypes.
CONCLUSIONS: Taken together, these data show that there are both behavioral and functional changes in the knock-in mice and these changes may account for some of the smoking-related behaviors seen in people with this SNP.

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Broad Abstract Category: Quantitative / Computer Methods
Keywords: Alcohol Epidemiology, Alcohol-Related Traffic Accidents, Motor-Vehicle Fatalities, Neighborhood Walkbility, Geo-Spatial Characteristics

MORE WALKABLE REGIONS HAVE ADVERSE ALCOHOL RELATED MOTOR VEHICLE FATALITY OUTCOME?

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BACKGROUND: As a demonstration of the importance of aspects of the physical and built environment on alcohol use outcomes, the current study will examine associations between neighborhood walkability and alcohol related motor vehicle (DUI) fatalities/crashes throughout Missouri.
METHODS: Walkscores, www.walkscore.com, give a walkability score (1-100) by considering a region's: distance to restaurants, coffee shops, grocery stores, and availability of public transits, with higher scores representing greater walkable access. DUI fatality numbers were obtained from National Highway Traffic Safety Administration (NHTSA). GPS coordinates of the alcohol outlets are derived from the addresses obtained from the Alcohol and Tobacco Control database. The association between the walkscore, alcohol outlets, demographics and per capita DUI fatalities for each region was assessed using Pearson Correlation Coefficients. Two levels of analysis were examined: state level and city level data with granularity of zipcodes.
RESULTS: Preliminary results suggest a positive correlation between walkscores and per capita DUI fatalities at both levels. State level analysis demonstrated this positive correlation with contribution from demographic factors and outlet densities ($R = 0.013$, $P = 0.000$). The Kansas City analysis points to walkscore as the only factor in determining the per capita DUI fatalities ($R = 0.235$, $P = 0.039$). The St. Louis analysis showed walkscore and some of the demographic and outlet densities correlate to per capita DUI fatalities ($R = 0.744$, $P=0.035$).
CONCLUSIONS: The analysis shows Kansas City, St. Louis and Missouri all have different sets of determining factors for the per capita DUI fatalities. The granularity of zipcodes does not provide a homogeneous population demographic nor outlet density distribution, thus hampering the analysis. The census block or block group level may provide more uniform/comparable regions for analysis. While this research demonstrates both the importance of aspects of the built environment on alcohol related risks and the feasibility of collecting and analyzing such data, future aims of this program of research will be to integrate objective measures of the environment, assessed using GIS technologies, and individual measures of risk (including genetic and self-reported information) to examine the interplay between genetic and environmental risks in the etiology of alcohol related harm

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Broad Abstract Category: Consequences of of Alcohol Consumption in Humans
Keywords: college students, sexual behavior, hooking up, women, casual sex

PREVALENCE AND PREDICTORS OF HOOKING UP AMONG FRESHMEN COLLEGE WOMEN

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BACKGROUND: The first year of college is a distinct transition period. Alcohol use is commonly a part of this process and may put students at risk for sexual risk behaviors, including uncommitted sexual encounters such as hook ups. The purpose of this study was to examine the prevalence and predictors of hook ups (defined as romantic or sexual encounters between two people who are strangers or acquaintances) among women during the transition to college.
METHODS: Female college freshmen (n=430) were recruited at the time of high school graduation and randomized to the control arm of a parent-based intervention to reduce alcohol-involved sexual risk behaviors. Baseline data were collected during the summer before college enrollment with two follow-up assessments during the fall and spring semesters of the first year of college.
RESULTS: Combining fall and spring semester reports, over the course of the first year of college, 44.7% of study participants reported at least one hookup encounter, with 60.4% of these engaging in penetrative hookups. Using multivariate logistic regression, heavy episodic drinking, more permissive attitudes towards sex, and living on campus were positively associated with hookup behavior in the first year of college. Multinomial logistic regression models found that peer injunctive sex norms and heavy episodic drinking were significant predictors of penetrative hookups relative to non-penetrative hookups. Additionally, women who reported penetrative hookups had more permissive attitudes towards sex, stronger peer injunctive sex norms, greater heavy episodic drinking, and were less likely to live at home compared to those who did not hookup.
CONCLUSIONS: Consistent with previous studies, we found that alcohol use was associated with any sexual hookup, and penetrative hookups in particular, during the first year of college. The current study contributes to the literature on sexual behaviors demonstrating that hookups are a prevalent type of sexual intimacy specifically among female college freshmen. Results suggest support for interventions to address alcohol use as a correlate of sexual hookup encounters as female students transition to college as well as normative interventions to address peer approval for uncommitted sexual activity.

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ETHANOL INHIBITION OF GLUTAMATE SYNAPTIC TRANSMISSION IN RAT BASOLATERAL AMYGDALA INVOLVES ENDOCANNABINOIDS

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BACKGROUND: Withdrawal-related anxiety during abstinence is both a hallmark of alcohol use disorders/physical dependence and one of the primary reasons cited for relapse. The endogenous cannabinoid system (eCB) is richly expressed in brain regions critical to the expression of anxiety, including the basolateral amygdala (BLA), and may play a significant role in the acute and chronic effects of ethanol in these regions. We have utilized field recordings of excitatory postsynaptic potentials (fEPSPs) and whole cell-patch clamp recordings of excitatory postsynaptic currents (EPSCs) to evaluate both the role of the eCB system in the effects of acute ethanol exposure within the BLA and the impact of chronic ethanol exposure on this role.
METHODS: *Ex vivo* recordings were performed in Sprague Dawley rats divided into either a control (CON) or a chronic intermittent ethanol vapor exposed (CIE) group. CIE animals underwent 10 cycles of 12h on/12 hr off ethanol vapor procedure and were sacrificed immediately following the final cycle (average BEC=200 mg/dl). CON animals were age matched to CIE animals and exposed solely to room air. All experiments were performed in the presence of the GABAA antagonist picrotoxin and select experiments in the presence of GABAB antagonist SCH 50911. fEPSPs and EPSCs were electrically evoked by stimulating the stria terminalis.
RESULTS: Following baseline in field recording, 80mM ethanol was bath applied either in the presence or absence of 5 μM SR141716 (RIM), a CB1 antagonist. In the CON group, pre-treatment with RIM significantly attenuated the inhibitory effect of 80mM ethanol on glutamatergic transmission within the BLA. This effect was occluded in the CIE group, with RIM application having no significant impact on ethanol inhibition of glutamatergic transmission. In whole cell patch-clamp recordings, changes to the paired-pulse ratio (PPR) following application of the CB receptor agonist WIN 55, 212-2 were compared to baseline PPR in both CON and CIE animals. CB1 agonism resulted in a significant decrease in presynaptic glutamate release in CON, with this effect attenuated in CIE animals.
CONCLUSIONS: Our data implicate a direct involvement of the eCB system in modulating the effects of acute ethanol on excitatory synaptic transmission within the BLA and may play a key role in the development of increased anxiety following chronic ethanol exposure and withdrawal.

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