1

HOOKAH USE AMONG MUSLIM U.S. COLLEGE STUDENTS.

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Aims: Hookah, a nicotine delivery system, is increasingly popular among college students. As tobacco use is frequently associated with alcohol use in the U.S., we examined prevalence and correlates of Hookah smoking in a sample of Muslim U.S. college students.
Methods: Respondent-driven sampling was used to recruit self-identified Muslim undergraduate students (n=156) at one urban university to complete a web-based survey.
Results: Almost half (44.3% sample adjusted; 95% CI 32.6 – 61.4%) of the sample reported Hookah use compared to 28.3% for cigarette use and 9.1% for alcohol use. Nonetheless, Hookah use was strongly associated with alcohol use (Odds Ratio=7.2, 95% CI 1.5-33.6). In unadjusted bivariate analysis, 5 variables (ever drank alcohol, proportion of friends who smoke Hookah, lower adherence to beliefs and practices of Islam, male gender, and living at home) were associated with Hookah use. In multivariate analysis, 2 variables (ever drank alcohol and proportion of friends who smoke Hookah) remained significant. Students who smoked Hookah scored higher on social motivations as reason to smoke than on conformity, cultural identity and perception that it is safer than cigarettes. The homophily for Hookah nonusers was low (.26), especially compared to that for alcohol nonusers (.43).
Conclusions: Hookah use was common and associated with alcohol use among this sample of proscriptive religiously affiliated college students. The low homophily among Hookah nonusers suggests lack of social stigma against Muslim students who smoke Hookah. Efforts to limit Hookah use, and thus exposure to tobacco smoke, need to address social influences and motivations.
Financial Support: Institute for Social Policy and Understanding

2

ALCOHOL INVOLVEMENT AND STI RISK DURING LATE ADOLESCENCE: MALE-FEMALE DIFFERENCES.

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Aims: To investigate sex differences in the associations among level of alcohol involvement, risky sexual behavior (RSB) and biologically-confirmed STIs during late adolescence in an urban, African-American sample.
Methods: Participants (n=308) were enrolled at birth in the longitudinal Miami Prenatal Cocaine Study. As a part of an ongoing 18/19-year follow-up (projected n=380), adolescents self-reported on alcohol consumption and RSB via computer-assisted self-interviewing software. HIV, Chlamydia, gonorrhea and syphilis screening was conducted by the University of Miami Adolescent Counseling and Testing Service.
Results: Lifetime alcohol involvement was defined as: no alcohol use (42%), non-problematic use (37%), and problematic use (binge drinking, or ≥ 1 symptom of abuse/dependence; 21%). There were no sex differences in level of alcohol involvement or having STIs (22% overall), but boys were more likely than girls to engage in past-year RSB. Problematic alcohol use was associated with having an STI in girls (OR= 3.3; p=0.04) but not in boys (OR= 0.9; p=0.86), controlling for age, prenatal alcohol and cocaine exposure, and illegal drug use. Problematic drinking was also related to past-year sex with a high risk partner, multiple partners, and an older partner (all $p<0.05$) only among girls. Non-problematic alcohol use was not related to RSB or STI outcomes.
Conclusions: This preliminary report highlights the importance of STI screening and RSB prevention among adolescent girls reporting problematic drinking. Possible psychosocial mechanisms accounting for the association between alcohol involvement and STI occurrence will be further explored.
Financial Support: ORWH/NIDA P50 DA 024584; NIDA R01 DA 006556, K01 DA 016720; and UM D-CFAR

3

DIFFERENTIAL PERFORMANCE ACROSS MULTIPLE MEASURES OF IMPULSIVITY AMONG CHILDREN WITH FAMILY HISTORIES OF SUBSTANCE USE DISORDERS.

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Aims: Previous research has shown that individuals with family histories of substance use disorders are more impulsive on some but not all laboratory behavioral measures, suggesting more pronounced deficits on specific forms of impulse control. However, these studies typically examined late adolescent or adult participants and excluded those with substance use disorders. This selection criteria may be biasing results by excluding the most impulsive individuals in from the study samples. The purpose of this study was to examine these measures in young children prior to the expected onset of regular substance use.
Methods: In the present study, we examined impulsive performance in a sample of healthy 10-12 year old children with (FH+; n=166) or without (FH-; n=42) family histories of substance use disorders. These children's performance was compared prior to regular alcohol or other drug use on behavioral measures of response initiation (Immediate Memory Task; IMT), response inhibition (GoStop Impulsivity Paradigm; GoStop), and consequence sensitivity (Two Choice Impulsivity Paradigm; TCIP; and Single Key Impulsivity Paradigm, SKIP) consequence sensitivity) impulsivity.
Results: FH+ children performed more impulsively than FH- children on the IMT and GoStop but not on the TCIP or SKIP. There were no differences in self-reported impulsivity (BIS-11) between the two groups
Conclusions: These results suggest that response initiation and response inhibition impulsivity are increased in children with family histories substance use disorders prior to any regular alcohol or other drug use, consistent with findings in FH studies examining older participants. As part of our ongoing longitudinal project, we examine how these and other processes both predict and are influenced by onset of substance use in this population.
Financial Support: Research supported by grants from the National Institute of Health (R01-DA026868 & KL2-RR025766).

4

COGNITIVE FUNCTIONING OF METHADONE MAINTENANCE CLIENTS ENGAGED IN A WEB-BASED PSYCHOSOCIAL INTERVENTION.

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Aims: 1. To characterize multiple dimensions of cognitive functioning in methadone maintenance clients enrolled in a study designed to evaluate a web-based psychosocial intervention; and 2. To determine the extent to which an interactive web-based intervention, which allows clients to control the pace of skills training and aims to train clients to become fluent in key skills and information despite their baseline knowledge/skills levels, can impact treatment outcomes among clients with varying levels of cognitive functioning
Methods: Clients entering methadone maintenance treatment were randomized to receive methadone plus either standard counseling (n=80) or treatment in which a web-based intervention replaced part of standard counseling (n=80). Participants were administered assessments at baseline and monthly for 12 months and provided weekly urine samples. Microcog, a comprehensive neurocognitive assessment, was completed at baseline. Analyses were conducted to characterize the sample on all Microcog domains.
Results: General Cognitive Functioning (M=78.5, SD=16.6) and General Cognitive Proficiency (M=77.7, SD=13.9) fell in the Low Average range. Information Processing Speed (M=85.0, SD=19.5), Spatial Processing (M=96.6, SD=14.7) and Reaction Time (MM=95.5, SD=17.3) fell in the Average range, while Information Processing Accuracy (M=80.8, SD=16.2), Attention (M=83.5, SD=17.8), Reasoning (M=81.7, SD=17.5) and Memory (M=82.8, SD=17.5) fell in the Low Average range. Demographic trends were similar to those in the general population. The relationship between the various dimensions of cognitive functioning and treatment outcome (retention and abstinence) will be examined by treatment condition.
Conclusions: Although scores were quite diverse, the sample of methadone maintenance clients generally demonstrated Average to Low Average neurocognitive functioning. An interactive, web-based intervention which can be used by clients with varying levels of cognitive functioning may be a promising component of treatment for this population.
Financial Support: R01DA021818, P30DA029926

5

DIFFERENCES IN REGIONAL CEREBRAL BLOOD FLOW RESPONSE TO A 5HT3 ANTAGONIST IN EARLY- AND LATE-ONSET COCAINE DEPENDENCE.

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Aims: 5-hydroxytryptamine 3 (5HT3) receptors are important modulators of mesostriatal dopaminergic transmission and have been implicated in the pathophysiology of cocaine reward and self-administration. In addition, the 5HT3 antagonist ondansetron is effective in treating early-onset, but not late-onset, alcohol-dependent subjects.
Methods: To explore the role of 5HT3 receptor systems in cocaine addiction using functioning imaging, we administered ondansetron to 23 abstinent, cocaine-addicted and 22 sex-, age-, and race-similar healthy control participants. Differences between early- (first use before 20 years, n=10) and late-onset (first use after 20 years, n=10) cocaine-addicted subjects were also assessed. On two separate days, subjects were administered ondansetron (0.15 mg/kg iv over 15 min) or saline. RCBF was measured following each infusion with SPECT.
Results: No significant rCBF differences between the cocaine-addicted and control participants were observed following ondansetron relative to saline. Early-onset subjects, however, showed increased ($p < 0.001$) right posterior parahippocampal rCBF following ondansetron. In contrast, late-onset subjects showed decreased rCBF following ondansetron in an overlapping region of the right parahippocampal/hippocampal gyrus. Early-onset subjects also displayed increased rCBF in the left anterior insula and subthalamic nucleus following ondansetron; late-onset subjects showed decreased rCBF in the right anterior insula.
Conclusions: These findings suggest that age of drug use onset is associated with serotonergic biosignatures in cocaine-addicted subjects. Further clarification of these alterations may guide targeted treatment similar to those successfully used in alcohol-dependent patients.
Financial Support: Funded by NIH DA11434 and supported by the VA North Texas Health Care System. Ceretec (HMPAO) was generously supplied by GE Healthcare.

6

EFFECTS OF SYNTHETIC CANNABINOIDS ON THE BLOOD BRAIN BARRIER.

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Aims: In recent years, many adolescents have started to use a popular legal alternative to marijuana called K2/spice, made primarily of a blend of synthetic cannabinoids. Many of the effects of these compounds are due to their actions on the central nervous system (CNS), hence causing the adverse effects and drug dependence among their users. The compound most commonly found in K2/spice is the potent CB1 agonist JWH-018; therefore, most of the research efforts have focused on CB1 agonists and the role of other JWH compounds with potent affinity for CB2 has not been elucidated yet. JWH-015 and AM-630 are cannabinoid (CB2) agonist and antagonist, respectively. Little is known about their effects on the Blood Brain Barrier (BBB) disruption. We hypothesize that synthetic cannabinoids will exert their effects on CNS cells such as human astrocytes (HA) and human brain microvascular endothelial cells (HBMECs), disrupting the BBB and facilitating an increased in transendothelial migration of monocytes.
Methods: The effects of JWH-015 and AM-630 were tested on an in vitro BBB model that was constructed with HA and HBMECs as described earlier. The integrity and function of the in vitro BBB was assessed by measuring transendothelial electrical resistance (TEER), FITC-dextran transport, and monocyte transmigration.
Results: Our results showed the synthetic cannabinoid JWH-015 caused a dose (1-5uM) and time dependent (2-24 hrs) decrease in TEER values of the BBB. However, the antagonist, AM-630, reversed the JWH-015-induced effects on BBB integrity.
Conclusions: In our study, we have observed that the CB2 agonist, JWH-015 induced a downregulation of BBB integrity in vitro; while the antagonist, AM-630, had a protective effect on the BBB integrity. These findings may further clarify the effects of synthetic cannabinoids and the role of CB2 on the CNS, specifically their degenerative or protective action on the BBB.
Financial Support: This work was supported in part by the National Institute on Drug Abuse grants R01MH085259, R01DA021537, R37DA025576.

7

MODAFINIL, COGNITION AND TREATMENT OUTCOME IN COCAINE-DEPENDENT OUTPATIENTS: PILOT RESULTS.

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Aims: Chronic cocaine abuse is associated with sub-clinical to severe cognitive deficits. Such deficits may impede patients' ability to benefit from interventions that require integrating information in order to change behavior. Medication that improves cognitive functioning could therefore positively impact treatment outcome. Studies suggest that Modafinil is a promising agent to reduce cognitive deficits in clinical populations. We conducted a small pilot study to test whether Modafinil would improve cognitive functions in cocaine dependent outpatients.
Methods: A double-blind, placebo-controlled 12-week trial with 15 cocaine dependent outpatients. Mean age was 41.3 (s.d., 5.9), 93.3% were male, 60% African-American. Participants had used cocaine regularly, average 14.4 years (s.d., 8.7). At baseline, mean days of cocaine use in the past 30 days was 19.9 (s.d., 8.1). Participants were free of significant medical and psychiatric conditions, including alcohol dependence. Eligible patients were randomized to Modafinil (n=8) or matching placebo tablets (n=7) . All patients received CBT.
Results: Cognitive functioning: patients treated with Modafinil did better. Compared to those on placebo, scores improved for those in the Modafinil group on the CVLT-II (verbal memory) ($p=0.02$) and on the Stroop interference task ($p=0.009$). Retention in the Modafinil group was slightly but not significantly higher in mean number of therapy sessions (10.57; s.d., 5.7) compared to patients treated with placebo (8.25; s.d., 4.3). Abstinence: mean weeks of cocaine abstinence trended towards significance in the modafinil group (mean weeks=4.7 s.d.4.3) compared to placebo (mean weeks=1.4 s.d.1.9; $p=.053$).
Conclusions: Our pilot results suggest strong promise for Modafinil as a cognitive enhancer in cocaine patients, and also suggest efficacy of Modafinil for the outcome of cocaine retention and abstinence.
Financial Support: NIDA K23DA16743, K05 AA014223, K24DA022412

8

ALCOHOL USE, RELIGIOSITY AND SOCIAL INFLUENCES AMONG U.S. MUSLIM COLLEGE STUDENTS.

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Aims: Alcohol use and related problems occur across religious groups, including those that are proscriptive. Past investigations have presumed that personal religious beliefs reflect formal religious doctrine or did not examine social influences. To test this assumption and assess the importance of social influences, we examined alcohol use among Muslim U.S. college students.
Methods: Respondent-driven sampling was used to recruit self-identified Muslim undergraduate students (n=156) at one urban university to complete a web-based survey.
Results: Alcohol use was uncommon (sample adjusted prevalence of 9.1 %; 95% CI 0.2 – 17.1%) but homophilies (measure of social network exclusiveness) were large (.36 for drinkers and .43 for abstainers). In unadjusted analyses, students who drank were more likely than life-long abstainers to report non-proscriptive personal belief (OR=8.4); did not strongly agree with intrinsic religiosity item of beliefs influence their decisions (OR=5.6); perceived most students (OR=5.8), most Muslim students (OR=9.8), and most friends (OR=23.6) used alcohol; attended high school with almost no Muslims (OR=3.4); and currently live in neighborhoods with almost no Muslims (OR=7.6). However, there was no difference in alcohol use by demographic characteristics, their estimates of the proportion of all students who were Muslim or their responses on extrinsic religiosity measures (i.e., importance of religious activities, attending services, and adherence to beliefs and practices of Islam).
Conclusions: These pilot findings suggest that alcohol use among Muslim students is associated with low intrinsic religiosity, personal nonproscriptive religious beliefs, and less proscriptive social influences. The high homophilies also suggest low overlap in social networks defined by alcohol use. As a pilot study, it showed respondent-driven sample was feasible in recruiting Muslim students, even with these high homophilies, to complete a web-based survey on alcohol use.
Financial Support: Institute for Social Policy and Understanding

9

LIFETIME PSYCHOPATHOLOGY AMONG IMPAIRED PHARMACISTS IN AN IMPAIRED HEALTH PROFESSIONALS PROGRAM: COMPARISON TO THE GENERAL POPULATION.

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Aims: The prevalence of substance abuse and other psychiatric disorders among pharmacists is not well-established. We determined differences in lifetime use, substance abuse or other psychiatric disorders comparing pharmacists undergoing monitoring with the general population.
Methods: Participants were 39 pharmacists recruited from an "Impaired Health Professionals" Program in Florida, and administered the Computerized Diagnostic Interview Schedule Version IV (C-DIS-IV) to determine the presence of psychiatric disorders. Pharmacists undergoing monitoring were compared to age, gender, and race/ethnicity matched cohorts from National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Wave 1, in a 10:1 ratio.
Results: Pharmacists undergoing monitoring had significantly higher odds of lifetime use of amphetamines (OR 10.62, 95% CI (4.96, 22.72)), cannabis (OR 2.79, 95% CI (1.42, 5.47)), cocaine (OR 5.54, 95% CI (2.54, 12.07)), opiates (OR 26.14, 95% CI (12.01, 56.91)), and sedatives (OR 19.52, 95% CI (9.01, 42.33)) than the general population. Pharmacists undergoing monitoring had higher odds of lifetime alcohol (OR 15.39, 95% CI (7.12, 33.24)), cannabis (OR 11.90, 95% CI (2.56, 55.35)), cocaine (OR 20.71, 95% CI (2.08, 206.65)), and opiate (OR 26.71, 95% CI (4.91, 145.38)) abuse/dependence than their matched controls, among those who had ever used. Pharmacists undergoing monitoring had higher odds of antisocial personality disorder (OR 12.38, 95% CI (5.01, 30.55)).
Conclusions: Pharmacists undergoing monitoring who had ever used alcohol, cocaine, cannabis, or opiates had significantly higher odds of abuse/dependence disorders than the general population. More research is needed to understand psychiatric morbidity in pharmacists –especially those designated as impaired or needing monitoring - due to their higher risk for exposure to medications and subsequent abuse.
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10

ABORIGINAL MENTAL HEALTH AND PATTERNS OF SUBSTANCE USE IN BRITISH COLUMBIA.

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Aims: Substance use among Aboriginals is a major concern in Canada, the USA, and other parts of the world. Currently limited data is available, specifically in marginal populations such as the homeless. The British Columbia Health of the Homeless Study has 38.9% of participants self-identified as Aboriginal (compared to 5% of the general population), allowing to study differences in substance abuse and related profiles.
Methods: Five hundred subjects were recruited from 3 urban regions in BC, Canada. Fifty percent were recruited from homeless shelters and 50% from the street. Standard assessments included the Mini-International Neuropsychiatric Interview and the Maudsley Addiction Profile.
Results: Aboriginals were much more likely to have no high school diploma (74.9% versus 56.2% among non-Aboriginals), suffer from any mental disorder (67.9% versus 59%), have a substance use disorder (88.9% versus 80.9%), and had higher rates of attempts at suicide (44.4% versus 32.8%). Interestingly, They were more likely to report current use of alcohol (70.9% versus 50.7%) but less likely to have used crystal meth (7% versus 16%), injected heroin (16.6% versus 30.3%) or injected drugs (21.6% versus 33.7%).
Conclusions: This study replicates findings indicating higher levels of substance use disorder and mental disorders in Aboriginal population as well as clear over-representation in the homeless population. Aboriginal and non-Aboriginal populations show differences in their use patterns. To better understand these patterns and allow for informed prevention and interventions, we will further analyze the data and use statistical modeling (e.g. logistic regression) to identify potential mediators and moderators: (sex, age, region, childhood trauma and neglect, and mental disorders).
Financial Support: BCMHA (PHSA)

11

PRESCRIPTION OPIOID USE IN LOS ANGELES COUNTY, CA.

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Aims: The purpose of this study was to evaluate synthetic opioid users in Los Angeles County, CA, who were receiving HIV prevention services.
Methods: This study of synthetic opioid users including those who reported using street methadone, Codeine, Vicodin, Morphine, Dilaudid, Demerol and Percodan recruited 2,122 participants throughout Los Angeles County, California as part of a Countywide Risk Assessment Survey in 2004.
Results: Of the participants, 13.4% (285/2122) reported using synthetic opioids within six months of receiving services. The participants ranged from 12 to 69 years old (M = 27.1, SD = 7.5) and those who reported recent opioid use ranged from 15 to 64 years old (M = 35.3, SD= 10.6). Synthetic opioid use was associated with polysubstance use, and synthetic opioid users were significantly older, had more sexual partners, and were more likely to trade sex for money or drugs, than non-opioid users. Logistic regression indicated that older age, past six-month use of heroin, cocaine, heroin and cocaine combined (speedball), marijuana, amphetamines, and ecstasy, as well as trading sex for drugs or money are associated with opioid use.
Conclusions: The associations observed between synthetic opioid use and polysubstance use, as well as sex trading, put this population at risk for contracting sexually transmitted diseases or developing drug dependence. These findings provide insight for developing strategies to identify and reduce risks in this population when encountered in public health or drug abuse treatment centers.
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12

DETERMINANTS OF COMMITMENT TO CHANGE IN HIV PRIMARY CARE PATIENTS RECEIVING A DRINKING-REDUCTION BRIEF MOTIVATIONAL INTERVIEW.

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Aims: Strengthening patient commitment to change is a central goal of motivational interviewing (MI). The strength of patients' language indicating commitment to change (e.g., substance use) in manualized treatment sessions has repeatedly been shown to predict treatment outcome. However, little is known about factors underlying the strength of patients' commitment language. Heavy drinking in HIV-infected patients predicts mortality and risk behaviors. In this study, urban HIV primary care patients who drank ≥4 drinks at least once in the prior 30 days (with or without alcohol dependence) participated in a session of MI aimed at drinking reduction. Linguistic and demographic factors potentially influencing commitment strength were investigated.
Methods: MI sessions of 95 patients were recorded. Patients' utterances related to change across session deciles were coded by trained raters with an objective scoring system. Variables included strength of commitment, desire, ability, need, readiness and reasons to reduce or maintain drinking. Two coders (inter-rater reliability=.73) rated 75 English and 20 Spanish sessions.
Results: Using repeated measures regression (SUDAAN), language factors predicting overall commitment strength included desire to change (β=.17, $p<.001$), ability (β=.21, $p<.001$), readiness (β=.04, $p<.05$) and reasons (β=.16, $p<.001$). Alcohol dependence (β=30, $p<.02$), older age (β=.03, $p<.001$)and lower drinking goal (β= -.10, $p<.01$)also predicted commitment strength. Years since HIV diagnosis, race, gender, depression, drug use, and housing status were unrelated to commitment strength. Significant predictors accounted for 36.2% of variance in commitment strength, *Wald* $F(7,94)=59.20$; $p<.001$.
Conclusions: Results extend earlier studies by indicating important determinants of patient commitment language that predicts improved treatment outcome in many studies. A predictive role for readiness to change, a primary construct in MI, is a new finding that may reflect an important distinctive characteristic for this treatment population.
Financial Support: R01AA014323, K05AA014223

13

DISRUPTION IN THE SEROTONIN 2C RECEPTOR (5-HT2CR) AND N-METHYL-D-ASPARTATE RECEPTOR (NMDAR) PROTEIN COMPLEX IN THE PREFRONTAL CORTEX REPRESENTS A NEUROMOLECULAR DRIVER OF IMPULSIVITY.

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Aims: Impulsivity is a complex, multifaceted personality trait broadly defined as action without sufficient foresight and individual sensitivity seems to determine the likelihood that drug use will escalate into dependence and relapse. Extensive lines of evidence implicate 5-HT and glutamate neurotransmission within the corticolimbic circuit as critical drivers of the cognitive and/or behavioral dimensions underlying impulsivity. Here, we focused on how 5-HT2CR:NMDAR interactions within the mPFC drive inherent impulsivity.
Methods: The proposed studies employed the one-choice serial reaction time task to identify high (HI) and low (LI) impulsive individual outbred rats to elucidate the neuromolecular biology of impulsivity. Rats were sequentially trained to nosepoke to receive food pellet rewards; premature responses resulted in further delays of reward presentation. The upper and lower 25% of animals were identified as HI or LI rats, respectively. Rats were sacrificed and mPFC synaptosomal protein extracted. We employed immunoprecipitation (IP) and immunoblot (IB) techniques to detect the synaptosomal association of 5-HT2CR with the NMDAR complex in the mPFC of HI vs. LI rats.
Results: The HI/LI phenotype is stable in that premature responses in HI rats remained significantly higher than those of LI rats across 70 days of training ($p<0.001$). We discovered that IP using the 5-HT2CR antibody followed by IB with the NMDA NR1 antibody yields a band at the expected MW (120 kDa) for the NR1 subunit, indicating the presence of a 5-HT2CR:NMDAR complex in the mPFC. The 5-HT2CR:NMDAR complex was decreased in HI vs. LI rats ($p<0.05$).
Conclusions: Disruption in the 5-HT2CR:NMDAR protein complex may drive high levels of impulsivity. The elucidation of the complex regulation of the 5-HT:glutamate balance within the mPFC as it relates to inherent impulsivity will lead to a better understanding of individual risk factors for psychostimulant addiction.
Financial Support: DA06511, DA024157, DA000403

14

POLYDRUG ABUSERS WHO FAIL TO DIFFERENTIATE OPIOID FROM PLACEBO IN LABORATORY CHALLENGE TESTING.

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Aims: Abuse liability assessments influence drug development, federal regulation, and clinical care. One suggested procedure to reduce variability in these studies is the use of a qualification phase. A qualification phase assesses whether study applicants adequately distinguish active drug from placebo; applicants failing to make this distinction are disqualified. The present analyses assessed the differences between qualifiers and non-qualifiers in an abuse liability trial.
Methods: Data were collected from 23 completers of the qualification phase of an abuse liability study. Participants were given 30 mg oxycodone and placebo on separate days and characterized as qualifiers (vs. non-qualifiers) if their peak visual analog scale liking score for active oxycodone was at least 20 points higher than placebo's peak rating. The two groups were compared on demographic, drug history, physiologic, subjective and observer-rated assessment time course data.
Results: 61% were qualifiers, 39% non-qualifiers. No significant differences were found between groups for demographics, drug use history, or pupillary constriction data. However, unlike qualifiers, non-qualifiers had an exaggerated placebo response (peak liking score 26 points higher than qualifiers; $p=0.03$) and an attenuated response to the oxycodone condition ($p< .0001$). Non-qualifiers' failure to differentiate oxycodone versus placebo was evident for both subjective reports and observer ratings.
Conclusions: The high prevalence and discrepant assessment responses of non-qualifiers suggest that a qualification phase may enhance an abuse liability study's sensitivity and validity. Further research may determine optimal qualification cut-off criteria and assessment variables, as well as the determinants and durability of some drug abusers' failure to differentiate active drug from placebo. Cost-benefit analyses would assist in determining the most cost-efficient qualification procedures.
Financial Support: NIDA grants T32-DA007209 and K24-DA023186.

15

ADDRESSING LOCAL SUBSTANCE ABUSE PROBLEMS: BINGE DRINKING AMONG MICHIGAN ARAB/CHALDEANS.

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Aims: Binge drinking, defined as 5 drinks in a setting for a man and 4 drinks for a woman, is a public health problem. Data from the 2007-09 Michigan Behavioral Risk Factor Surveys indicated that past month alcohol use rate among Arab/Chaldeans (45.6%) was significantly lower than among non-Hispanic Whites (59.4%) but that Arab/Chaldean past month binge drinking rate (17%) was almost identical to that of non-Hispanic Whites (18.7%). To develop culturally appropriate response for this local problem, more information was needed.
Methods: To obtain the Arab/Chaldean context of binge drinking, we conducted 12 focus groups in English and Arabic with a total of 82 young (18 – 29 year old) self-reported Arab/Chaldeans in 6 distinct Detroit metropolitan areas. The participants included Muslims (48%), Chaldeans (32%) and Orthodox Christians (21%). Participants were asked what they saw in their community to avoid disclosing potentially shameful activities.
Results: Most of the participants were already aware of the problem. Differences by groups within the larger Arab/Chaldean community included context for drinking and gender roles. Similarities across the groups included availability of alcohol, importance of parents, conformity to the behaviors of the group, and social aspect of drinking. Findings were mixed for saliency of stress, discrimination, and acculturation.
Conclusions: High rate of binge drinking among Arab/Chaldeans who drink is recognized by young Arab/Chaldeans as a problem and, importantly, as a problem across different religious and ethnic groups within the community. These findings were used to recommend local interventions.
Financial Support: Southeast Michigan Community Alliance

16

MANAGING ABERRANT DRUG BEHAVIOR IN PRIMARY CARE.

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Aims: To provide recommendations for primary care physicians on managing aberrant behavior in patients prescribed opioids.
Opioid prescribing has increased, accompanied by increases in overdose deaths and addiction. Current guidelines suggest that physicians ask about current and past substance use and apply risk screening tools before initiating opioid therapy. High risk patients should only be prescribed opioids if they have a well-defined pain condition that has been shown to be opioid-responsive. Managing comorbid pain and addiction is particularly challenging. If a trial of opioids is indicated, weak opioids should be used first. Factors making certain opioids more attractive for abuse, such as reputation among abusers, street value, and ease of tampering for inhalation or injection should be considered. High-risk patients should be prescribed small amounts of opioids and undergo frequent urine testing and pill or patch counts. High-dose administration (>200 mg/d morphine equivalent) should be avoided, if possible. Substance-abusing patients often display aberrant behaviors such running out early, snorting or injecting oral tablets or acquiring opioids from multiple doctors or the 'street'. If abuse is suspected, patients should undergo a time-limited structured trial (with a different opioid) that includes frequent dispensing of small amounts of opioid, use of sustained-release preparations, preparations formulated to resist tampering, and tapering to <200 mg/d morphine equivalent. If the structured trial fails, methadone or buprenorphine treatment is indicated, which involves daily supervised dispensing, gradual introduction of take-home doses, and frequent urine testing.
Conclusions: Prescribing opioids to high risk patients requires careful patient selection, dose titration and dispensing, close monitoring, and possibly referral for substance abuse treatment.
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17

HOW INTERACTIONS WITH A COMPUTER-BASED VIDEO INTERVENTION CAN AFFECT HIV TEST RATES.

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Aims: The current research examines how baseline HIV knowledge deficits and time spent with a computer based video intervention designed to increase HIV testing can impact HIV test rates.
Methods: 202 patients in a high volume urban hospital emergency department used inexpensive netbook computers to view videos designed to increase HIV test rates, and respond to pre- post-intervention questions. The videos were roughly 2.5 minutes long, patients could rewind, pause, and fast-forward. At the end of the intervention, the computer program asked patients if they would like an HIV test. Chi-square analyses were run to examine relationships between: time spent with the intervention, pre-intervention knowledge, participant race, and HIV test rates. A Generalized Linear Model was run to examine pre-intervention knowledge and test acceptance while controlling for self-reported pre-intervention likelihood of testing.
Results: Participants who incorrectly answered questions about HIV symptoms at pre-test (i.e. that people with HIV may look and feel healthy) were more likely to accept a test [$F(14, 201) = 4.48$, $p = .000$]. White participants were less likely to accept a test compared to African American, Latino or Other patients [$c2 (3, N = 202) = 10.39$, $p. = .02$], and were also the least likely to incorrectly answer symptoms questions at baseline [$c2 (6, N = 202) = 18.16$, $p = .01$]. Participants who accepted an HIV test at the end of the intervention took longer to respond to post-intervention questions, which included the offer of an HIV test, [$F(1, 195) = 37.72$, $p = .000$] than participants who did not accept a test.
Conclusions: These analyses suggest that a brief video addressing specific knowledge deficits can encourage participants to test. Results may also indicate that after watching a video, participants who accepted an HIV test spent more time deciding whether or not to learn their HIV status than those who chose not to test.
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18

DISCONTINUOUS ENROLLMENT DURING COLLEGE: ASSOCIATIONS WITH DRUG USE AND MENTAL HEALTH.

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Aims: Examine the prospective relationships of marijuana use and mental health with the risk of discontinuous enrollment during college.
Methods: Participants were 1145 college students interviewed annually at one large public university, beginning at college entry (Year 1). Discontinuous enrollment was defined as a gap in enrollment of one or more semesters and operationalized as "early" (during the first two years of college) and "late" (during the second two years of college) versus "none" (continuously enrolled throughout). Independent variables measured in Year 1 were Beck Depression Inventory (BDI) score; Beck Anxiety Inventory (BAI) score; past-year marijuana use; and typical number of alcohol drinks consumed per drinking day. Self-reported lifetime history of clinically diagnosed ADD/ADHD, depression, and/or anxiety was captured in Years 3-4, including age at diagnosis, which was later recoded into pre-college or during-college. Multinomial logistic regression was used to evaluate the association between the explanatory variables and discontinuous enrollment, holding constant gender, race, SES, and high school GPA.
Results: Higher BDI scores were associated with early discontinuity but not late discontinuity, whereas marijuana use was associated with late discontinuity but not early discontinuity. Depression diagnosis during college was associated with both early and late discontinuity. None of the pre-college diagnoses tested were related to discontinuous enrollment once demographic factors were taken into account.
Conclusions: Students experiencing depressive symptoms and/or seeking treatment for depression during college may be at risk for interruptions in their college enrollment, which could lead to dropout and/or delayed graduation. Marijuana use appears to add to this risk. Students entering college with pre-existing depression or anxiety diagnoses are not necessarily at risk for enrollment problems.
Financial Support: NIH/NIDA: R01-DA14845, A. Arria, PI

19

RELATIVE REINFORCING EFFICACY AND ABUSE LIABILITY OF ORAL TRAMADOL IN HUMANS.

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Aims: Tramadol, a monoaminergic reuptake inhibitor, is metabolized hepatically to an opioid known as M1. This atypical opioid analgesic is generally considered to have limited abuse liability and is not scheduled by the DEA. Recent reports of its abuse have increased, leading to more stringent scheduling in some U.S. states. The purpose of this study was to examine the relative abuse liability and reinforcing efficacy of tramadol to both a high (oxycodone) and low efficacy opioid agonist (codeine).
Methods: Healthy, non-dependent prescription opioid abusers (n=9) participated in this within-subject, randomized, double blind, placebo-controlled study. A total of 14 paired sessions (7 sample, 7 self-administration) were conducted. During each sample session, an oral dose of tramadol (200, 400 mg), oxycodone (20, 40 mg), codeine (100, 200 mg) or placebo was given and a full array of abuse liability measures was collected. During self-administration sessions, volunteers were able to work on 7 trials (via progressive ratio) for some, none or all of the sample dose (in 1/7 increments) or money ($21 available in $3 increments).
Results: All active doses were self-administered, but placebo engendered no responding. Tramadol and oxycodone functioned as dose-dependent reinforcers, as the higher doses were readily self-administered (70%, 59% of available drug, respectively), while the lower doses and both doses of codeine maintained intermediate levels of drug taking (in the range of 31-44%). All three drugs dose-dependently increased measures typically associated with abuse liability (e.g., drug liking, high), relative to placebo ($p < .05$); however, the magnitude and time course of these and other pharmacodynamic effects varied qualitatively across drugs.
Conclusions: This study demonstrates that, like other opioids, higher doses of tramadol function as reinforcers in opioid abusers, providing new empirical data for regulatory evaluation.
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20

MDMA IMPAIRS RESPONSE TO FLUID INTAKE IN HUMANS: A CONTROLLED STUDY OF HYPONATREMIA MECHANISMS.

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Aims: Hyponatremia (lowered serum sodium concentration) is a potential complication of illicit MDMA use that is seen primarily in female MDMA users. Hyponatremia is of particular concern because it occurs after relatively low doses, has high risk of mortality, and has poorly understood mechanisms. Case reports suggest MDMA may impair water balance after ingestion of hypotonic fluid, possibly by increasing antidiuretic hormone (ADH) secretion. Lab studies suggest MDMA may modestly elevate ADH, but there are no controlled laboratory studies of whether MDMA alters response to fluid intake. We sought to elucidate the mechanisms of MDMA-related hyponatremia. We hypothesized that MDMA would increase the effects of standardized water intake on serum sodium concentrations compared to placebo.
Methods: In a double-blind, placebo-controlled within-subjects, 2-session study, 12 (6M/6F) healthy MDMA-experienced participants received MDMA (1.5 mg/kg oral) or placebo. Drug administration was followed, one hour later, by standardized water intake (20 mL/kg water within 30 minutes). Serum sodium, ADH, and copeptin were measured at timed intervals and analyzed using mixed-effects models.
Results: Two participants vomited after water intake; these data (both MDMA sessions) were excluded from analyses. Procedures were otherwise well tolerated. Water loading reduced serum sodium more after MDMA than placebo (delta Cmin: :-3.35 mmol/L, $t= -3.122$, $p= 0.01$). There was no main effect of gender, although there was trend for a significant interaction ($p = 0.07$). Despite the effect of dosing condition on serum sodium, we detected no effect of condition on ADH or copeptin.
Conclusions: MDMA may create a vulnerability to hyponatremia by mechanisms other than ADH secretion.
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21

INTEGRATED SUBSTANCE ABUSE TREATMENT: BUPRENORPHINE IN A PRIMARY CARE CLINIC.

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Aims: Since 2004, Stanley Street Treatment and Resources Inc. (SSTAR) has offered buprenorphine in our PHS 330 Federally Qualified Health Center (FQHC). Medical care is provided by waivered, family practice physicians working closely with nurse care coordinators. We have developed nursing protocols for medication induction and maintenance. Manualized, evidence-based group therapy is required and delivered by mental health providers employed by the clinic. Over the years, the clinic has transitioned from an abstinence-only focus (three infractions of the program's requirements resulted in medication taper) to a harm-reduction model that increases support and substance abuse counseling when illicit use occurs. Behavioral health treatment has become more integrated by use of electronic medical records and regular team meetings. These analyses describe the patient demographics, enrollment process, treatment outcomes and profits.
Methods: Medical records, state tracking reports and internal accounting records were reviewed.
Results: Since 2004, we have treated 865 patients. The current patient population is male (60%), white (88%) and IV heroin abusers (75%). We maintain rapid access with 4.62 days between initial contact and enrollment vs the state average of 16.6 days. We provide evidence-based protocols with 59% of our clients receiving 20 mg or less of Suboxone. We demonstrate retention consistent with the national average and have a current length of stay of 892 days. 2400 group sessions are delivered annually. In 2010, the total revenue generated by the medical component was $636,000; after expenses a $282,000 profit was demonstrated. Mental health services were billed separately and generated $73,000.
Conclusions: Buprenorphine can be successfully provided in a primary care setting. Care is best delivered in a team model with integrated electronic medical records. Such programs can be financially viable.
Financial Support: No financial support.

22

FEEDING CONDITION, BUT NOT TYPE OF REINFORCER, IMPACTS THE RELATIVE CONTRIBUTION OF DOPAMINE RECEPTOR SUBTYPES TO THE DISCRIMINATIVE STIMULUS EFFECTS OF QUINPIROLE IN RATS.

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Aims: Feeding condition can impact the role of dopamine (DA) receptor subtypes in the behavioral effects of direct-acting DA receptor agonists. For example, it appears as though the discriminative stimulus effects of quinpirole are mediated predominantly by D3 receptors in free-feeding rats and predominantly by D2 receptors in food-restricted rats. However, comparisons among feeding conditions often occur across different experimental conditions (e.g., type of reinforcer [food or shock avoidance] used to maintain responding); the current study examined whether type of reinforcer impacts the role of DA receptor subtypes in the discriminative stimulus effects of quinpirole.
Methods: Food-restricted male Sprague Dawley rats (n=6/group) were trained to discriminate quinpirole (0.032 mg/kg) from saline under a schedule of either stimulus shock termination or food presentation.
Results: Stimulus control was established after an average of 26 +/- 9 and 42 +/- 8 training sessions in rats under a shock or food schedule, respectively. Regardless of type of reinforcer, the direct-acting DA receptor agonists lisuride and apomorphine occasioned responding predominantly on the quinpirole-associated lever, being less potent in food-restricted rats compared with free-feeding rats. Amphetamine and morphine occasioned responding predominantly on the saline-associated lever in all rats. The DA D2 receptor antagonist L-741,626 and the D3 receptor antagonist PG01037 shifted the quinpirole dose-response curve to the right in both groups of food-restricted rats.
Conclusions: Depending on feeding conditions, different receptors can mediate the discriminative stimulus effects of some DA receptor agonists. This study provides clear evidence that those differences are due to feeding condition per se and not to the type of reinforcer used to maintain operant responding.
Financial Support: CPF is supported by Senior Scientist Award DA17918.

23

DIFFERENTIAL ASSOCIATIONS OF BIOLOGICAL VS. NON-BIOLOGICAL NETWORK MEMBER PSYCHOPATHOLOGY ON DRUG USE DISORDERS IN VIETNAM VETERANS AND NON-VETERANS: A 25-YEAR LONGITUDINAL STUDY.

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Aims: Little is known about Vietnam veteran and non-veteran family and friend network psychopathology on drug use disorders in adulthood. We first attempt to differentiate vertical vs. horizontal associations of drug use disorders while controlling for other confounding variables. Next we examine the associations of drug use over 25 years with spouse's psychopathology.
Methods: Participants (index participants, n=839) were Vietnam veterans and matched non-veterans who were a part of a longitudinal study of substance abuse and co-morbidity. Network member information included psychiatric and drug abuse problems, and was ascertained on parents, siblings, children, spouses and friends. Generalized estimation equation (GEE) modeling was used to differentiate effects of biological versus non-biological network psychopathology on participants' drug dependence/abuse over the 25 year period. Additionally we performed bi-variate and multivariate analysis to examine associations with female spouse characteristics in particular for this all male index participant group.
Results: Non-biological drug use measures predicted participant's drug dependence/abuse (OR =2.86; CI = 1.89 & 4.32) over 25 years, in addition to biological network drug abuse (OR =1.54; CI = 1.07 & 2.22). In additional analysis, controlling for race-ethnicity, education level, veteran status, and alcohol dependence, spouse's drug problem (OR=9.77; CI = 3.13 & 30.48) and depression (OR = 1.93; CI = 1.09 & 3.39) were associated with participant drug dependence/abuse over 25 years. Further, Post traumatic stress disorder over 3 consecutive year period (OR = 2.52, CI = 1.57 & 4.04) and alcohol dependence/abuse were co-morbid conditions (OR = 5.61, CI = 3.71 & 8.49).
Conclusions: Our findings suggest the significant role of non-biological network psychopathology characteristics in particular those of spouses on persistence of drug abuse among war veterans in their adulthood.
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24

A COTININE URINALYSIS-BASED EVALUATION OF THE RELIABILITY OF SELF-REPORTED TOBACCO USE AMONG PSYCHIATRIC PATIENTS.

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Aims: There is a complex and significant correlation between respiratory disorders and psychiatric conditions. Reliability of self-reported tobacco use has been questioned in recent times.
The current study aims at assessment of accuracy of self-reported tobacco use (both smoked and smokeless) among psychiatric out-patients. We recruited 131 consecutive subjects from the out-patient psychiatry department of a tertiary care hospital.
Methods: Male patients meeting the study criteria were approached for participation in the study. They were asked about their recent tobacco use history. Those reporting recent use were assessed for severity of dependence using FTND-smoking and FTND-smokeless scales. Quantitative urine cotinine analysis was performed using the ELISA method. Based on this method, a (50 ng/ml) cut off score for urinary cotinine level for tobacco use was set.
Concordance between the self-report of tobacco use and urinary cotinine level was assessed using the Cohen's kappa. Additionally, Pearson's correlation coefficient was used to examine the correlation between the FTND-smoking and FTND-smokeless scales and the urinary cotinine levels.
Results: The values of Cohen's kappa suggest no significant concordance between the self-reported recent tobacco use and urinary cotinine levels for both smoking and smokeless tobacco forms. The discordance was present irrespective of a higher (550 ng/ml) or a lower (50 ng/ml) cut off score for a urinary cotinine level. Pearson's correlation coefficient failed to reveal any significant direct correlation between the FTND scores and urinary cotinine levels.
Conclusions: It is recommended to use biological markers such as urinary cotinine levels to corroborates the information provided by the patients.
Financial Support: NONE

25

ACUTE D-AMPHETAMINE IMPAIRS MEMORY RETRIEVAL AT DOSES THAT ENHANCE LEARNING.

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Aims: Moderate doses of stimulant drugs enhance learning in animals and humans. There is also evidence that stimulants can improve retrieval of previously-learned information in animal models, but these drugs' effects on memory retrieval have not been tested in humans. Thus, we set out to determine whether the prototypic stimulant drug d-amphetamine (AMP) enhances memory retrieval in humans at doses known to enhance learning.
Methods: Healthy volunteers (N=30; 18-35 yrs) received AMP (10, 20 mg) or placebo at the time of retrieval across three sessions, in a double-blind, counterbalanced, crossover design. These doses of AMP were previously shown enhance learning when administered prior to encoding. Each drug condition consisted of two laboratory visits: 1) an Encoding Phase, where participants viewed pictures and words under sober conditions, and 2) a Retrieval Phase 2 days later, where drug or placebo was administered before memory was tested. Participants viewed 60 unique pictures and 30 unique words during each Encoding Phase. At Retrieval, memory was assessed by free recall, and then by recognition among novel distractors. No feedback was provided during testing, and stimuli were not re-used across sessions. Hit and false alarm rates, and overall accuracy (hit – false alarm rates) were analyzed using 2-way repeated-measures ANOVA.
Results: AMP did not enhance retrieval. Instead, it impaired memory accuracy by increasing false alarm rates without affecting hit rates for previously-studied information.
Conclusions: At doses that facilitate learning, AMP can impair memory retrieval in humans. This impairment is due to an increased tendency towards false recollection, rather than to reduced access to previously-learned information. That stimulant drugs may interfere with retrieval by increasing false alarms has clinical implications for individuals who use these drugs for cognition-enhancement.
Financial Support: This research was supported by NIDA DA02812 & T32 DA007255

26

KETAMINE REDUCES NEGATIVE AFFECT: RESULTS OF A WEB-BASED SURVEY.

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Aims: Ketamine is a widely used dissociative anesthetic and drug of abuse that is also being studied for use an antidepressant. We sought to determine whether non-medical ketamine users with depressive personality traits report a more favorable response to ketamine than do users without such traits.
Methods: Visitors to the erowid.org website between 5/23/11 and 7/29/11 were invited to participate in a survey of non-medical drug use and mood. Participants completed the Depressive Personality Disorder Inventory (DPDI) and retrospectively reported affect (using the Positive and Negative Affect Scales, PANAS) occurring during abstinence and 2 days after drug use.
Results: 18,848 participants completed the survey. 1084 (5.7%) had used ketamine in the last six months and 211 (19.5%) had elevated (≥170) scores in the DPDI. PANAS positive affect was not elevated at 2 days after ketamine use relative to baseline in subjects with depressive personality. However, those without depressive personality (N=873) reported significantly lower positive affect post-ketamine (Δ from baseline=-3.05; 95%CI -3.56 to 2.53) compared to those with depressive traits. Both groups reported lower PANAS negative affect after ketamine use compared to baseline. The magnitude of this change was greater in the depressed group (Δ from baseline=-6.87; -8.04 to -5.70) than in the non-depressed group (Δ from baseline=-2.42; -2.78 to -2.06).
Conclusions: Participants reported lowered negative affect but not elevated positive affect after ketamine. This reduction in negative affect after ketamine was greater in high-DPDI participants, consistent with a possible antidepressant-like effect. Future research is needed to determine whether those with clinical depression report a clinically significant change in mood after non-medical ketamine use. Large samples can be rapidly assembled using Web-based surveys.
Financial Support: None

27

WHEEL RUNNING, GROUP HOUSING AND SPONTANEOUS MORPHINE WITHDRAWAL IN MICE.

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Aims: The present study investigated the effects of group housing and wheel access on thermal sensitivity following termination of daily morphine administration (i.e. during spontaneous withdrawal).
Methods: C57Bl6J mice were housed in three different conditions: 1) singly housed, with running wheels, 2) singly housed, no running wheels and 3) group-housed (4 mice/cage) no running wheels. Mice in all groups received either saline or 56 mg/kg morphine (s.c.) twice daily for 5.5 days. Following the 5.5 days of saline or morphine treatment, spontaneous withdrawal was observed by measuring thermal sensitivity on a hotplate set at 50, 52, 54 and 56 °C (n=7-8). Measurements were taken at 8, 24, 32 and 48 hrs after the final injection. Mice with access to running wheels were given free access to the wheels during a 1week acquisition phase and again during the withdrawal phase. Thermal sensitivity was quantified by calculating the temperature that produced a 50% reduction in response latency on the hot plate (ET10).
Results: Thermal sensitivity was greater in singly housed mice that received 5.5 days of morphine treatment (average ET10=52.9°C) than in mice that received saline (average ET10= 54.5), suggesting that increases in thermal sensitivity provide a sensitive measure of changes that occur during morphine withdrawal. In group-housed mice, thermal sensitivity was also greater in morphine treated mice (ET10=53.8, 53.4°C) as compared to saline treated mice (ET10 =54.6, 54.4°C) at 32 and 48 hours after the last injection. The enhanced thermal sensitivity observed in the morphine-treated mice during withdrawal (average ET10=52.9°C) was significantly attenuated in those mice that had access to running wheels during the withdrawal period (average ET10 = 54.4°C).
Conclusions: Access to running wheels produced a significant attenuation of the enhanced thermal sensitivity observed during spontaneous morphine withdrawal. Although group housing also attenuated thermal sensitivity, its effects were less robust.
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28

DOES EXECUTIVE FUNCTIONING PREDICT MARIJUANA INVOLVEMENT BY MID-ADOLESCENCE?

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Aims: To estimate the degree to which executive functioning during early adolescence predicts level of marijuana involvement through the mid-adolescent years and to examine potential sex differences.
Methods: The sample was drawn from the longitudinal Miami Prenatal Cocaine Study cohort. 403 African-American adolescents completed executive functioning (EF) assessments at age 12/13-years and had at least one completed measure of marijuana involvement at 12/13, 14/15, and/or 16/17 years. EF level was derived as a undimensional factor score tapped by indicators from the NEPSY, Stroop Color and Word Test, Wisconsin Card Sorting Test, Trail Making Test, Verbal Fluency, and Rey-Osterrieth Complex Figure. Marijuana (MJ) involvement was assessed by self-report, toxicology and caregiver report and defined as: no involvement; opportunity to try; initial use; repeated use; and problem use/positive toxicology. Statistical analysis involved multiple logistic regression and Poisson regression with robust variance estimation of relative risk (RR).
Results: EF level predicted risk of MJ opportunity by age 16/17 years for males and females, before and after adjustment for prenatal drug exposures (adjusted RR, aRR = 2.0; $p<0.05$), including and excluding those with MJ involvement before the age 12/13 study visit. MJ use by the 16/17-year follow-up was also predicted by EF level (aRR = 1.45; $p<0.05$), but this relationship was due to the EF-associated increased risk of a chance to try. EF was not related to repeated or problem MJ use.
Conclusions: Higher EF was predictive of MJ involvement via its prediction of chance to try MJ, but not of higher MJ levels once use occurred. Future work will examine other possible neurocognitive predictors and correlates of MJ involvement through late adolescence.
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29

THE RELATIONSHIP BETWEEN COURT-MANDATE STATUS AND PSYCHIATRIC DISORDERS IN INPATIENT DRUG TREATMENT.

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Aims: The criminal justice system is the primary referral source for drug treatment, but little research has examined differences in rates of psychiatric/substance use disorders as a function of referral (voluntary; VO, court-mandated; CM). A better understanding of this could inform treatment planning and improve our understanding of the different outcomes observed between these groups. This study compared rates of specific DSM-IV Axis I/II diagnoses/comorbidities by referral.
Methods: 463 inpatients (M age=43.3; 69.7% male; 88.4% Black; 57.6% CM) in substance use treatment completed the Structured Clinical Interview for the DSM-IV. X2 tests for categorical variables and ANOVAs for continuous variables were used to examine differences in diagnoses by referral status.
Results: 85.1% of CM patients had substance dependence (SD) versus 71.3% of VO patients ($p = .001$). CM patients were less likely to have current and past alcohol dependence ($\chi2 = 26.26$, $p < .001$; $\chi2 = 14.27$, $p < .001$, respectively) or past cocaine dependence ($\chi2 = 10.98$, $p = .001$). 55.2% of CM patients had Axis I and II psychiatric disorders versus 68.7% of VO patients ($p = .003$).18.0% of CM patients had major depressive disorder (MDD) versus 36.8% of VO patients ($p = .001$). Lower rates of borderline personality disorder (BPD) and generalized anxiety disorder were observed among CM patients ($\chi2 = 6.15$, $p = .013$; $\chi2 = 4.27$, $p = 0.039$, respectively), but antisocial personality disorder rates did not differ by referral status. There were significantly lower rates of comorbid SD and psychiatric disorders among CM patients ($\chi2 = 11.98$, $p = .001$); CM patients were less likely to have comorbid cocaine dependence and depression, or cocaine dependence and BPD than VO patients. They had significantly lower rates of comorbid alcohol dependence and mood, anxiety, BPD, or ASPD than did CM individuals.
Conclusions: Rates of psychiatric and SUDs differ as a function of referral status and should be considered when formulating treatment strategies.
Financial Support: This work was supported in part by NIDA grant R01 DA19405 awarded to Carl W. Lejuez.

30

INCREASES IN HEROIN TREATMENT ADMISSIONS ACROSS WASHINGTON STATE: DEMOGRAPHIC AND GEOGRAPHIC CORRELATES.

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Aims: Heroin treatment and adverse consequences have increased dramatically in Washington State. To shed light on this phenomenon we conducted analyses of treatment data to: 1) describe changes in heroin admissions and 2) determine factors associated with rapidly changing admission rates.
Methods: Admission data included all state funded treatment and private pay methadone treatment in the State from 1999 to 2010 where heroin was the drug of choice (57,050 admissions). Epidemiological analyses consisted of a series of stratified, bi-variate trend analyses that accounted for demographic and geographic characteristics of interest.
Results: Heroin treatment admissions increased 66%, with all of the increase outside of the Seattle area. The median age at treatment entry for heroin users decreased from 40 to 29 from 2004 to 2010. In 1999, 43% of treatment admissions were to opiate substitution treatment, this declined to 22% in 2010. A substantial increase in the proportion who report initiating prescription opiates prior to using heroin corresponded with the increase in the heroin admission rate. Geographically, outside of the Seattle area, the increase in treatment admissions for prescription-type opiates preceded the increase in heroin admissions by 5 years.
Conclusions: The increase in heroin treatment admissions is not uniform across Washington, with a much faster rate of increase in admissions outside of the largest metropolitan area. This geographic change corresponded with a dramatic decrease in the age of those entering treatment. Prescription opiate use prior to heroin use is associated with the increase in the heroin admission rate. The rapid increase in heroin use in areas with little experience dealing with heroin use and its consequences represent a serious, long term challenge to drug treatment and public health systems.
Financial Support: Alcohol & Drug Abuse Institute, University of Washington

31

DEPRESSION AS A MEDIATOR IN THE LONGITUDINAL RELATIONSHIP BETWEEN STRESS AND ALCOHOL USE.

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Aims: The objectives of this study were to determine whether change in depression mediated the relationship between change in stress on later alcohol use, and to examine if differences in age, gender and rurality affected the relationship.
Methods: Utilizing a longitudinal study of 527 community-dwelling, middle-aged participants, latent growth structural regression modeling was used to test the hypothesis that the Center for Epidemiological Studies Depression Scale (CES-D) mediated the relationship between the Perceived Stress Scale (PSS) and the Alcohol Use Disorders Identification Test (AUDIT), over 14 years. Age, gender, and distance from the city center were then added to the model to determine if those variables influenced the mediation model.
Results: The slope of the CES-D mediated the relationship between the slope of the PSS and current AUDIT scores. This statistically significant relationship remained so when age, gender, and distance from the city center were added into the model. Additionally, men had higher AUDIT values and lower PSS intercept scores compared to women, younger participants had a greater increase in PSS values over time, and participants living further from the city center had a greater increase in PSS values over time, while participants living closer to the city center had higher AUDIT values.
Conclusions: In a predominantly healthy, middle-aged sample, the relationship between change in stress and alcohol use is mediated by change in depression. This relationship highlights the need for prevention and early interventions for stress and depressive symptomology in order to help prevent increased alcohol use in at-risk demographic groups.
Financial Support: This research was supported by a grant from the Life Science Discovery Fund to the Rural Mental Health and Substance Abuse Treatment.

32

ETHNIC VARIATION IN METHADONE PHARMACOKINETICS.

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Aims: Retention in treatment and reduction in illicit opiate use during methadone maintenance therapy is often dose related with most patients responding to doses between 80-120 mg daily. We previously identified an ethnic minority (the Hmong from Laos) with greater 1-year retention on significantly lower methadone doses than other ethnicities. We hypothesized that this lower dose requirement in Hmong was due to decreased methadone clearance (CL).
Methods: Hmong and non-Hmong subjects who had been on methadone for at least 2 months with no dose changes for 5 days prior to study were recruited from a single urban methadone clinic. Those who were pregnant, had end stage liver disease, or were taking medications known to interact with methadone were excluded. Blood samples were obtained approximately 2 (peak) and 24 (trough) hours after taking once daily methadone. Plasma levels of R-methadone were measured using HPLC-MS. A linear one-compartment population pharmacokinetic model with FOCE-I was used to evaluate methadone CL and volume of distribution (V). Diagnostic plots and the generalized additive models procedure were used to assess covariates including ethnicity, weight, BMI, age, and methadone dose. Improvements in Akaike Information Criterion and objective function value were seen for a final model that included only ethnicity and age as covariates.
Results: From 75 Hmong (71% males) and 143 (61% males) non-Hmong subjects, the mean (SD) methadone dose was 53.8 (19.1) and 86.7 (35.7) mg, respectively. In the final model, R-methadone CL was 14.7 L/h and V 712 L for a standard 40 year-old non-Hmong subject. After adjusting for age, the Hmong had a 25% lower CL and 41% lower V compared to non-Hmong. The interindividual and residual variabilities were 37.3% and 17.8%, respectively.
Conclusions: While the Hmong have significantly lower methadone dose requirements, the CL and V are significantly less than non-Hmong. With similar changes in CL and V, it may be that the Hmong have a greater bioavailability than non-Hmong.
Financial Support: K23DA024663

33

SMOKING AND NON-ALCOHOL SUBSTANCE USE IN VETERANS WITH PTSD AND ALCOHOL DEPENDENCE.

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Aims: To describe co-occurring non-alcohol substance use in veterans with PTSD and alcohol dependence entering a controlled trial of topiramate.
Methods: Background: PTSD and alcohol dependence are both common and frequently coexist in veterans. Co-occurring substance use may affect the severity of these disorders.
Methods: Baseline psychological, alcohol and non-alcohol substance use (NASU) measures are reported for the first 27 subjects in a pilot controlled trial of topiramate treatment for alcohol dependence and PTSD in veterans. PTSD, anxiety, and depression, as well as smoking, non-alcohol substance use (NASU) and NASU disorder diagnoses (NASUDs) were calculated. Subjects with and without smoking or NASU were compared on alcohol use PTSD, depression, and anxiety severity.
Results: Mean age was 50, 93% were male. 48% were Vietnam era and 19% were Iraq/Afghanistan veterans. All had current alcohol dependence and PTSD. 78% had combat-related PTSD. Mean Clinician Administered PTSD Scale (CAPS) score was 77; mean Beck Depression and Anxiety scores were 26 and 25 respectively. Past 90 day mean % drinking days was 79%. 44% were smokers and 44% reported NASU in the past 30 days: 33% cannabis, 19% cocaine, 19% other drugs. Urine drug screens were positive for cannabis in 15%, cocaine in 7%, and other drugs in 15%. 22% met SCID NASUD criteria. Smokers did not have higher mean CAPS, BDI, or BAI scores than nonsmokers. Smokers had fewer drinking days in the past 30 (17 vs 24, $p < .05$; $\eta 2 = .17$) than nonsmokers. Baseline NASU other than smoking was associated with higher BDI scores (34 vs 24, $p = .07$), but not higher alcohol use, CAPS, or BAI scores.
Conclusions: Smoking and other non-alcohol substance use were not associated with greater alcohol use, PTSD or anxiety severity in veterans with PTSD and alcohol dependence entering a pharmacotherapy clinical trial.
Financial Support: Department of Defense Grant No: W81XWH-05-2-0094

34

ENGAGEMENT MODELS FOR ADOLESCENTS: ETHNIC DISPARITIES.

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Aims: Treatment readiness has consistently been the best predictor of therapeutic engagement. Moderators of this relationship and intervening variables have been infrequently addressed for adolescents. Ethnicity may interact with social and personality factors thereby differentially affecting the engagement process. The purpose of the current study is to examine variations in adolescent engagement models across different ethnic groups. Do relationships among treatment readiness, social factors, and therapeutic engagement differ between Hispanic and White clients? It is hypothesized that level of social support and hostility will influence the degree to which readiness influences engagement, with social support as a mediator for Hispanic adolescents.
Methods: Data were collected in 2011, as a part of the TCU Adolescent Project and represent 390 adolescents (75% Hispanic origin) within 8 residential therapeutic communities located in Texas, New York, and California. Age, primary drug and gender did not differ by ethnicity. Hispanics were less likely to be chemically dependent and more likely to report criminal justice involvement within the 30 days prior to treatment. Measures of motivation, hostility, and social support were assessed at intake, with therapeutic engagement measured at 45 days of treatment, and multiple regression analysis was used to test hypotheses.
Results: Treatment readiness was predictive of participation and counselor rapport for both Hispanic and White clients. A series of regression models indicated that social support mediates the relationship between motivation and engagement for White clients and that hostility drops as a predictor of engagement when social support is added for both ethnicities.
Conclusions: Preliminary results suggest that the influence that the level of motivation has on engagement for White clients is accounted for by social support, while the relationship for Hispanic clients deserves further explanation. Social support serves as a protective barrier to the detrimental role of hostility on engagement for both ethnicities.
Financial Support: NIDA grant R01DA013093.

35

SPORTS PRACTICE AND ALCOHOL USE BY ADOLESCENTS: A BRAZILIAN STUDY.

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Aims: The aim of this study was to verify the association between sports practice and alcohol use by adolescents.
Methods: A national sample from high-schools of 27 Brazilian capitals (n=19.132) was assessed by the means of an anonymous self-report questionnaire applied in the classrooms. Only those students who answered about sports practice were included in this study (n=13.873). Logistic regression models were used to estimate the Odds Ratio (OR) for alcohol use and binge drinking on the last month. The main independent variables were type of sports, frequency and motivation for sport practice.
Results: The most frequent sport was soccer 26.3% (99%CI: 25.0-27.7). Sports practice was more related to alcohol use on the last month (OR: 1.2[1.1-1.4]) and binge drinking (OR: 1.2[1.1-1.5]) compared to non-practicing students. However, team sports students were less likely to report alcohol use (OR: 0.7[0.6-0.8]) or binge drinking (OR: 0.8[0.6-0.9]). Compared to non-practicing students, gym was associated to the risk of alcohol use (OR: 2.2[1.6-2.5]) and binge drinking (OR: 1.9[1.6-2.4]) as well as soccer, respectively: OR: 1.2[1.1-1.4] and OR: 1.3[1.1-1.5]. When included friend's drunkenness, gym were still risk for alcohol use (OR: 2.0[1.6-2.5]) and binge drinking (OR: 1.5[1.2-2.0]). The frequency of 20 or more days practicing sports per month were more associated with the risk of alcohol and binge drinking compared to 1-5 days per month.
Conclusions: These data indicate that sports are associated to alcohol use and binge drinking among Brazilian students, especially gym and soccer players. However, sports characteristics are also involved and should be considered in future studies. Our findings should be taken into account to elaborate preventive programs of alcohol use among this population.
Financial Support: The CEBRID (Centro Brasileiro de Informações sobre Drogas) provided database for analyses. FAPESP (Fundacao de Amparo a Pesquisa do Estado de Sao Paulo), SENAD (Secretaria Nacional de Políticas sobre Drogas) and AFIP (Associação Fundo de Incentivo à Psicofarmacologia) provided financial support.

36

COUNSELORS' ATTITUDES TOWARD PAIN TREATMENTS IN METHADONE MAINTENANCE TREATMENT.

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Aims: Despite calls for improved treatment for co-occurring chronic pain (i.e., pain lasting at least 3 months) and opioid dependence (POD) in methadone maintenance treatment (MMT), little is known about MMT counselors' attitudes toward pain treatment. This study explored counselors' a) attitudes toward the efficacy of various conventional and unconventional pain management interventions, including 9 specific cognitive-behavioral therapy (CBT) for POD modules; b) willingness to refer their POD patients to such treatments; and c) interest in learning CBT for POD components for use with their pain patients.
Methods: Thirty MMT counselors completed an interview and survey developed by the authors.
Results: Mean counselor age was 43.6 years (SD = 12.8); 20 (67%) were women, 20 (67%) described themselves as white, and their mean years of clinical experience was 5.8 (SD = 5.3). On average, the highest and lowest ratings on 0-4 scales for perceived efficacy and willingness to refer for conventional pain treatments were CBT (3.5 and 3.8) and physical exercise (2.6 and 3.1), respectively, and the highest and lowest ratings for unconventional pain treatments were acupuncture (3.2 and 3.7) and magnets (2.0 and 2.4), respectively. On average, all 9 CBT for POD modules were rated highly on perceived efficacy, willingness to refer, and interest in learning (the lowest ratings on 0-10 scales were 8.9, 9.2, and 9.0, respectively).
Conclusions: Counselors exhibit positive attitudes toward specific conventional and unconventional pain treatments, and, in particular, CBT. Counselors' highly favorable ratings of the perceived efficacy of CBT for POD modules, their high ratings on willingness to refer their POD patients for these interventions, as well as their elevated interest in learning these CBT components suggest that the introduction of specialized chronic pain counseling into opioid treatment programs may be well-received.
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37

ETHNICITY AS A MODERATOR OF HIV/STD SEXUAL RISK REDUCTION GROUPS FOR WOMEN IN SUBSTANCE ABUSE TREATMENT PROGRAMS.

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Aims: High-risk sexual behavior is an important vector of the HIV/AIDS epidemic, particularly among female substance abusers. Effective interventions to reduce unprotected sexual occasions (USO) and increase condom skills in this population are needed. Literature suggests ethnicity may influence risk behavior and participant response to intervention. We therefore performed a secondary analysis on a gender specific controlled multi-site trial of a 5-session HIV/STD risk reduction intervention, Safer Sex Skills Building (SSB), compared to a 1-session Health Education (HE) control. SSB was skills-oriented but not ethnically tailored. Based on literature, it was hypothesized that ethnicity would moderate the intervention effects of SSB: reducing USO and increasing condom use skills among Caucasians but not minorities.
Methods: 515 eligible participants (298 Caucasian,125 African American,92 Hispanic and others), from 12 methadone and psychosocial outpatient treatment programs, were randomized to either SSB or HE. PROC GLIMMIX in SAS was used to test ethnic group effects on USO and condom skills.
Results: For the primary outcome USO, there was a significant main effect of treatment, reflecting lower USO in the SSB group, but no ethnicity by treatment interaction. For male condom use skills, there was an interaction between ethnicity and time ($F(1,212)=4.75, p=0.03$),reflecting significantly greater skills among minorities at the 6-month follow-up. For female condom use skills, there was an interaction between ethnicity and treatment($F(1,257)=6.94, p<.01$), reflecting significantly higher skills among minorities in the SSB group.
Conclusions: Contrary to the original hypothesis, a skills based HIV risk reduction intervention was equal to or more effective among minorities on the outcomes of USO and condom use skills.
Financial Support: Grant support:2U10 DA013035(Nunes & Rotrosen),K24 DA022412 (Nunes)

38

DIFFERENCES IN PRETREATMENT CHARACTERISTICS AND HEALTH DISPARITIES AT INTAKE AND 3 MONTHS AMONG ASIAN SUBGROUPS.

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Aims: Studies that indiscriminately combine Southeast Asians (SE Asians), Asian Pacific Islanders (APIs), and Native Hawaiians/Other Pacific Islanders (NHOPI) with other Asians are not uncommon in the substance abuse literature. Such studies yield results that Asians are lower in severity of substance use disorders compared to other groups. However, recent research indicates highest treatment rates for NHOPI and high risk for SE Asians given refugee issues within this group. Research also indicates Asians as a whole receive fewer services, but it is unclear if this is true for subgroups or if services are commensurate to needs. This study aims to provide evidence for distinctions between Asian subgroups and test for health disparities in treatment needs.
Methods: Asians who completed the Global Appraisal of Individual Needs prior to entering treatment were classified based on ethnicity, location, and Asian identification. 50 APIs were compared to 117 SE Asians and also to 48 NHOPI who did not identify as Asian. A comparison group of multiethnic Asians who typically exhibit high severity and a "combined Asian" group were also included. Group differences on intake characteristics were examined using odds ratios and Cohen's d. Chi-square analyses were used to test if those with mod/hi needs at intake were targeted (proportion of services provided to those with mod/hi need) or unmet (proportion of those with mod/hi need who did not receive services) at 3 months across ASAM dimensions.
Results: APIs are more likely to have lifetime and past-year dependence, moderate pathological gambling, conduct disorder, ADHD, commit crimes, use cocaine, self-harm, and receive non-evidence-based treatment. 95% of APIs versus 70% of SE Asians endorsed mental health need at intake. SE Asians have the highest proportions of unmet need for ASAM B2, B3, B5, & B6. Subgroups are more severe than the combined group.
Conclusions: Combining all Asians may cause failures in noticing severe subgroups, such as APIs. Dialogue on why unmet needs are higher for some groups and ways to address such disparities is needed.
Financial Support: SAMSHA contract no:#270-07-0191

39

BODY WEIGHT LOSS AS A MEASURE OF PHYSICAL DEPENDENCE AFTER ABRUPT WITHDRAWAL OF BUPRENORPHINE IN RATS.

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Aims: Traditionally, it has not been possible to demonstrate physical dependence in rats receiving multiple injections of buprenorphine after naloxone challenge or abrupt withdrawal of the analgesic. Previous work involving a heroic s.c. dosing schedule (daily injections of 3 mg/kg of buprenorphine for 28 days, followed by saline) uncovered only one sign of withdrawal - sudden weight loss on day 6 of saline injections. Here, we monitored rat weight during 4, 7 or 14 day induction periods with buprenorphine (0.5, 1.5 or 3 mg/kg) as well as during subsequent "withdrawal" (saline) periods. Parallel experiments with methadone (5 or 10 mg/kg) afforded positive control data. Our ultimate goal was to provide a shortened dosing protocol with consequent weight loss that would become a standard for preclinical buprenorphine research.
Methods: Male S.D. rats (175-200 g; n=6-10) were weighed and injected s.c. at 9 AM daily with buprenorphine, methadone or saline as indicated above.
Results: The mean weight of rats receiving buprenorphine during induction did not differ significantly from that of control (saline) animals. Animals on methadone during induction all lost weight relative to controls (and 4 out of 6 rats on 10 mg/kg methadone for 14 days died). Sudden, impressive weight loss (on day 5 of "withdrawal") was associated with only the 3 mg/kg - 14 day buprenorphine dosing schedule (9 ± 2 g). Rats on 5 mg/kg methadone for 7 days lost 5.5 ± 4.5 g on day 1 of "withdrawal".
Conclusions: The 3 mg/kg - 14 day buprenorphine dosing schedule is associated with convincing "withdrawal day 5 weight loss" and is recommended as the standard experimental protocol for academic pursuits and for facilitating comparative structure-activity studies of buprenorphine-like compounds.
Financial Support: DA0294414 and DA031605.

40

THE INFLUENCE OF ALTERNATIVE REINFORCER RESPONSE COST ON METHAMPHETAMINE CHOICE.

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Aims: Methamphetamine use disorders are a persistent public health concern. Behavioral treatments have demonstrated that providing alternative reinforcers reduces methamphetamine use. The purpose of this experiment was to determine how response cost for alternative reinforcers influenced methamphetamine choice in the human laboratory. It was hypothesized that methamphetamine choice would increase as response cost for the alternative reinforcer increased.
Methods: Seven subjects with histories of recreational stimulant use completed a placebo-controlled, crossover, double-blind protocol in which they first sampled doses of oral methamphetamine (0, 8 or 16 mg) and completed a battery of subject-rated and physiological measures. In subsequent sessions, subjects made eight choices between 1/8th of the sampled dose and an alternative reinforcer (US$0.25). The response cost to earn a methamphetamine dose was always 500 responses (FR500). The response cost for the alternative reinforcer varied across sessions (FR500, FR1000, FR2000, FR3000). Data were analyzed using repeated-measures ANOVA.
Results: Methamphetamine was chosen to a greater degree than placebo. As alternative response cost increased, methamphetamine and placebo choice also increased. Methamphetamine produced typical stimulant-like subject-rated and physiological effects (e.g., increased ratings of Stimulated; elevated blood pressure).
Conclusions: These data demonstrate that making alternative reinforcers more difficult to earn increases methamphetamine self-administration, which has implications for treatment efforts. Future research should determine how putative pharmacotherapies for methamphetamine use disorders alter methamphetamine choice under this arrangement.
Financial Support: Supported by a grant from NIDA (R01 DA 025032) to CRR.

41

DISCOUNTING OF FUTURE REWARDS AND BRAIN ACTIVATION IN HEALTHY 10-14 YEAR-OLDS.

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Aims: Increased discounting of delayed rewards is one measure of impulsivity that has been linked to risk for substance use disorders (SUD). In healthy adults, greater discounting has been shown to be positively correlated with brain activation during reward tasks. Whether this relationship exists in children and adolescents has yet to be determined.
Methods: Eight healthy 10-14 year-olds completed a behavioral measure of delay discounting (Monetary Choice Questionnaire) and an event-related fMRI task (Monetary Incentive Delay). The main contrast of interest was anticipation of $5 reward versus $0. We tested for a correlation between the behavioral measure of delay discounting and activation in bilateral nucleus accumbens region of interest using SPM5 with statistical threshold $p < .05$. Post-hoc correlation provided an estimate of effect size (r).
Results: Rate of discounting of future rewards was positively correlated with activation in both left nucleus accumbens (cluster size=18 voxels) and right nucleus accumbens (cluster size=30 voxels) during anticipation of monetary reward. Effect sizes were r=0.86 for left and r=0.85 for right nucleus accumbens.
Conclusions: Preference for immediate reward, indicated by greater delay discounting, positively correlates with brain activation in nucleus accumbens in healthy children and adolescents. These data are similar to studies previously reported in adults, providing preliminary evidence of a consistent relationship between these variables across developmental stages. This pilot study in healthy children will serve as a foundation for future work examining the developmental trajectory of discounting and neurobiological correlates of reward processing as well as comparison of these traits in youth at high risk for SUD.
Financial Support: Supported by grant number K12DA000357, awarded to the American Academy of Child and Adolescent Psychiatry (AACAP) by the National Institute on Drug Abuse (NIDA).

42

ANALYZING HUMAN COCAINE USE PATTERNS TO INFORM ANIMAL ADDICTION MODEL DEVELOPMENT.

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Aims: The goal of this project was to evaluate patterns of cocaine use in humans with the long term goal of developing more accurate animal models of drug taking.
Methods: Participants (N=189) included cocaine-dependent individuals who were screened in person as a part of ongoing inpatient laboratory studies. In order to more closely investigate the influence of history of cocaine use, the sample was split into quartiles according to number of years they had used cocaine. Quartiles one (HiYrs: N=48) and four (LoYrs: N=49) were targeted.
Results: Participants were primarily African American males who were ~40 years of age. Individuals in the HiYrs group used for 28.3±3.2 (mean±S.D.) years while those in the LoYrs category used for 6.5±2.9 years ($p<0.001$). Surprisingly, HiYrs and LoYrs participants used cocaine an equivalent number of days per month (20.8±8.1 vs. 20.0±8.0, respectively), purchased an equivalent amount of cocaine in grams each time (1.5±1.2 vs. 1.6±1.9), and consumed cocaine over a similar period of time in hours (5.1±11.3 vs. 6.7±10.0). In contrast, subjects in the HiYrs group used cocaine fewer times, and by implication in larger amounts (3.7±3.5 vs. 6.1±8.4, $p=0.064$).
Conclusions: The lack of differences between these two distinct groups suggests that patterns of drug use may be generated early in the course of drug-taking. The main difference observed was that HiYrs users consumed their purchased cocaine in the same amount of time as LoYrs but did so in fewer intervals; presumably producing higher "spikes" and "troughs" in their blood/brain concentrations of cocaine. Recent animal data suggest that spiking (rather than sustained) brain cocaine levels are more important in the addiction process and appear to be in agreement with these data. Development of more accurate animal models in which different patterns of intake can be investigated will perhaps lead to identification of more effective medications.
Financial Support: This study is sponsored by NIH via support to RDLG (DA023624, DA023588, DA028387) and TFN (DA017705, DA018197).

43

KAPPA OPIOID AGONISTS, NOT ANTAGONISTS, STIMULATE PHOSPHORYLATION OF C-JUN N-TERMINAL KINASE.

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Aims: A previous study reported that long-acting κ opioid antagonists stimulated the phosphorylation of c-Jun N-terminal kinase (JNK) as measured by Western blot analysis using HEK 293 cells expressing the rat κ opioid receptor labeled with green fluorescent protein (Bruchas et al., JBC, 2007). Seldom do opioid antagonists act as agonists. This current study used an ELISA to characterize total JNK and phosphorylated JNK (pJNK) levels mediated by the human κ opioid receptor.
Methods: Chinese hamster ovary (CHO) cells stably transfected with the human κ opioid receptor (KOR) were used in an ELISA to determine if κ full agonists, partial agonists, and antagonists altered the levels of total JNK and pJNK.
Results: Within 5 min after incubating KOR-CHO cells with the κ-selective agonist U50,488, the level of pJNK was increased 130% above basal pJNK levels. This pJNK level remained constant for 40 min. The pJNK levels gradually attenuated until they had returned to basal levels after 5 hr of incubation of the cells with U50,488. The total JNK levels did not change regardless of whether the cells were treated with agonists or antagonists. U50,488 stimulated pJNK levels with an EC_{50} value of 0.60 nM and an E_{max} value of 130%. Other κ full and partial agonists also stimulated pJNK levels. The long-acting κ antagonists, nor-BNI and GNTI, completely inhibited U50,488-stimulated pJNK levels. However, these antagonists at concentrations up to 10 μM did not stimulate pJNK levels.
Conclusions: This current study found that U50,488 was very potent in stimulating pJNK levels. An EC_{50} value of 0.60 nM was obtained for U50,488-induced stimulation of pJNK levels. In contrast, an EC_{50} value of 1240 nM was obtained for U50,488 in the previous study using Western blot analysis. Unlike the previous study, we did not find any stimulation of pJNK levels by long-acting opioid antagonists.
Financial Support: Paul Stark Endowed Professorship and the Margo Cleveland Fund.

44

ADHD, CONDUCT DISORDER, AND INITIAL PHYSIOLOGICAL REACTIONS TO CIGARETTES AND ALCOHOL IN FEMALE ADOLESCENTS: EVIDENCE FOR THE LINK BETWEEN ADHD AND RISK FOR TOBACCO USE.

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Aims: To characterize associations among Attention-Deficit Hyperactivity Disorder (ADHD) symptoms, Conduct Disorder (CD) symptoms, and initial reactions to cigarettes and alcohol in an epidemiological sample of female adolescents.
Methods: Participants were female twin pairs identified through Missouri birth records (n=1290 individuals). DSM-IV symptoms of ADHD were assessed via parent interview when the twins were adolescents (mean age = 18.2, s.e. = .03). CD and initial reactions (i.e. 9 items reflecting subjective responses to first experiences with the substance) were assessed by twin self-report. Linear regression (adjusting for the non-independence of members of twin pairs) was used to examine relationships among ADHD Inattentive Symptoms, ADHD Hyperactive/Impulsive Symptoms, CD symptoms, and self-reported initial reactions to cigarettes and alcohol.
Results: ADHD Inattentive symptoms significantly predicted the overall magnitude of initial responses to first cigarettes, after controlling for CD and Hyperactive/Impulsive symptoms ($t = 2.34$, $B = 0.07$, $p = .02$). CD symptoms significantly predicted the overall magnitude of initial responses to first drinks of alcohol, after controlling for ADHD Inattentive and Hyperactive/Impulsive symptoms ($t = 2.84$, $B = 0.33$, $p = .005$).
Conclusions: These results show that ADHD Inattentive symptoms are differentially associated with increased reactions to first cigarettes, whereas Conduct Disorder is differentially associated with increased initial reactions to alcohol. These results add to a growing body of literature suggesting that ADHD is an important risk factor for tobacco use, specifically, after controlling for CD.
Financial Support: Supported by AA11998 (Heath), DA16184 (Bidwell), DA023134 (Knopik)

45

GENDER DIFFERENCES IN DRUG-RELATED AND SEXUAL RISK BEHAVIORS AFTER RELEASE FROM PRISON.

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Aims: Prison inmates have a high prevalence of HIV and substance use disorders. Following release from prison, former inmates have opportunities to engage in risk behaviors that put themselves and community members at risk for HIV. The study aims were to characterize and examine gender differences in risk behaviors during the first 3 weeks after release from prison.
Methods: We recruited 125 former inmates 18 and older and within 21 days of release to the Denver area from community sites and correctional programs. We conducted in-person interviews using computer-assisted survey software for sensitive questions and rapid HIV testing. Analyses included descriptive statistics, and chi-squared and Fisher's exact tests for baseline measures.
Results: Participants enrolled an average of 13.5 days after release (Standard Deviation [SD] 6.4). The mean age was 41 (SD 8.9); 22% were female; and 46% were African American, 29% Latino, 22% white and 5% another race/ethnicity. Nearly one third (31%) reported having hepatitis C, 27% had ever been treated for an overdose, and 8% had HIV. While 42% had ever injected drugs, only one participant injected drugs in the prior 7 days. In terms of sexual risk behaviors, 37% had at least one sexual partner since their release. In the last 7 days, 17% of men and 44% of women had unprotected oral sex (P<0.01), 18% of men and 37% of women had unprotected vaginal sex (P=0.04), and 5% of men and 7% of women engaged in unprotected anal sex (P=0.64).
Conclusions: Former inmates reported substantial sexual risk behavior in the immediate post-release period with greater sexual risk behavior among women. Former inmates had a high prevalence of drug-related medical complications, including HIV, hepatitis C, and history of overdose. These results support the inclusion of women in interventions to prevent sexual risk behavior in the post-release period and a greater emphasis on the medical consequences of drug use in former inmates.
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46

A CONTROLLED TRIAL OF MEMANTINE AS AN ADJUNCT TO LONG-ACTING NALTREXONE FOR OPIOID DEPENDENCE.

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Aims: Preclinical research suggests that inhibition of NMDA-receptor glutamatergic neurotransmission may be beneficial in the treatment of opioid dependence. We hypothesized that addition of memantine, an NMDA receptor antagonist, to a long-acting preparation of naltrexone would be safe and effective in preventing relapse to opiate use in detoxified individuals.
Methods: Opioid-dependent participants seeking treatment (N = 82) were admitted for detoxification and initiation of treatment with long-acting injectable naltrexone (Vivitrol, 380 mg i.m.). During detoxification participants were randomized to adjunctive memantine 20 mg p.o. bid or placebo, in combination with Vivitrol (monthly for 3 months) and individual relapse-prevention therapy. The primary outcome was retention in treatment since treatment dropout is most commonly associated with relapse to opiate use.
Results: Twenty-seven (33%) participants withdrew from treatment during detoxification and prior to starting naltrexone or adjunctive study medication. Of those that were randomized (N=55), 80% completed 4 weeks only, and 56% completed all 12 weeks of treatment. Retention in treatment was significantly lower in participants that received adjunctive memantine, as compared to those receiving placebo (43% vs. 70% respectively; p=.047).
Conclusions: The efficacy of memantine 40 mg/d as an adjunct to naltrexone for the relapse prevention in opiate dependence was not supported. To the contrary, it appears that memantine may worsen the effectiveness of long-acting naltrexone.
Financial Support: NIDA grants: RO1 DA15822

47

COMPUTER USE AND ATTITUDES AMONG PATIENTS WITH CO-OCCURRING DISORDERS: IMPLICATIONS FOR COMPUTER-BASED INTERVENTIONS.

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Aims: The aim of this study was to explore the feasibility of computer-based interventions for adults with severe mental illness and substance use by describing computer access, attitudes, and skills in a sample of psychiatric outpatients.
Methods: Participants' computer attitudes, access, and skills were assessed by self-report and direct observation task analysis. Qualitative data were collected during a "think aloud" exercise in which patients navigated through an instructional website. Descriptive statistics were calculated for questionnaire and task-analytic items. Anecdotal comments were independently reviewed and grouped into themes.
Results: Twenty-eight psychiatric outpatients participated in the study. All reported recent cocaine use. A small proportion (11%) reported owning a computer, but the majority (61%)had regular computer access. Participants self-reported having basic computer skills but many expressed negative attitudes about using computers. Task analysis revealed participants could complete most steps of navigating a fairly complex website with verbal prompting. More assistance was needed to type in designated spaces. Use of the mouse and small font caused frustration for some participants.
Participant comments were categorized into themes of Suspicious, Insecure, Awe, Motivated/Interested, Experienced, Capable, Lack of Exposure/Ignorance, and Willing.
Conclusions: Although many participants reported negative attitudes and/or limited computer skills initially, all could navigate a reasonably complex website with some training, and many reported satisfaction with the experience.
Results suggest feasibility and acceptability of computer-based interventions for adults with co-occurring disorders may be increased by (1) providing access to computers (2)assessing basic skills initially and providing instruction and assistance to ensure full program access (3) providing options to navigate the program without a mouse (4)minimizing complexity of program content and layout.
Financial Support: This study was funded by NIDA: R01DA12952, R01DA025613.

48

METHAMPHETAMINE USE AND DIAGNOSED STD/HIV IN THE COMMUNITY: UNITED STATES, 2005-2009.

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Aims: In this cross-sectional study, we aim to estimate the degree to which being a methamphetamine (METH) user is associated with being a case of a sexually transmitted disease (STD) and/or being infected with the human immunodeficiency virus (HIV). The study has the strengths of rigorous sampling of community residents across the range from adolescence through adulthood, and confidential audio-enhanced computer-assisted self-interview methods (ACASI) to promote accuracy and completeness in self-report measurements.
Methods: Data are from the US National Surveys on Drug Use and Health (NSDUH) 2005-2009, yielding nationally representative samples of community-dwelling methamphetamine users and non-users age 12 years and older (n= 278,130). The ACASI elicited self-reported METH use and history of STD/HIV as diagnosed by a medical professional. A bivariate generalized estimating equations approach (GLM/GEE) estimated the prevalence odds ratios (POR), with due attention to complex survey design and weights.
Results: The bivariate GLM/GEE model produced a moderately strong POR estimate such that the odds of diagnosed STD/HIV was 4.6 times greater for METH users as compared to non-users (p<0.05), with no need for separate METH-STD and METH-HIV estimates; the common slope estimate served well to summarize the evidence. A regression-based covariate adjustment yielded modest attenuation of the estimate (POR = 3.9; p<0.05, with control for age, sex and race/ethnicity; POR = 3.6; p<0.05, with these additional covariates: marital status, education, use of alcohol, tobacco, or other drugs, injecting drug use).
Conclusions: The main finding is a predicted substantial association of METH and the STD/HIV diagnosis, based upon a rigorous nationally representative community sample. Continued research will identify subgroups where comorbid METH and STD/HIV diagnosis is exceptional. This search for subgroup variation in a nationally representative sample may help identify new target groups for public health outreach and intervention.
Financial Support: D43TW005819; T32DA021129; K05DA015799

49

CHARACTERISTICS OF PEOPLE WHO INITIATE INJECTION DRUG USE LATER IN LIFE: PRELIMINARY QUANTITATIVE RESULTS FROM A MIXED METHOD STUDY.

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Aims: Very little is known about people who initiate drug injection at the age of 30 or older. We aim to describe characteristics of people who initiate drug injection at the age of 30 or older (Late Initiates) and to compare the drug use, health, and drug injection initiation characteristics to people who initiate injection prior to the age of thirty (Typical initiates).
Methods: As part of a mixed method, exploratory study on injection drug initiation, computer-assisted personal interviews were conducted with injection drug users recruited at outreach sites in California (n=356). Interviews covered demographics, family history of drug use, drug use initiation, drug injection initiation, current drug use patterns, and health issues among others. A multivariate logistic regression model was developed comparing Late to Typical initiates.
Results: The sample was: 31% White, 30% Black, and 28% Latino; 26% female; 75% 40 years of age or older; and 62% homeless. Typical and Late initiates did not differ on most variables including first drug injected, drug use pattern, homelessness, health status, gender, income, family alcohol and drug abuse, or exposure to childhood physical or sexual abuse. In a multivariate model comparing Late to Typical initiates, we found Late initiates more likely to report non-injection use of first drug injected (adjusted odds ratio [AOR]=3.83, 95% confidence interval [CI] = 1.81, 8.17), to be initiated by someone the same age (AOR=2.59, 95% CI= 1.18, 5.66) or younger (4.16, 95% CI = 1.54, 11.22) as opposed to older, to be Black (AOR=2.77, 95% CI = 1.12, 6.82) as opposed to White, and to not have ever been in residential drug treatment (AOR=0.40, 95% CI=0.18, 0.89).
Conclusions: Late initiates appear similar to Typical IDUs. We are using a qualitative, life course approach to better understand why some drug users initiate drug injection later in life.
Financial Support: NIDA grant number R01DA027689

50

PTSD HISTORY AND EMERGENCY DEPARTMENT PRESENTATION DUE TO VIOLENT INJURY: EXAMINING A POSSIBLE CONNECTION AMONG DRUG-USING YOUNG ADULTS.

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Aims: Prior research has reported that young adults seeking emergency department (ED) care for violent injury (VI) have higher levels of drug use and exposure to prior violence compared with those seeking ED care for other reasons. It is not known, however, whether PTSD history plays a role in this relationship, i.e., whether it is related to presentation to ED for VI.
Methods: Young adults ages 18-24 years presenting to an urban ED in 2010 with a VI and history of past six month drug use self-administered a computerized survey (n= 298). An age and sex-matched comparison group of ED patients with histories of past six month drug use presenting for other reasons was also recruited, and self-administered the same survey (n=212). Validated instruments assessed the main independent variables of interest including PTSD and type of drug use. Multiple logistic regression modeling was used to estimate associations between independent variables and presentation to ED for VI.
Results: Prevalence of prior PTSD was greater among the VI ED group compared with the other ED group (13% vs. 7%, respectively; $p<0.05$). Prevalence of other illegal drug use, primarily reflecting cocaine and heroin use, was also more pronounced in VI ED group (VI=13% vs. other=8%; $p<0.05$). Multiple logistic regression modeling yielded similar results, with PTSD and other illegal drug use positively associated with being in the VI ED group (AOR=2.0 for both; $p<0.05$).
Conclusions: Young adults seeking ED care for VI are more likely to have a prior history of PTSD and use illegal drugs such as cocaine and heroin compared with similar drug using young adults seeking ED care for other reasons. Possible explanations for this association will need to be examined in future work. Nonetheless, based on previous research, individuals with prior PTSD may be more likely to experience subsequent PTSD from their presenting VI, and may need greater mental health resources.
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51

THE EFFECT OF PARENTAL DEPENDENCY DRUG COURT COMPLIANCE ON CHILD WELFARE OUTCOMES.

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Aims: This workshop will provide participants with research findings on the predictors of monthly dependency drug court (DDC) compliance for parents participating in substance abuse treatment services in the Sacramento DDC.
Methods: Using a sample of 843 children and 447 parents participating in the Sacramento DDC from January 2006 to April 2009, a multilevel random effects growth analyses was employed to address the following questions: (1) What are behavioral and demographic markers of compliance in the DDC? (2) What is the impact of timing regarding enrollment and engagement on DDC compliance? (3) What are the effects of compliance trajectories and timing of compliance on children's child welfare outcomes? (4) Do latent class profiles modeled as growth mixture models provide further predictive validity of parental characteristics or child outcomes?
Results: Preliminary analyses are evidencing greater risk of non-compliance in the first three months of participation in the DDC and significant individual differences in compliance trajectories across time. In particular, noncompliance at the Month 1 hearing significantly reduced the likelihood of graduation, which in turn, decreased the likelihood of reunification with children. Compliance was relevant at each hearing, and increased relevance over time.
Conclusions: Noncompliance significantly reduced the likelihood of reunification starting at the Month 1 hearing. This effect was accounted for by compliance effects on likelihood of graduation. Surprisingly, parental characteristics were not strong predictors of graduation and or compliance, meaning successful treatment was the key predictor of graduation and reunification for all parents. Noncompliance was relevant starting at month one and became more relevant over time for successful outcomes. This underscores the need for successfully maintained treatment.
Financial Support: This work was conducted through a subcontract to Children and Family Futures by the Sacramento County Alcohol and Drug Services Division.

52

THE ASSOCIATION OF PERCEIVED SEVERITY OF AND PERCEIVED SUSCEPTIBILITY TO NON-FATAL OVERDOSE WITH LIFETIME OVERDOSE AMONG NEEDLE EXCHANGE ATTENDEES.

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Aims: The study examines the association of two social cognitive variables (perceived susceptibility to, and perceived severity of, non-fatal overdose), adapted from the Health Belief Model, with history of overdose (OD) among injection drug users (IDUs) attending needle exchange programs.
Methods: IDUs (N = 91) completed surveys assessing health beliefs, drug-use, and demographics. Participants were mostly non-white (54%) males (77%) with a mean age of 45 years (SD = 11); 88% reported heroin as their drug of choice. Logistic regression was used to evaluate the association between demographics (age, gender, race/ethnicity), substance use (lifetime prescription opioid use, lifetime cocaine use), perceived severity of OD, and perceived susceptibility to OD with lifetime history of non-fatal OD.
Results: Age and perceived severity were associated with OD in bivariate analyses; participants who had overdosed were older and viewed OD as less severe than those who had never overdosed. In the multivariable logistic regression model, age (OR = 1.05, 95% CI = 1.01-1.10) and perceived severity (OR = .58, 95% CI = .37-.91) were significantly associated with OD history, but perceived susceptibility was non-significant (OR = 1.40, 95% CI = .77–2.54).
Conclusions: These findings indicate that individuals who viewed non-fatal OD as relatively severe were less likely to have overdosed in their lifetime but perceived susceptibility was not related to overdose history. Although causal inferences are beyond the scope of these data, it is possible that severity may influence IDUs' use of protective behaviors that reduce overdose risk. Future research is needed to explore the impact of social cognitive factors on risk behaviors and OD.
Financial Support: This work was conducted as part of the doctoral dissertation of the first author who was supported by a dissertation fellowship from the Bowling Green State University Graduate College; no external funding was received.

53

MISUSE OF MARIJUANA AND CONTROLLED MEDICATIONS BY ADOLESCENTS: PARENTAL MONITORING AND OTHER RISK FACTORS.

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Aims: To compare risk factors associated with adolescents' past year nonmedical use of controlled medications and marijuana use. Given legal, social and medical differences between marijuana misuse and controlled medications misuse, we hypothesized that risk factors would differ between marijuana use and nonmedical use of controlled medications (opioid, anti-anxiety, stimulant and sleep).
Methods: The Secondary Student Life Survey is a web-based survey that was administered from December 2009-April 2010 in classroom settings. Sample was comprised of 2744 secondary school students residing in southeastern Michigan. The mean age was 14.8 years; 50.4% were female, 64.1% were Caucasian and 30.6% were African-American.
Results: There were notable differences in risk factors for marijuana and nonmedical use of controlled medications. For instance, higher levels of parental monitoring were significantly associated with lower odds of using marijuana (OR=0.89, 95% CI= 0.80, 0.99, p<.05), but not with nonmedical use (OR=.97, 95% CI=0.87, 1.07, ns). Other risk factors for nonmedical use included past year alcohol (OR=2.4, 95% CI=1.6, 3.8, p<.01) and marijuana use (OR=2.0, 95% CI=1.2, 3.3, p<.01), and externalizing behaviors (OR=1.05, CI=1.02-1.08, p<.01). Other risk factors for marijuana use included: being in high school (OR=6.5, 95% CI=3.0, 14.4, p<.05), past year alcohol (OR=5.4, 95% CI=3.6, 8.2, p<.05), tobacco (OR=7.7, 95% CI=5.2, 11.3, p<.05) and nonmedical use (OR=2.0, 95% CI=1.2, 3.4, p<.05) and externalizing behaviors (OR=1.07, 95% CI=1.04, 1.10, p<.05).
Conclusions: Parental monitoring provided reduced risk for marijuana use but not for nonmedical use of controlled medications, whereby parental monitoring had no significant effect on nonmedical use. Efforts to prevent nonmedical use might benefit from raising parents' awareness about the risks of nonmedical use of controlled medications.
Financial Support: This study was supported by NIDA research grants R01DA024678 and R01DA031160.

54

INTRA-VTA CRF-R1 AND CRF-R2 ANTAGONISM PREVENTS SOCIAL-STRESS INDUCED ESCALATION OF COCAINE BINGE.

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Aims: Intermittent social defeat can induce long-term synaptic plasticity within the mesolimbic circuit that may influence escalated cocaine-taking behavior. Stressful confrontations can lead to hyperactivation of dopamine neurons particularly within the ventral tegmental area (VTA) that may be modulated by corticotropin releasing factor (CRF). Separate experiments examined intra-VTA antagonism of CRF-R1 subtype or CRF-R2 subtype prior to each stress episode on the subsequent expression of locomotor sensitization and cocaine self-administration during fixed ratio, progressive ratio, and a continuous 24-h "binge". Additionally, we aimed to investigate the neurochemical modulation of dopamine (DA) and serotonin (5-HT) in the nucleus accumbens (NaC) by CRF receptors in the VTA.
Methods: Long-Evans rats were submitted to four intermittent social defeat experiences separated by 72 h over 10 days. Following the last social defeat, stressed and non-stressed rats either underwent catheterization for cocaine self-administration or were surgically implanted with unilateral intra-VTA and intra-NaC cannulation for simultaneous microinjection and microdialysis measurements.
Results: Pretreatment with either a CRF-R1 or CRF-R2 antagonist into the VTA prior to each social defeat episode prevented escalated cocaine self-administration during a 24-h "binge," but only CRF-R1 antagonism prevented stress-induced locomotor sensitization to a cocaine challenge. Intra-VTA treatment of a CRF-R1 antagonist (CP 154,526; 0.3μg/0.5μL) prior to a cocaine challenge may prevent the escalated extracellular release of DA and 5-HT in the NaC, where as CRF-R2 antagonism (Astressin-2B; 1.0μg/0.5μL) may be less effective.
Conclusions: These results suggest that social stress affects differentially CRF receptor subsystems in the VTA, particularly the CRF-R1 sutype may be critical for escalated cocaine taking behaviors.
Financial Support: NIH RO1 DA 031734

55

PREVENTING SUBSTANCE USE DISORDERS IN FOSTER YOUTH: A FEASIBILITY STUDY.

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Aims: Youth aging out of foster care are at disproportionate risk of developing substance use disorders (e.g., within a year of exit, a 13% increase in drug abuse diagnoses). Traditional interventions with this population may not be feasible, due to challenging psychosocial histories. Developing innovative models of care for this group is essential, as both prevalence of disorder and barriers to care represent a substantial health disparity.
Methods: To understand potential pathways to reducing substance use among this population, focus groups were conducted with foster care staff (n=15) and parents (n=8) at a Rhode Island agency. Groups provided feedback on the feasibility of using two common interventions (Brief Motivational Interviewing and Screening, Brief Intervention, and Referral to Treatment). Participants were also asked to design a hypothetical intervention based on their experiences with foster youth. Focus group transcripts were analyzed for thematic content using ATLAS.ti software.
Results: Participants were all female, 87% Caucasian, 9% African-American, and 4% Latina. Staff ranged in foster care experience from 1-23 years (M=6.0, SD=6.7). Support for the two proposed interventions was low. Major themes that emerged were:
1) Longer-term solutions are needed, rather than brief approaches;
2) Breaking off newly-formed relationships with interventionists could be damaging;
3) Disclosure of substance use is unlikely;
4) Approaches should be creative and engaging.
Participants generated a range of intervention ideas, some unsupported by research, some extremely innovative.
Conclusions: Despite innovations in adolescent substance use research, reaching those with significant abuse and neglect histories may require more creativity. In addition to more detailed focus group data, we will also present a resulting novel approach to working with this population.
Financial Support: Pacific Institute for Research and Evaluation Corporate Development Award

56

RESPONSE INHIBITION AND PSYCHOMOTOR SPEED IN COCAINE-DEPENDENT INDIVIDUALS: EFFECTS OF SLEEP DEPRIVATION.

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Aims: Cocaine-dependent (COC) individuals have deficits in cognitive functioning, which may be exacerbated by withdrawal- or binge- associated sleep deprivation (SD).
Methods: To assess cognitive function and the influence of SD, 14 healthy control (HC) adults (34±3.1 yrs.) and 8 COC adults (44.5±1.8 yrs.) completed the Continuous Performance Task (CPT) after a baseline night of sleep, a night of total SD, and two recovery (RE) sleep nights. The Digit Symbol Substitution Task (DSST) was completed at bedtime and each morning. To assess subjective mood and sleep, the Post Sleep Inventory (PSI) was completed on mornings after baseline, RE1 and RE2 sleep. Data were analyzed with linear mixed model ANOVAs with sleep night and treatment group as fixed factors.
Results: At baseline, compared to HCs, COC participants had slower reaction times (RTs) during the CPT (p<0.001), and completed fewer accurate substitutions on morning and evening DSST (both p<0.01). The effect of sleep night and the sleep night by group interaction were not statistically significant, but across all four days COC participants made more errors of omission (p<0.01), had slower RTs on the CPT (p<0.0001), and completed fewer accurate substitutions on both the evening and morning DSST (both p<0.0001). At baseline and across all sleep nights, COC participants reported higher mood (p<0.05), less difficulty waking (p<0.01) and fewer physical ailments (p<0.01) than HCs. COC participants also reported less depth of sleep after RE1 (p<0.05).
Conclusions: One night of SD did not exacerbate cognitive performance deficits in cocaine-dependent individuals. However, altered DSST and CPT performance were detected, which is indicative of altered psychomotor performance, and selective attention and/or impulsivity, respectfully. Collectively, these data suggest that COC subjects have disrupted cognitive function, which could impair daily functioning and decision making.
Financial Support: NIDA Grants: DA016542, T32DA15036, K24DA15116, 5K01DA025125, and KO5DA00343

57

INVESTIGATION OF SENSITIVITY TO SMOKING-RELATED STIMULI AS A FUNCTION OF INITIAL ABSTINENCE DURATION.

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Aims: Initial sustained smoking abstinence (ISSA) is a robust predictor of longer-term smoking cessation. We have been investigating whether ISSA directly lowers relapse risk in a human lab model. Our prior studies have shown that ISSA decreases nicotine withdrawal, and the relative reinforcing effects of smoking vs. money, and increases ratings of ease of abstaining. The present study aims to examine whether ISSA changes behavioral and neurobiological sensitivity to smoking-related stimuli.
Methods: Participants were randomly assigned to one of two 15-day conditions in which payment was contingent on abstinence across all 15 days (15C) or just the final 2 days (2C). Participants completed fMRI sessions at baseline and on day 14 during which they viewed smoking-related and neutral stimuli and completed cigarette-craving scales (1-10). On day 15 participants completed a smoking preference session in which they made exclusive choices for smoking vs. money.
Results: Ratings of nicotine withdrawal decreased and ease of abstaining increased in the 15C vs. 2C conditions, and 15C participants were less likely to smoke in the preference session. Craving ratings in response to smoking-related and neutral stimuli were more than 2-fold lower in the 15C than 2C conditions on day 14, although in both conditions smoking-related stimuli continued to occasion higher ratings than neutral stimuli. There were no significant differences between treatment conditions in neural response to smoking-related or neutral stimuli.
Conclusions: 15 days of ISSA compared with 2 days reduced indicators of relapse risk (e.g., withdrawal and relative reinforcing effects of smoking) and decreased overall craving for cigarettes, independent of stimulus type. This suggests that reduction in overall craving during an ISSA period may be more important to lowering relapse risk than reduction in sensitivity to smoking-related stimuli per se.
Financial Support: R01 DA008076-15A1 & T32 DA07242-17 from NIDA

58

A COMPARISON OF DSM-IV AND DSM5 SUD CRITERIA IN A SAMPLE OF ADOLESCENTS.

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Aims: This study examined diagnostic agreement between DSM-IV-TR and DSM5 criteria for substance use disorders (SUD) in a nationally-representative sample of adolescents. This study investigated two questions: (1) Are there high levels of diagnostic agreement between DSM-IV and DSM5 criteria? and (2) Do youth diagnosed with a SUD in DSM-IV only, DSM5 only, both classification systems, or neither differ in severity of substance use?
Methods: The sample consisted of adolescents ages 12-18 (N =20,421) that completed the 2009 National Survey on Drug Use and Health. The sample was 51% male, 59% Caucasian, 17% Latino, 14% African-American, and 10% other race. Analyses focused on past year use for the following substances: alcohol, cannabis, cocaine, opioids, inhalants, hallucinogens, stimulants, and sedatives. Descriptive analyses were conducted to examine DSM-IV and 5 prevalence rates for each substance. Diagnostic agreement and kappa coefficients were calculated to assess agreement between DSM-IV and 5 criteria. A series of ANOVAs compared the frequency of substance use for youth that met DSM-IV criteria only, DSM5 criteria only, both DSM-IV and 5 criteria, and neither.
Results: Diagnostic agreement between the DSM-IV and 5 criteria ranged from 88% to 94% for the eight substances examined (κ = .71 to .79, $p<.01$). A series of ANOVAs revealed significant differences in days of use across diagnostic groups for all 8 substances, with youth that met both DSM-IV and 5 criteria reporting the most use followed by DSM5 only, DSM-IV only, and no diagnosis ($p<.05$).
Conclusions: Results from the present study indicate high rates of diagnostic agreement between DSM-IV and DSM5 SUDS criteria across all substances. Furthermore, youth that met criteria for DSM-IV and 5 criteria or DSM5 only reported more frequent use than youth who met DSM-IV criteria only. These findings provide preliminary support for the proposed DSM5 criteria to accurately detect problematic substance use among adolescents. Limitations of the study and implications for future research will be discussed.
Financial Support: None

59

POSITIVE RESULTS FROM PROJECT LAZARUS COMMUNITY-BASED PRESCRIPTION OPIOID OVERDOSE PREVENTION.

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Aims: The Aims of this project are to learn from implementation of a community-based prescription overdose prevention program and to evaluate the results of the intervention from 2007 through 2011.
Methods: In response to the 3rd highest drug overdose death rate, Wilkes County, NC initiated a public health prescription opioid overdose prevention program that includes supply reduction, demand reduction, diversion control and harm reduction. The intervention includes: 1) community coalition building, 2) epidemiologic monitoring, 3) primary overdose prevention efforts, 4) naloxone prescribing to community members, and 5) program evaluation. Primary prevention efforts included: one-on-one physician education, pill take-back days, fixed disposal sites, community awareness, expanded access to drug treatment, and other measures. Evaluation data were obtained from vital statistics, hospital emergency admissions and prescription monitoring program (PMP).
Results: The overdose death rate dropped from 46.6 per 100,000 in 2009 to 24.5 in 2010, a 47.4% decrease. Hospital emergency admissions dropped 15.3% from 2009 to 2010. (The first 11 months of 2011 show further decreases in deaths and admissions.) More than 70% of controlled substance prescribing clinicians are registered to use the state's PMP (NC average: 21%). Decedents who received prescriptions for the opioid implicated in their fatal overdose from a Wilkes County physician decreased from 82% in 2008 to 10% in 2010; no OD deaths in the first 11 months of 2011 involved an opioid prescription from a Wilkes practitioner.
Conclusions: Project Lazarus has begun to reduce the burden of opioid overdose mortality through a novel and comprehensive community-wide approach. However, public health programs must openly acknowledge the difficulties in changing behavior and set realistic time frames for intervention to take effect.
Financial Support: Community Care of North Carolina and Drug Policy Alliance. One-time funding from Purdue Pharma LP via unrestricted educational grant. Purdue made no contributions to design, implementation, evaluation, or publication.

60

JOINT TRAJECTORIES OF METHAMPHETAMINE, CANNABIS, AND ALCOHOL USE FOLLOWING TREATMENT FOR METHAMPHETAMINE USE.

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Aims: For methamphetamine(meth) users, research on posttreatment drug use outcomes has focused primarily on meth with little attention to concurrent patterns of other substances. This paper examines joint trajectories of meth, cannabis, and alcohol use during a period of up to 13 years following a treatment episode in the mid-1990s, identifying trajectories, and comparing trajectory groups on demographics, drug use history, and characteristics measured at different points in the posttreatment period.
Methods: Data are from a longitudinal study of 351 meth users with intensive Natural History interviews conducted at 3, 6, and 15 years following treatment. Use patterns were examined with group-based trajectory models. Chi-square or general linear models compared pattern groups on selected user characteristics.
Results: For meth, 5 distinctive use patterns were identified: consistent no/low, increasing to high, low/mid but increasing, gradual decline, rapid decline. For cannabis, 4 patterns emerged: no/very low, consistent low(weekend), consistent high, increasing. Comparison of selected joint pattern groups suggest that the low meth/low cannabis group (26% of total) were most likely to be female (58% vs. 13-40% for other major groupings), more likely to have been employed early in trajectory (51%), and had highest participation in self-help (average 31 months over trajectory period). The group with gradual or rapid decline in meth use while high or increasing cannabis use was least likely to have been employed at first interview (8%), had the highest depression score at recent interview (16 vs. 10 for other groups) and the lowest participation in self-help (11 months). The group with low meth but high cannabis use (5% of total) was most likely to be male (87%). Additional comparison results are presented, as well as patterns and comparisons for alcohol use pattern groups.
Conclusions: Results may help identify meth users at risk for continued use or relapse, not only of meth but also of cannabis and alcohol, and optimal periods for intervention along their substance use trajectories.
Financial Support: NIDA DA025113, P30 DA016383-06

61

RELATION OF IMMEDIATE TREATMENT RESPONSE AND END-OF-TRIAL OUTCOMES IN PLACEBO-TREATED METHAMPHETAMINE-DEPENDENT PATIENTS.

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Aims: Placebo effects exist across a broad range of medical treatments, impact both self-reported and biologically-verified outcomes and complicate interpretation of clinical trials data. Research examining placebo responding in addiction medicine trials is scarce. Data from clinical trials of psychiatric medications suggest that placebo responding is characterized by immediate improvement followed by symptom fluctuation. Among methamphetamine (MA) dependent individuals randomized to a placebo and behavioral support condition, we hypothesized that immediate abstinence would be a necessary but insufficient predictor for end-of-trial (EOT) abstinence.
Methods: Participants were treatment-seeking individuals randomly assigned to conditions that delivered placebo pills and behavioral support from medication trials for methamphetamine dependence. Receiver operating characteristic (ROC) analyses assessed the predictive power of immediate abstinence, assessed by thrice weekly urine screening, for EOT abstinence.
Results: Sixty percent of individuals with complete abstinence in the first two weeks of treatment were abstinent at EOT while 18% of people who failed to meet this standard were abstinent at EOT. ROC analysis suggested that three MA positive screens within the first two weeks of treatment optimally predicted persistent EOT methamphetamine use. The inability to achieve at least three MA negative screenings in the first two weeks is associated with greater than 90% likelihood of treatment failure. A third week of screening added minimally to the prediction of EOT outcomes. The prediction of treatment failure was more precise than the prediction of treatment success.
Conclusions: The absence of a clinical response in the first two weeks of placebo treatment combined with behavioral support signals high risk of treatment failure. The vast majority of information regarding placebo response from a12-week trial is obtained in early in the trial. These effects have important implications for clinical practice and research design.
Financial Support: NIDA P50 DA18185 & T32 DA026400.

62

A RANDOMIZED PILOT OF COMMUNITY REINFORCEMENT AND FAMILY TRAINING FOR TREATMENT RETENTION.

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Aims: Aim is to conduct an initial evaluation of the efficacy of Community Reinforcement and Family Training for Treatment Retention (CRAFT-T) relative to treatment as usual (TAU), in helping persons with opioid dependence remain in treatment following a short-term BUP/NX taper. It is hypothesized that CRAFT-T will be significantly more effective than TAU at retaining IP's in treatment.
Methods: This Univ. of Cincinnati IRB approved randomized pilot consists of screening/baseline, treatment, and follow-up. Participants are 50 dyads, including an opioid dependent person (IP) and their concerned significant other (CSO), recruited from a community based detoxification. CRAFT-T consists of 2 joint sessions (CSO & IP) followed by 10 individual CSO sessions in a 14 week period, with 2 optional sessions within 6 months. IP's receive either TAU or TAU + CRAFT-T. The primary outcome is IP's time to first drop of 30 days from treatment.
Results: Between 1/7 & 8/26/11 50 dyads randomized to TAU + CRAFT-T (n=27) or TAU (n=23). Urn randomization balanced on 3 variables: a) CSO relationship to IP = parent or other, b) race of CSO = African American or other, c) location Delaware or Columbus, OH. CSOs were; 92% females, 50% parents, 92% white, average 43 years old. IP's were; 100% opioid dependent, 82% male, 96% white, and average 29 years old. IPs attended 91% of the planned sessions and, CSO's attended 64% and 19% of the planned & optional sessions respectively. The primary outcome is IPs time to first drop from treatment therefore no missing data on primary outcome. Three IPs remain in treatment; the primary outcome will be presented.
Conclusions: Opioid dependent persons and their CSOs volunteered to participate in this intervention. Opioid dependent IPs received short-term (13 day) taper detoxification without ongoing medication assistance which lead to rapid relapse. While relapses had a demoralizing effect on CSOs they continued to participant in CRAFT-T and some successful at re-engaging the IP in treatment.
Financial Support: NIDA #1K23DA021512 (PI Brigham)

63

PSYCHOSOCIAL PROBLEMS AMONG TRUANT YOUTH: A MULTI-GROUP, EXPLORATORY STRUCTURAL EQUATION MODELING ANALYSIS.

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Aims: Truant youth represent a critical group needing problem-oriented research and involvement in effective services. There is a need to examine the interrelationships among multiple domains of psychosocial functioning among this population.
Methods: Recruitment of truant youth occurred in two locations. For interested families, an in-home meeting is scheduled to discuss the project and to conduct baseline interviews. Subsequently, youth and parent/guardian are randomly assigned to one of three project service conditions: the Standard Truancy Services, two BI sessions with the youth, or two BI sessions with the youth and one BI session with the parent. The BI sessions are based on the work of Winters and Leitten (2007).
Results: EFA with Geomin rotation was used to estimate a factor solution involving seven variables: anxiety, depression, mania, ADHD, trauma, delinquency, and substance use diagnosis. A two-factor solution was obtained. Factor 1 appears to be a general factor-all variables except substance use diagnosis are significantly loaded. Factor 2 is more problem specific with significant loadings for delinquency and substance use diagnosis. The two factors are not significantly related to one another.
We also examined the fit of the two factor model across demographics. Multi-group model specification involved measurement invariance across the various comparison groups. Girls are more likely to experience the issues reflected in Factor 1, as are younger youth, and non-Hispanics.
Conclusions: Our results document the high prevalence of psychosocial difficulties experienced by the truant youths. This study provides an informed understanding of such youth and their families, and indicates the serious need for ongoing, in-depth assessments.
Financial Support: This study is an on-going NIDA funded project, Grant Number DA021561.

64

EVIDENCE-BASED MULTIMEDIA TOOLKITS DURABLY IMPROVE COUNSELOR ADHERENCE IN GROUP COUNSELING WITH MINIMAL TRAINING: 6-MONTH FOLLOW-UP RESULTS.

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Aims: Adapting evidence-based psychosocial treatments into disseminable formats suitable for community treatment programs is challenging. We translated proven psychosocial treatments into a multimedia curricula toolkit (TK) to help counselors deliver clinically useful group sessions that convey core elements of cognitive-behavioral relapse prevention (RP). We tested the durability of counselor adherence improvements and found post-training and describe counselor use of core RP skills of homework review and functional analysis.
Methods: We coded 3 sets of treatment groups run by 14 counselors prior to receiving the TK curricula, post-training, and at 6-months follow-up. Each counselor's best effort on 2 preselected RP topics, Coping with Craving (CC) and Drug Refusal (DR), was coded at baseline. Counselors attended a 3-hour training to familiarize them with the TKs; they received no additional direct training or supervision on these particular sessions. Observers then attended 4 post-training groups and 4 follow-up groups run by counselors using the TKs, including the TK groups for CC and DR topics.
Results: There were significant, large effect improvements in frequency and extensiveness in delivering CC ($F(2, 12) = 10.94$, $p = 0.002$); and DR content ($F(2, 12) = 8.40$, $p = 0.005$) with TKs; adherence improvements were durable out to 6 months. Skillfulness of delivery did not significantly improve. The majority of counselors conducted functional analysis (83%) and assigned homework (57%) at a criterion skill level, but rates of counselor engagement declined over repeated sessions; rates of engagement showed slight, non-significant declines at 6-months.
Conclusions: Multimedia toolkits may be a cost-effective, disseminable approach to improve group counseling in community treatment with minimal training; however, controlled trials are needed and ongoing supervision may be critical to improve skillfulness and counselor engagement with core RP skills.
Financial Support: NIDA R01 DA025034

65

IDENTIFYING ADULT ADHD IN ADULT MARIJUANA TREATMENT SEEKERS.

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Aims: Co-occurrence of cannabis dependence and ADHD is prevalent among adolescents (ADHD rates range from 34%-48%). To our knowledge, there are no published rates of adult ADHD in marijuana using adults (MUA) seeking treatment. This study aims to estimate prevalence of adult ADHD among MUA and to identify a scale that would have the most utility to screen for this co-morbidity.
Methods: Adults seeking treatment for marijuana use completed the ADHD Rating Scale (AARS), Wender Utah Rating Scale (WURS) and Adult ADHD self-report scale (ASRS). The observed proportion of positive ADHD scores for each scale was calculated. Previously, using the CAADID, the sensitivity and specificity of these scales were calculated in a cocaine dependent population (Levin et al, CPDD 2009). Using the law of total probability, algebra and probability identities, a population proportion (P(D)) of ADHD was expressed as a function of the sample proportion of positive findings (P(+)), the sensitivity and specificity (Pavlicova and Glass; technical report). This function was used to estimate the (P(D)) of adult ADHD in MUA.
Results: Ninety-nine participants completed the ADHD scales; 74% male, 45% Caucasian, 25% African American, 21% Hispanic, 9% Other. The average age was 35. The (P(+)) ranged from 29%-53% and the calculated (P(D)) ranged from 34%-46% for all scales; the AARS alone and the AARS+WURS were the most comparable and produced prevalence estimates of 33%-34% and 29%-36%, respectively.
Conclusions: Prevalence of adult ADHD in MUA may be strikingly greater than rates in other substance using populations and up to 6 times greater than the general population. Substance abusers with ADHD do less well in treatment, therefore, treating ADHD may improve the outcome of treatment for cannabis abuse. The AARS and WURS can efficiently screen for adult ADHD in this population and get a population estimate quickly and accurately. There is the limitation that the sensitivity and specificity were calculated using a sample of cocaine treatment seekers.
Financial Support: NIDA grants: P50DA09236-16, K24 DA029647

66

IMPLEMENTATION OF AN ELECTRONIC INFORMATION SYSTEM TO ENHANCE PRACTICE AT AN OPIOID TREATMENT PROGRAM.

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Aims: The Addiction Research and Treatment Corporation is an outpatient opioid treatment program that provides primary medical care, including HIV/AIDS care for approximately 3,000 predominantly minority adults in New York City. We received National Institute on Drug Abuse R01 funding to study the implementation of an electronic health information system integrating counseling, social services, medical services, case management, HIV services, methadone dispensing, and administrative/fiscal data.
Methods: Four domains (Quality, Productivity, Satisfaction, and Financial Performance) were evaluated utilizing a pre and post-implementation research design. A fifth domain, Risk, was dropped from the analysis due to insufficient numbers for valid statistical comparison.
Results: For Quality, pre-implementation annual medical assessments and annual, 30-day, and 90-day multidiscipline assessments were timely for 83% and 70%, 72%, and 42% of cases, respectively. Post-implementation, timeliness of annual medical and annual multidiscipline assessments was 97% and 96%, 87%, and 70% respectively, all highly statistically significant improvements. Also in the Quality domain, hepatitis C viral load was appropriately performed in 85% of cases pre-implementation and 81% post-implementation; a non-significant difference. For Satisfaction, there was no change for patients and a non-statistically significant upward trend post-implementation for staff. Productivity tended to decline post-implementation; reaching statistical significance for counselors. Financial Performance (revenue per capita staff; cost per patient visit) did not change significantly.
Conclusions: Despite results that were somewhat less robust than expected in some of the domains examined; had we not implemented the electronic information system, healthcare reform and recent changes in documentation and reimbursement for services would have paralyzed our agency.
Financial Support: National Institute on Drug Abuse (R01 DA022030)

67

SELF-EFFICACY, COPING SKILLS, AND PROBLEMS RELATED TO MARIJUANA USE IN COMPUTER-ASSISTED AND THERAPIST-DELIVERED INTERVENTIONS.

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Aims: This study compared therapist-delivered and computer-delivered interventions for cannabis use disorders on putative mechanisms of change and outcome indicators. The primary hypothesis was that computer-delivered therapy would produce at least comparable positive change lending empirical support for this treatment modality.
Methods: 75 adults (60% African American, 57% male) seeking treatment for cannabis use were randomized to a 2-session Motivational Enhancement Therapy (MET), therapist delivered MET/Cognitive Behavioral Therapy plus Contingency Management (tMET/CBT+CM), or computer delivered MET/CBT plus CM (cMET/CBT+CM). Self-efficacy (Stephens et al., 1995), coping strategies (Litt et al., 2005) and marijuana-related problems problems (Stephens et al., 2000) were assessed at intake, end of treatment, and 3 months post-treatment. Mixed model analyses of variance (ANOVA) compared treatment conditions.
Results: No significant main effects for treatment condition or interaction effects for treatment condition and time were observed for any of the dependent variables. A significant effect of time was observed for all three variables. Post-hoc analyses showed MET produced a significant improvement over time only for marijuana problems ($p<.02$). For both tMET/CBT+CM and cMET/CBT+CM, significant improvement over time was observed for self efficacy ($p<.01$) coping skills ($p<.02$), and marijuana problems ($p<.01$).
Conclusions: Findings suggest therapist delivered and computer delivered MET/CBT+CM engender comparable changes in self efficacy and coping skills and equivalent impact on problems related to marijuana. Computerized interventions are a viable method of treatment delivery and have become increasingly more important to enhance access to and reduce costs associated with substance abuse treatment. Of note, the changes observed with these MET/CBT+CM did not clearly differ from those observed with MET, perhaps indicating limited change across all conditions or inadequate power to detect differences.
Financial Support: NIDA: DA023526; T32DA022981; CTSA: 1UL1RR029884

68

RELIGIOUS ATTENDANCE AND SMOKING BEHAVIOR IN BALTIMORE: A PROSPECTIVE ANALYSIS USING THE EPIDEMIOLOGIC CATCHMENT AREA (ECA) STUDY.

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Aims: This prospective study examined the relationship between religious attendance and smoking cessation.
Methods: Participants (n=666) who smoked at wave three (1993-1996) of the Baltimore ECA study were sampled and followed until wave four (2004-2005). A Generalized linear model (GLM) was used to assess the relationship between religious attendance and smoking cessation between waves while controlling for confounders. Smoking cessation was defined as having stopped smoking completely between waves three and four. Religious attendance categories ranged from attending more than once per week to never.
Results: Attending religious activity more than once per week (vs. never) was associated with a 44% increase in smoking cessation (adjusted relative risk [ARR] = 1.44; 95% confidence interval [CI]=1.02-2.00). Those attending about once per week (vs. never) were 36% more likely to stop smoking (ARR= 1.36; 95% CI = 1.02-1.80). Lower frequencies of religious attendance were not significantly related to cessation.
Conclusions: The prospective nature of this study underscores the potential benefits of religious attendance on smoking cessation. Future research should evaluate how faith-based interventions may be used in smoking cessation programs.
Financial Support: This research was supported by the National Institute of Mental Health grant R01-MH47447 (P.I. William Eaton, PhD); and the National Institute on Drug Abuse grant T32DA007292 (P.I. Debra Furr-Holden, PhD).

69

SEX DIFFERENCES IN THE DISCOUNTING OF SEXUAL AND MONETARY REWARDS IN COCAINE DEPENDENCE.

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Aims: There is a well-established link between drug abuse and increased delay discounting. There have been inconsistent findings in the delay discounting literature regarding sex differences in the discounting of delayed monetary rewards. The aim of the present study was to examine sex differences in the discounting of both hypothetical sexual rewards and real monetary rewards. Both types of rewards were assessed to determine if any sex differences in discounting were specific to sexual outcomes or generalized to non-sexual outcomes.
Methods: Sixty-six cocaine-dependent individuals (46 males, 20 females) completed a Sexual Discounting Task assessing decisions between immediate unprotected sex and delayed sex with a condom across four hypothetical partners: most (and least) likely to have a sexually transmitted infection (STI), and most (and least) sexually desirable; a money delay-discounting task assessing decisions between smaller immediate and larger delayed money rewards, with actual reward delivery in one randomly selected trial.
Results: Male participants discounted sex with a condom at a statistically significant greater rate (i.e., preferred unprotected immediate sex to waiting for delayed sex with a condom) than female participants in three of the four conditions (i.e., no difference found in the most likely to have an STI condition). There were no statistically significant differences found between the sexes in the discounting of real monetary rewards.
Conclusions: The greater discounting of sexual outcomes, but not money outcomes, for males compared to females suggests a domain specific sex difference in delay discounting, and may be consistent with the evolution of different mating strategies between the sexes. These findings may have implications for informing sex-specific strategies in HIV prevention efforts.
Financial Support: NIH grants R21 DA026967 and T32 DA07209.

70

ECSTASY DEPENDENCE: IS THERE EVIDENCE FOR THIS SYNDROME IN FREQUENT ECSTASY CONSUMERS?

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Aims: In Australia, past-year ecstasy use is prevalent (3% of adults) yet primary treatment presentations are rare (6 per 100,000 adult population). Case studies of dependence exist but studies of the syndrome are limited.
Methods: Cross-sectional face-to-face interviews with 672 frequent (at least monthly; on average fortnightly) ecstasy consumers, including standardised measures of DSM-IV and working DSM-5 substance use disorder criteria.
Results: Using conservative assessments, 52% met past 6 month abuse criteria, 21% experienced significant withdrawal (multiple concurrent, distressing symptoms) and 24% met DSM-IV dependence criteria. Those classified dependent were more likely to initiate ecstasy use in adolescence, consumed ecstasy more frequently and in larger amounts, and experienced more health harms, psychological distress and service contact. Polysubstance use was similar between groups. Confirmatory factor analysis demonstrated that, consistent with amphetamines, DSM-IV dependence items for ecstasy fit a single syndrome model well, although a 2-factor structure comprising 'compulsive' and 'escalating' use factors fit significantly better, in keeping with findings for hallucinogens. Similarly, the DSM-5 single substance use disorder structure had superior fit than the DSM-IV structure of separate abuse and dependence factors.
Conclusions: Ecstasy dependence does appear to be a valid syndrome, as it identifies individuals experiencing increased problems with use, and is largely consistent with the syndrome structure for other drug classes. Screening for ecstasy use disorder is appropriate if coming into contact with this group. Unresolved questions include determining how the notion of dependence fits with the non-daily consumption patterns apparent in this sample, and the clear delineation of post-acute 'crash' from true withdrawal symptoms in survey instruments.
Financial Support: Australian Government Department of Health and Ageing

71

INCUBATION EFFECTS OF NICOTINE ARE DIFFERENTIALLY REGULATED BY ERK ACTIVITY IN THE PREFRONTAL CORTEX AND NUCLEUS ACCUMBENS SHELL.

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Aims: Chronic nicotine administration leads to elevations phosphorylated (active) ERK in the prefrontal cortex (PFC) but not the nucleus accumbens (NAc). These functional studies sought to determine if ERK activation in these mesolimbic projection areas contributes to nicotine self-administration during daily exposure to nicotine and following protracted abstinence from the drug.
Methods: Male Long Evans rats were trained to self-administer nicotine using a fixed ratio 1 schedule of reinforcement for at least 10 days and then changed to a progressive ratio (PR) schedule of reinforcement. Responding on an active lever led to presentation of a tone plus light stimulus paired with i.v. injection of 0.03 mg/kg nicotine (NIC) or light plus tone in the absence of nicotine (CUEonly). Immediately prior to PR, rats received local infusions of 0.2, or 0.4 ul U0126 (a selective inhibitor of the MEK kinase that phosphorylates ERK) or vehicle (VEH) into the NAc shell or PFC using a within-subject Latin-Square design. Following protracted abstinence from nicotine, animals received local infusion of VEH or 0.4 ul U0126 into the PFC or NAc shell using a between subject design.
Results: Consistent with previous neurochemistry data, local infusion of U0126 into the PFC but not the NAc shell resulted in dose-dependent decreases in active lever pressing and breakpoints of NIC animals during daily exposure to nicotine. Protracted abstinence from nicotine led to a significant increase in active lever presses and breakpoints of NIC animals that was not observed in CUEonly rats. Inhibition of ERK phosphorylation in the NAc shell blocked this increase in responding.
Conclusions: These data suggest that the ERK signaling contributions to motivation to work for nicotine is neuroanatomically selective. Activation of ERK in the PFC appears critical for daily administration whereas ERK activity in the NAc shell appears to regulate the incubation effects of nicotine.
Financial Support: This research was funded in part by the Virginia Foundation for Healthy Youth grant 8520667.

72

CONTEXT OF ADOLESCENT ALCOHOL SUPPLY IN A NATIONAL AUSTRALIAN COHORT.

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Aims: Parents are the largest supplier of alcohol to adolescents. Alcohol-specific rules and monitoring have been identified as important factors in adolescent alcohol use. However, to date, little research has addressed how such factors relate to adolescent alcohol initiation and parental supply. This research reports baseline data from a cohort investigating the context of alcohol supply to adolescents from parents and other sources. It is hypothesised that parental monitoring and alcohol-specific rules will be related to early adolescent alcohol use.
Methods: Parent-child dyads were recruited via schools. In total, 1808 dyads completed baseline surveys. Descriptive analyses were conducted in SPSS.
Results: Sixty-eight percent of children (M=12yrs) had tried alcohol; first trying at an average age of 9.7 years. Children who had tried alcohol were more likely to report less parental monitoring ($F=2.04$, $p=0.015$), and less strict alcohol rules ($F=14.65$, $p<0.005$). Those parents supplying alcohol had children who reported less strict alcohol rules ($F=12.78$, $p<0.005$). Regression analyses indicated that in addition to parental monitoring and alcohol-specific rules, externalising and depression scores predicted child alcohol involvement ($F=8.45$, $p=.000$).
Conclusions: Research on how parental monitoring and alcohol rules impact upon adolescent alcohol initiation and use is minimal. This research has significant implications for prevention and policy.
Financial Support: This research is funded by: Australian Research Council Discovery Project (DP1096668), Australian Rotary Health Mental Health Research Grant and Whitcroft Family Scholarship, and Foundation for Alcohol Research & Education Project Grant.

73

SHOULD CAFFEINE WITHDRAWAL AND CAFFEINE USE DISORDER BE INCLUDED IN THE DSM-V: A SURVEY OF PROFESSIONALS IN ADDICTION-RELATED ORGANIZATIONS.

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Aims: Caffeine Withdrawal was included in the DSM-IV as research diagnosis to encourage research that might help determine if it warranted inclusion in future taxonomies. Caffeine Dependence (not listed in DSM-IV) has received less attention in the literature, with findings suggestive of a significant Caffeine Use Disorder that is not exceedingly rare. The DSM-V Substance Use Work Group is developing recommendations on how to handle these diagnoses in DSM-V. This survey was conducted to obtain data on how professionals involved in the addictions field view caffeine.
Methods: A web-based survey was administered to members of four addiction-related organizations via e-mail requests sent by the organization (n=501). Six questions asked participants to rate beliefs about caffeine's addictive potential and diagnostic classification on a 7-pt Likert scale. General comments were solicited.
Results: A great majority believed cessation of caffeine could cause a withdrawal syndrome (95%) that is clinically important (73%). Less consistent responding was observed when asked if Caffeine Withdrawal should be in the DSM (48% positive, 28% negative, 24% neutral). The majority believed that some people develop a Caffeine Use Disorder (58%), but less unanimity was observed when asked if Caffeine Use Disorder should be in the DSM (44% positive, 38% negative, 18% neutral). The majority (60%) believed that some people could benefit from professional help for quitting caffeine. Psychiatrists were more likely than Psychologists to believe that Caffeine Withdrawal and Use Disorders should be in the DSM (62% vs. 45% and 55% vs. 40%, respectively).
Conclusions: Findings indicate more agreement across professionals on the prevalence and clinical importance of Caffeine Withdrawal than Caffeine Use Disorder. Clearly the field is divided on how to handle caffeine in the DSM. Resolution of such issues requires a clear definition of what criteria are necessary to determine whether a syndrome should be classified as a Substance Use or Mental Disorder.
Financial Support: CTSA: 1UL1RR029884

74

LIFE SATISFACTION AND ITS RELATION WITH TOBACCO CONSUMPTION IN SCHOLARS OF VALENCIA (SPAIN).

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Aims: To determine the relationship of perceived satisfaction with life at the moment and consumption of tobacco among school students in Spain.
Methods: Sample: 1698 students, mean age 14.88 (SD=1.85); 51,6% (n=876) are female. Instrument: "Pre-Chat Survey on Drug Addiction; during 2010-2011". It was used Chi-square test with an independent variable (satisfaction with life at the moment) with three categories (satisfied; regular; unsatisfied); and three dependent variables: 1) consuming tobacco only in special occasions; 2) all the weekends; and 3) every day.
Results: 7,1% (120) answered consuming tobacco only in special occasions (5,7% males; 8,3% females); 35 (2,1%) consume tobacco all the weekends (1,8% males; 2,3% females), and consuming daily 192 (11,3%) (10,8% males; 11,8% females). Significant association was found between the satisfaction with life at the moment and all dependent variables. Compared to those who not consume tobacco, has lower satisfaction with life those who consume only in special occasions ($X2 = 15,17$; $p<0.001$); all the weekends ($X2=9,25$; $p<0.01$); and every day ($X2=34,42$; $p<0.001$). Considering the males, significant association was found only among those who consume tobacco daily ($X2=5,79$; $p<0.05$); and among females, association was found in: consuming only in special occasions ($X2=18,79$; $p<0.001$); consuming all the weekends ($X2 = 15,75$; $p<0.001$); and consuming daily ($X2=31,07$; $p<0.001$).
Conclusions: Less satisfaction with life at the moment is associated with consumption of tobacco in scholars, especially in girls.
Financial Support: Plan Municipal de Drogodependencias (PMD), Ayuntamiento de Valencia, and Universitat de València.

75

OXYTOCIN: SHIFTING THE BALANCE BETWEEN DRUG AND SOCIAL REWARDS?

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Aims: Oxytocin is known for its role in birth, bonding and social relations. More and more researchers are demonstrating that oxytocin plays a direct modulating effect on the rewarding and entactogenic effects of drugs as well. The balance between the rewarding properties of social relations and external rewards such as alcohol and drugs can influence initiation of drug use, escalation of use and relapse. It is therefore very important for the addiction field to understand the role that oxytocin plays in susceptibility to addiction and it's possible use in treatment.
A strong social network and strong relations have been known to delay initiation of drug use and have a positive effect on treatment outcome when dependence has developed. Recent studies show that social relations have directly rewarding properties, which are mediated via a direct interaction between of the dopamine and oxytocin system. Special social relations can be rewarding in itself and can therefor balance the need for external, drug rewards; we suggest that the oxytocin system is important in setting this balance. Drugs reduce the value of social relations and visa versa.
The paper will discuss the biological bases of this balance. Direct modulation by oxytocin of the HPA-axis and the dopamine reward system are possible routes to translate experiences into changed sensitivity to reward and relapse.
Conclusions: The balance between the rewarding effects of drugs and social relationships could play a major role in drug initiation, continuation and relapse. Oxytocin might affects this balance in the brain by direct interaction with key regulatory systems. Understanding this balance opens pathways for early intervention and treatment.
Financial Support: This research was supported by the University of Adelaide (FBP) and by a Veni grant (MT) of the Netherlands Organization for Scientific Research (NWO) (451-07-013).

76

ALCOHOL USE AND COGNITIVE IMPAIRMENT AMONG OLDER HOMELESS PERSONS.

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Aims: Introduction: Alcohol abuse/dependence and traumatic brain injury are highly prevalent among persons with a history of homelessness. Both conditions are associated with cognitive deficits that can affect the extent to which an individual is able to function independently in the community.
Aims: To measure the association between alcohol use disorders and cognitive impairment in older Australians who are homeless.
Methods: Fifty clients were recruited from an inner–city crisis accommodation centre. Clients were were aged 45 years or older and had been homeless within the past 6 months. Participants were administered a face-to-face survey to assess alcohol use disorder and cognitive impairment.
Results: The lifetime prevalence of alcohol use disorders in the sample was 95.5%; the median age that these participants first drank alcohol was 13 years while the median age of onset of regular drinking was 16 years. The prevalence of any acquired brain injury (ABI) was 88% with alcohol-related brain injury (ARBI) being the most common type. Indeed, among those with any ABI, 86% had experienced an ARBI and the mean number of incidents experienced was 17. The next most common form of ABI was traumatic brain injury (TBI), which also had the second highest frequency of exposure with a mean of 8 incidents. The prevalence of hypoxic events was 53% and the mean number of events was 4. In comparison, infectious events were rare. Seventy-seven percent of the total sample screened positive for mild cognitive impairment (MCI), and this rate was higher for participants diagnosed with lifetime alcohol dependence (77%) compared to participants diagnosed with lifetime alcohol abuse (43%).
Conclusions: A need exists for the expansion of services of neuropsychologists for the care of older people who are homeless with a history of alcohol related disorders. Compromised executive functioning (due to alcohol misuse) requires adjustments to client management including flexibility in services delivery and the need for mainstream aged care services to accept and manage the needs of these individuals.
Financial Support: Funded bu the Alcohol Education & Rehabilitation Foundation

77

HEALTH AND SOCIAL CHARACTERISTICS OF PRESCRIPTION OPIOID-ABUSING MEN.

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Aims: To examine health and social characteristics of high risk prescription opioid abusing men who have sex with men (MSM) in Miami, FL, enrolled in a randomized clinical intervention trial. Hypothesis: Prescription opioid abuse among MSM will be associated with stimulant (cocaine and/or methamphetamine) use and increased health and social risks.
Methods: Computer-assisted personal interviews included well-tested, comprehensive measures of substance use and health and social risks. Eligible MSM were 18-55 years old and reported heavy drug and/or alcohol use (6 or more times) and unprotected anal sex in the past 90 days (N=515).
Results: The sample included non-Hispanic White (N=250), African American/Black (N=110), and Hispanic (N=133) MSM. Median age was 40. 129 (25%) men reported current (past 90 days) prescription opioid abuse. Mean days cocaine use for current opioid abusers were 2.2 times higher than for non-opioid abusing MSM (p<.000). Current opioid abusing MSM were more likely to report DSM-IVR substance dependence (p<.000), severe mental distress (p=.011), and histories of substance abuse treatment (p=.001), victimization (p=.031) and arrest (p<.000) than non-opioid abusers. Further, current opioid abusers had higher odds of drug injection during the past 90 days compared to non-opioid abusers (p=.011), with methamphetamine being the most prevalent injected drug. There were no significant differences in age or race/ethnicity.
Conclusions: Among high risk MSM in South Florida, opioid abusing men report higher levels of prior and ongoing mental health and social risks than their non-opioid abusing counterparts. The use of prescription opioids is associated with more frequent cocaine use, presumably to moderate effects of cocaine. Similarly the strong association between opioid abuse and methamphetamine injection is also likely for the purpose of moderating the effects of methamphetamine use.
Financial Support: This research was supported by DHHS Grant DA024579 from the National Institute on Drug Abuse.

78

DOES CLINICAL MONITORING IMPACT TREATMENT OUTCOMES?

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Aims: Monitoring clinical status of clients during outpatient substance abuse treatment (SAT) is recommended for decision making, quality improvement, and reporting at the individual and program level. Pilot data are reported from a randomized trial to determine preliminary efficacy of a Monitoring and Feedback Intervention (MFI) compared to treatment as usual (TAU) for clients in outpatient SAT. It was hypothesized that the MFI would positively impact the treatment process, as well as during treatment and short-term outcomes.
Methods: 6 counselors from an outpatient clinic were randomly assigned to provide MFI or TAU. 96 new admissions were randomly assigned to receive MFI (n=54) or TAU (n=42). During individual treatment sessions, clients in MFI completed a weekly, counselor-administered, web-based assessment of 19 clinical monitoring items. Clients in TAU received standard weekly individual sessions. MFI counselors received training to administer assessments, review system case reports, and respond clinically to data collected. Outcomes were measured during the 3-month intervention.
Results: More MFI clients were in treatment at 30 days post admission compared to TAU clients (86% vs. 74%); 60 days (65% vs. 48%), and 90 days (49% vs. 38%). Results were not significant and effect sizes were small (>0.1 to <0.2). At 1 month a urine screen showed that 35% of MFI clients and 53% of TAU clients tested positive for at least one drug; at 3 months 39% of MFI clients and 52% of TAU clients tested positive. Similarly, these results were not significant and effect sizes were small. Receipt of past 30 day multi-domain treatment services was measured at month 1; while there were no significant group differences, there was a small effect for employment/support services (MFI 40% vs. TAU 27%). Therapeutic alliance did not differ significantly for the two groups.
Conclusions: The MFI is an innovative treatment enhancement for outpatient SAT. Counselor and client acceptability were high, and initial results suggest a small intervention effect on important variables.
Financial Support: NIDA Grant R01 DA021154

79

GENDER DIFFERENCES OF HETEROSEXUAL ANAL SEX AMONG MEN AND WOMEN IN SUBSTANCE ABUSE TREATMENT.

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Aims: Heterosexual anal intercourse (HAI) is a higher risk behavior for HIV transmission than vaginal intercourse. The NIDA Clinical Trials Network Safe Sex for Men/Women protocols (CTN 0018/0019) provided a unique opportunity to examine this understudied high risk behavior in men and women in substance abuse treatment.
Methods: Men(n=539)and women(n=422)enrolled in CTN 0018/0019 reporting engaging in heterosexual activities in the 90 days prior to baseline assessment were included. Rates of engaging in HAI were determined for any, main and casual partners. Gender differences were analyzed with contingency table analysis utilizing the χ^2 statistic. Based on prior research, the following variables have been thought to be related to high risk sexual behavior among substance abusers: age, psychiatric severity, lifetime history of sexual abuse, ethnicity, stimulant use, number of sexual partners. These variables were entered into separate logistic regression analyses for men and women in an effort to identify correlates associated with HAI.
Results: More men (32.8%) than women (27.1%, χ^2=3.7, p=.05) report engaging in HAI. These rates are higher than the prior 90 day rates reported for both men (6.0 to 15.9%) and women (3.5 to 13.0%) age 25-59 in the National Survey of Sexual Health and Behavior. Men (28.6%) and women (23.2%) reported similar rates of engaging in HAI with their main partners (p=.09). Men were much more likely to report HAI with their casual partners (34.1%) than women (16.7%, $\chi^2$19.4, p<.001). In the logistic regression model for men, having more sex partners, being younger, and white were significantly associated with engagement in HAI. For women, stimulant use and younger age were the significant associations.
Conclusions: HAI is a behavior practiced by more men and women in substance abuse treatment than in the general population, and is a logical target of HIV prevention interventions.
Financial Support: NIDA grant U10 DA13714 (D. Donovan, PI)

80

BASELINE CHARACTERISTICS BY PRIMARY SUBSTANCE OF ABUSE OF OUTPATIENT CLIENTS IN A WEB-BASED INTERVENTION TRIAL.

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Aims: The purpose of this study is to compare demographic and clinical differences across classes of substances among clients recruited into an effectiveness trial of the Therapeutic Education System (TES), an efficacious, web-based version of the Community Reinforcement Approach.
Methods: Clients were recruited from 10 outpatient drug treatment programs within NIDA's Clinical Trials Network from June 2010-August 2011. Participants completed a brief eligibility screen followed by baseline assessment and randomization. Inclusion criteria were broad: 1) 18 years or older; 2) illicit substance use in the prior month; and 3) within the first 30 days of treatment. Those receiving opioid replacement medication were excluded. Assessment included sociodemographics, substance use, mental health, and internet use.
Results: 1,781 participants completed screening; 850 were ineligible (primarily absence of recent drug use) and 424 were eligible but not randomized. The randomized sample (n=507) was 38% female, an average of 41.5 years old, with varied primary substances of abuse (marijuana 23%; alcohol 21%; opioids 21%; cocaine 20%; stimulants 11%; other 5%). No differences by substance were detected on the Brief Symptom Inventory somatization or anxiety subscales; however depression scores differed (p=.02): alcohol (M=6.3), cocaine (M=6.0), opioids (M=4.8), stimulants (M=4.4); marijuana (M=4.3). Differences in frequency of internet use was found (p=.03). Primary marijuana (58%) and alcohol users (55%) reported daily internet use more than cocaine (35%), stimulant (38%), and opioid users (46%). Results of additional clinical characteristics will be reported.
Conclusions: This study was successful in recruiting a diverse, treatment-seeking sample. Clinical differences across primary substance of abuse have implications for treatment engagement and planning, as well as overall trial outcomes.
Financial Support: This research was supported by the NIDA National Drug Abuse Treatment Clinical Trials Network, U10 DA13035 (EV Nunes, J Rotrosen, Co-PIs) and NIDA K24 DA022412 (EV Nunes, PI).

81

OCCULT HEPATITIS B AMONG IN-TREATMENT NON-INJECTING DRUG USERS IN WEST CENTRAL MEXICO.

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Aims: Occult hepatitis B (OHB) infection is a nearly silent form of hepatitis B, but one which nevertheless can be associated with cirrhosis and hepatocellular carcinoma. There has been little research on OHB among non-injecting drug users (NIDUs). This is the first study to examine the prevalence of OHB among NIDUs receiving drug treatment in west central Mexico.
Methods: We sampled clients attending Centros de Integración Juvenil (CIJ) treatment programs in the west central Mexico states of Jalisco, Colima and Michoacan: 122 NIDU clients from nine community clinics and 30 NIDU clients from an in-prison program. Blood samples were analyzed for hepatitis B surface antigen (HBsAg), hepatitis B anticore antibody (anti HBc), antibody to hepatitis C and antibody to HIV. HBV DNA was detected by nested PCR of HBV genome; HBV genotypes were determined. Occult hepatitis B was defined as the presence of hepatitis B virus (HBV) DNA in individuals testing hepatitis B surface antigen negative.
Results: 10 (8.2 %) of the 122 community clinic clients were occult hepatitis B positive; 8 (26.6 %) of the 30 in-prison treatment clients were occult hepatitis B positive. For the two groups taken as a whole, the most frequent genotype was F (68%).
Conclusions: The prevalence of occult hepatitis B was relatively high for both the community NIDUs and the in-prison NIDUs. Although genotype H and G are the most common hepatitis B genotypes among the Mexican general population, the predominant genotype among this study's NIDUs was F. This is a concern as F is one of the three genotypes known to be associated with chronic hepatitis B infection leading to hepatocellular carcinoma and suggests different reservoirs of HBV. Non-injection drug users, particularly prison clients, could represent a high risk group for OBH
Financial Support: PROINV program from the Universidad de Guadalajara

82

SMALL VILLAGE/LARGE HELL: INCARCERATION AND GENDERED WORK IN DRUG TRAFFICKING.

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Aims: This research analyzes the ways in which women's economic and social positions in the Santa Monica prison in Lima, Peru are shaped by their labor in the global illicit drug trade.
Methods: Research methods for this ethnographic project included participant observation, life history and in-depth interviews with female prisoners over a period of 9 months. Analysis of fieldwork data included qualitative content analysis.
Results: This research shows that the transnational cocaine commodity chain is structured by race, class, gender and nationality and that incarcerated women in the Santa Monica prison are inserted into particular "links" of this chain based on the intersections of these systems of power. Furthermore, fieldwork demonstrates how the labor a woman performs in this chain determines her pathway into the prison as well as her socio-economic position inside the prison.
Conclusions: The results from this project are important for understanding specific processes of the global illicit trafficking of cocaine. It demonstrates how processes of drug trafficking are not only gendered, but also structured by race and class transnationally. This research also adds to an understanding of the gendered effects of War on Drug policies in the Latin American region. This is important in an analysis of how certain policies emanating from the United States are exported, reconfigured, contested and eventually lived out by individuals in "target" regions. Finally, this research project demonstrates how globalized drug trafficking affects localities and how it is also shaped by local sites such as the prison.
Financial Support: The author was supported as a predoctoral fellow in the Behavioral Sciences Training in Drug Abuse Research program sponsored by Public Health Solutions and National Development and Research Institutes with funding from the National Institute on Drug Abuse (5T32 DA007233).

83

MODERATE EXERCISE IMPROVES METHAMPHETAMINE USERS' PERFORMANCE ON NEUROCOGNITIVE TESTS.

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Aims: The aim was to characterize the effects of aerobic and resistance exercise versus health education on the neurocognitive function of treatment seeking methamphetamine users.
Methods: Participants completed baseline cognitive testing during the two weeks of treatment as usual in a residential treatment center. After stratifying by high or low methamphetamine use in the prior 30 days and gender, the participants were randomly assigned to receive the Exercise condition or Health Education (control condition) 3 x weekly for 8 weeks in conjunction with their substance abuse treatment. The ANAM cognitive battery, consisting of motor speed, logic, memory and attention tasks, repeated post-discharge at week 9 with follow-up testing at 3 and 6 months. Data represent the first 44 participants (22 in each group) to complete the intervention.
Results: GEE analyses of the DVs throughput and response time indicated that there were significant group by timepoint interactions on memory and motor speed tests with the exercise group exhibiting better performance than the education group (p's <.05).
Conclusions: Moderate exercise improves performance of methamphetamine users more than a health education intervention on several areas of neurocognition and in some areas improvements are still seen at 6 months.
Financial Support: Funded by NIDA grant DA027633 (Rawson, PI).

84

BENZODIAZEPINE DEPENDENCE: PERSONAL DEFINITIONS OF OLDER WOMEN.

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Aims: To examine the cultural experience and personal definitions of benzodiazepine (BZD) dependence among a sample of community-dwelling older women.
Methods: Women age 65 and older who reported regular use of a BZD over the previous 3 months at minimum were recruited via flyers. Three semi-structured ethnographic interviews were conducted in a mutually agreed upon place, were digitally recorded, and transcribed. Data were coded and analyzed for experience in order to access what was significant to informants.
Results: Though many informants self-reported dependence to their BZD, they did not meet the criteria for dependence based on the Severity of Dependence Scale. No informant reported that during the previous month their BZD use was out of control and only a few reported that either the prospect of a missed dose made them anxious or worried or that they worried about their use of their BZD. Women were more likely to report that over the previous month they wished they could stop using their BZD and that it would be difficult to stop or to go without their BZD. Informants based their personal definitions of dependency on information gathered over their lifetimes, from their culture, from experiences with family members and close friends who had dependence or addiction problems, and even from previous personal experiences with addiction and dependence. These definitions of dependence impacted informant's BZD usage patterns.
Conclusions: The available methods of identifying dependence in older adults have been shown to not necessarily reveal dependence in this population and future tools need to be developed that take older adults' reports into consideration. Uncovering personal definitions and the individually-mediated manner in which older women consume potentially addictive medications can help identify potential strategies for enhancing well-being in later life.
Financial Support: This research was supported by a predoctoral award from NIDA (F31DA025391); current funding on the Drug Dependence Epidemiology Training Program, with the Johns Hopkins University Bloomberg School of Public Health that receives support from NIDA (T32DA007292).

85

PRENATAL NICOTINE EXPOSURE MODIFIED BRAIN MYELINATION WITH SEX AND AGE DIFFERENCES.

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Aims: Children whose mothers smoked during pregnancy are more likely to develop drug addiction and psychiatric disorders such as conduct disorder, depression and autism. Most of these disorders are related to the deficits in the central myelination. We therefore tested the hypothesis that gestational exposure to nicotine (GN), the major psychoactive component in tobacco, changes central myelination.
Methods: Pregnant Sprague Dawley rats were treated with nicotine (3 mg/kg/day) or saline via osmotic minipumps from gestational days 4 to 18. Both male and female offspring were sacrificed during childhood [postnatal day (PD) 20-21], adolescence (PD 35-36), or adulthood (PD 59-60). The mRNA expression of thirty-two myelin-related genes in the prefrontal cortex (PFC) and caudate putamen (CPu) was examined using quantitative RT-PCR. The protein expression of myelin basic protein (MBP) was further evaluated using western blotting and immunohistochemistry.
Results: In the PFC, GN downregulated the mRNA expression of most myelin genes in both male and female juveniles. During adolescence, these genes remained downregulated in GN-treated females but became upregulated in GN males. In contrast, GN had no effects on myelin-gene expression in the PFC in either male or female adults. In the CPu, most myelin genes were upregulated by GN in female juveniles, showed normal expression in female adolescents and were downregulated in female adults. In contrast, these genes were generally upregulated in the male CPu during adolescence while they expressed normally in both juvenile and adult males. Furthermore, the unique modifications during adolescence were confirmed by analysis of protein expression.
Conclusions: Together we revealed that GN altered the expression of myelin genes, which differed across ages, sexes and brain regions. This study indicates that central myelination links neurological disorders with prenatal exposure to maternal smoking.
Financial Support: DA-012844, DA-013783 and DA-026356.

86

METABOTROPIC GLUTAMATE2/3 RECEPTORS DIFFERENTIALLY MODULATE DISCRIMINATIVE STIMULUS EFFECTS OF HALLUCINOGENS.

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Aims: Hallucinogenic drugs cause profound changes in human consciousness and perception, but the mechanism of action is not well understood. The 5HT2A receptor has been the only consistent mechanism of action. More recently, studies found that mGlu2 receptors are co-localized along with 5HT2AR and may be crucial for hallucinogenic activation within the brain. N,N-Diisopropyltryptamine (DiPT) is a synthetic hallucinogen that produces auditory effects in humans in contrast to the structurally similar analogue, dimethyltryptamine (DMT) which produces short lasting visual, episodic hallucinations. The role of mGluR2 was assessed in both DiPT and DMT.
Methods: Two-lever drug discrimination was used to investigate the mGlu2 receptor as a mechanism of action of DiPT and DMT in vivo. Adult male rats were trained to discriminate DiPT (5 mg/kg, 15 min) and DMT (5 mg/kg, 5 min) from saline under a FR10 schedule. The mGluR2/3 agonist LY379268 was tested for antagonism and the mGluR2/3 antagonist LY341495 for potentiation of hallucinogenic effects.
Results: The mGluR2/3 agonist (LY379268; 0.005-2.5 mg/kg) partially blocked the discriminative stimulus effects of DMT, but not DiPT. The mGluR2/3 antagonist (LY341495; 1- 2.5 mg/kg) facilitated the effects of DMT, but not DiPT.
Conclusions: The mGluR2 agonist and antagonist altered the discriminative stimulus effects of DMT, but not DiPT. Thus the mGluR2 may have a greater effect in visual hallucinations than auditory hallucinations. LY379268 did not fully block the discriminative stimulus effects of DMT, indicating that other receptors such as the 5HT2AR may contribute to the stimulus effects. Research on the mechanisms of DiPT and DMT may give further insight into the mechanisms of auditory versus visual hallucinogens. This may be of direct relevance to understanding why humans use hallucinogens and in the mechanism of auditory hallucinations in schizophrenia.
Financial Support: Supported by T32 AG020494, NIH N01DA-2-8822 and NIH N01DA-7-8872.

87

EFFECTIVENESS OF HARM REDUCTION SUBSTANCE ABUSE TREATMENT WITH METHAMPHETAMINE-USING MSM.

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Aims: Prior clinical research established the effectiveness of culturally tailored, cognitive-behavioral substance abuse treatment with methamphetamine-using men who have sex with men (MSM). This study examined the effectiveness of cognitive-behavioral substance abuse treatment that is being implemented from a harm reduction perspective.
Methods: Methamphetamine-using MSM enrolled in a treatment outcome study during the first 60 days of outpatient substance abuse treatment at the Stonewall Project, which assists clients with pursuing self-identified goals related to methamphetamine use and sexual risk taking behavior. To date, 38 methamphetamine-using MSM have completed the 6-month assessment (95% follow-up rate) for this ongoing study. Using repeated measures ANOVAs, we examined changes in self-reported frequency of methamphetamine use (past 30 days), number of anal sex partners (past 3 months), and affective states (using the Differential Emotions Scale) over the 6-month follow-up period.
Results: Most participants were HIV-positive (63%), middle-aged (M = 44, SD = 11), Caucasian (63%), and attended at least some college (58%). Participants reported a clinically interesting, 37% reduction in the frequency of methamphetamine use, but this trend was not statistically significant ($F(1, 37) = 3.06$, $p = .09$). However, participants reported significant decreases in overall number of anal sex partners ($F(1, 37) = 7.10$, $p = .01$; 6.9 (SD = 12.4) to 2.4 (SD = 3.8)) and anal sex partners while feeling the effects of methamphetamine ($F(1, 37) = 5.30$, $p < .05$; 5.7 (SD = 12.2) to 1.4 (SD = 3.4)). Finally, participants reported significant increases in positive affect ($F(1, 37) = 5.30$, $p < .05$) and decreases in negative affect ($F(1, 37) = 11.42$, $p < .01$).
Conclusions: Harm reduction approaches to substance abuse treatment may be an effective method of addressing the co-occurring epidemics of methamphetamine use and HIV/AIDS among MSM.
Financial Support: California HIV/AIDS Research Program (CR08-SFAF422; CR08-SF423)

88

CHANGE IN ROUTES OF ADMINISTRATION FOR OXYCONTIN AND COMPARATORS FOLLOWING INTRODUCTION OF REFORMULATED OXYCONTIN® AMONG INDIVIDUALS ASSESSED FOR SUBSTANCE ABUSE.

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Aims: Reformulated OxyContin® (oxycodone HCl controlled-release) Tablets (ORF) has physiochemical barriers to crushing and dissolving to reduce abuse by non-oral routes of administration (ROA, e.g., injecting, snorting, and smoking). Shipments of original OxyContin (OC) stopped on August 5, 2010, and ORF started on August 9, 2010. We assessed changes in ROA for OxyContin, ER oxymorphone and ER morphine among individuals assessed for substance abuse problems after ORF introduction.
Methods: The NAVIPPRO system uses a computer-administered interview (ASI-MV) for adult treatment planning that collects self-report of past 30 day substance abuse, including prescription opioids. Respondents differentiate abuse of prescription products and ROA using screen images. Historical rates and ROA patterns of OC were measured over 14 months before ORF introduction (June 2009 - August 8, 2010) and compared to ORF in the 11 months following ORF introduction (August 9, 2010 - June 2011).
Results: In the before period, there were 67,165 assessments, of which 12,035 reported prescription opioid abuse and 2,835 reported OxyContin abuse. In the after period, 7,233 of the 37,465 assessments reported prescription opioid abuse and 786 reported ORF abuse. Among OxyContin abusers, the percent reporting injecting decreased from 34.7% for OC in the before period to 14.0% for ORF in the after period, snorting reduced from 58.5% to 27.6%, and smoking reduced from 7.0% to 4.2%. Since this analysis was restricted to OxyContin abusers, the proportional decrease in non-oral abuse was associated with a proportional increase in oral abuse (54.3% to 76.7%); however overall, the number of oral OxyContin abusers per 100 assessments declined. No significant change in ROA patterns were observed for the comparator opioids.
Conclusions: While promising, these early results require continued monitoring to assess longer term impacts of the OxyContin reformulation on its abuse patterns.
Financial Support: Purdue Pharma & Inflexxion, Inc.

89

ASSOCIATIONS BETWEEN SELECTED STATE LAWS AND TEENAGERS' DRINKING AND DRIVING BEHAVIORS.

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Aims: To examine the associations between selected state level graduated driving licensing laws (GDL) and use-and-lose laws (laws that allow for the suspension of a driver's license for underage alcohol violations including purchase, possession, or consumption) with individual level alcohol-related traffic risk behaviors among high school youth.
Methods: Logistic regression models with fixed effects for state were used to examine the associations between the selected state-level laws and youth (ages 16-17 years old) drinking and driving behaviors (obtained from the Youth Risk Behavior Surveillance System, responses dichotomized as "0 times" or "1 or more times") over an extended period of time (1999-2009).
Results: 11.7% of students reported having driven after drinking any alcohol and 28.2% reported riding in a car with a driver who had been drinking on one or more occasions in the past 30 days. Restrictive GDL laws and use-and-lose laws were associated with decreased driving after drinking any alcohol and riding in a car with a driver who has been drinking alcohol.
Conclusions: Restrictive graduated driving licensing laws and use-and-lose laws may help to bolster societal expectations and values about the hazards of drinking and driving behaviors and are therefore partly responsible for the decline in these alcohol-related traffic risk behaviors.
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90

GENETICALLY INFLUENCED DEFICITS IN INHIBITORY CONTROL ARE ASSOCIATED WITH PROPENSITY FOR ADDICTION-RELATED BEHAVIORS IN MICE.

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Aims: Various dimensions of impulsivity have been implicated in addiction. While initial studies attributed these impairments in inhibitory control to exposure to and continued use of drugs, recent work has shown that individual differences in impulsive traits can predict propensity for aspects of addiction, suggesting a bidirectional relationship between addiction and impulsivity. As previous experiments in our lab have determined that impulsive responding in a reversal learning task is heritable, we aimed to test whether genetically-determined differences in this phenotype predicts propensity for addiction-related behaviors; specifically, we hypothesized that strains with poor impulse control would also exhibit a propensity to engage in high levels of cocaine self-administration and have difficulty in extinguishing this behavior.
Methods: BxD mice from strains exhibiting either good or poor reversal ability were implanted with jugular catheters and tested for acquisition of cocaine self-administration under FR1, FR2, and FR5 schedules and subsequently tested for drug-seeking behavior under extinction conditions. Psychomotor effects were also assessed after IP cocaine administration.
Results: Mice from high impulsive responding strains exhibited higher rates of cocaine self-administration than low impulsive responding strains. During extinction, they exhibited a slower rate to decrease drug-seeking responses, and persistant conditioned responding on the active lever. They also exhibited larger locomotor responses to cocaine at higher doses.
Conclusions: In summary, strains with a phenotype of poor inhibitory control over impulsive responses show an increased sensitivity to the psychomotor, reinforcing, and conditioning effects of cocaine. These data suggest that genetically-influenced deficits in this form of impulsivity are predisposing factors for susceptibility to substance abuse.
Financial Support: UL1-DE019580, RL1-MH083270, PL1-NS062410, T32-DA024635 and P50-MH077248

91

MENTAL HEALTH SERVICES UTILIZATION TRAJECTORY OVER TIME AND LONG-TERM PSYCHIATRIC OUTCOMES AMONG DRUG-DEPENDENT WOMEN.

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Aims: The aims of this study are: 1) to assess long-term psychiatric outcomes among drug-dependent women; 2) to examine the mental health services utilization trajectory during 6 years period after the enrollment of drug abuse treatment; and 3) to examine whether mental health services utilization improves long-term mental health status among this population.
Methods: The study includes 713 women who attended drug abuse treatment programs in 13 California counties during 2000-2002, and they completed a follow-up interview survey in 2010-11. The Addiction Severity Index was assessed at treatment enrollment and at follow-up, and the mental health services utilization data were obtained from the California Department of Mental Health (DMH). The 6-year trajectory of mental health services utilization after treatment enrollment was examined using growth mixture model.
Results: At the follow-up survey, study subjects demonstrated better psychiatric assessment results than the assessments at treatment enrollment ($p<0.01$). During the 6 years after treatment enrollment, the mental health services utilization significantly decreased over time ($p<0.01$); and the slope of trajectory significantly differed between subjects with and without psychiatric symptoms at baseline ($p<0.01$). Additionally, we fitted regression models and found that an increase in mental health services utilization over time is a significant predictor of better long-term psychiatric outcomes, after controlling for baseline psychiatric assessment, drug use at baseline and follow-up, and other demographic variables.
Conclusions: Findings suggest that interventions should encourage appropriate mental health services utilization and provide related resources for drug-dependent women, in order to improve their long-term mental health outcomes.
Financial Support: Supported by NIDA R01DA021183, P30DA016383, & K05DA017648 (PI: Hser)

92

USING TECHNOLOGY TO INCREASE ACCESS TO SUBSTANCE ABUSE TREATMENT IN PRISON.

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Aims: To test, among a sample of incarcerated offenders with mostly mild to moderate substance use disorders, the comparative effectiveness of the Therapeutic Education System (TES), a computer-based psychosocial treatment program, versus Standard Care on measures of self-reported drug use (e.g., weeks of abstinence), HIV risk behavior (both sex- and drug-related) and reincarceration.
Methods: Employs random assignment to either (1) TES, or (2) Standard Care, in a multi-site trial conducted in 4 States and 10 prisons. This prospective longitudinal study obtains follow-up data post prison discharge; interviews at 3- and 6-months to examine the comparative effect of these interventions on self-reported involvement in criminal activity, substance use and HIV-risk behavior and official record data of re-incarceration ranging from 8 to 14 months post discharge.
Results: A total of 513 subjects were recruited to participate in the study (TES N=258; Control N=255). Preliminary findings indicate that there are no significant differences between TES and Standard Care on measures of self-reported criminal activity, substance use and HIV risk behavior at both 3- and 6-months post prison release. In addition, there were no significant differences between groups on rates of reincarceration at 12 months post-prison release.
Conclusions: Preliminary results suggest that TES and Standard Care are comparably effective interventions as both produced substantial and significant reductions in self-reported criminal behavior, substance use and HIV risk behavior along with similarly low rates of reincarceration. If found to be cost-effective, TES could improve access to quality psychosocial interventions by providing a means by which substance abuse treatment in criminal justice settings could be expanded to reach a large portion of offenders that typically are not treated.
Financial Support: This ongoing ARRA-funded NIDA study, begun in 2009, and is supported by Award Number RC2DA028967 from the National Institute on Drug Abuse (NIDA)

93

PARENT-ADOLESCENT INTERACTIONS AND ADOLESCENT SUBSTANCE USE.

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Aims: Aims: One important factor in adolescents' development of substance abuse is their family environment. The present laboratory study examined observed parenting behaviors (support, structure, criticism) in parent-adolescent interactions, adolescents' heart rate (HR), blood pressure (BP), emotional, and cortisol responses to these interactions, and adolescent substance use initiation.
Methods: Methods: Fifty eight 10-16 year olds and their parents completed a 10 minute parent adolescent interaction task (PAIT) in which they discussed a personal conflict topic. Parental supportive, structuring, and critcizing behaviors were coded from the interaction. Before, during, and at repeated time-points after the PAIT, adolescents' HR, BP, reported emotions (anxiety and anger), and salivary cortisol were assessed. In a separate session, youth reported on their lifetime use of substances on the Youth Risk Behavior Survey (YRBS; Brener et al., 2002) and completed urine drug screens.
Results: Results: Findings indicated that lower parental structure was associated with youth's greater diastolic BP reponse ($F[3, 162] = 2.68$, $p < .05$) and lower parental support was associated at a trend level with youth's higher anger response ($F[3, 54] = 2.63$, $p = .06$) to the PAIT. Furthermore, higher systolic BP response to the PAIT and higher anxiety before and after the PAIT were associated with youth's substance use history (for systolic BP, $F[2, 52] = 3.34$, $p < .05$, for anxiety, $F[1, 56] = 5.68$, $p < .05$).
Conclusions: Conclusion: Findings suggest that heightened emotional and physiological responses to parent-adolescent conflict interactions in youth may be one pathway by which poor parenting is associated with youth's substance use and risk for abuse. Such arousal responses could be targeted in family-based substance abuse prevention programs for adolescents.
Financial Support: Supported by: NIH Grants (K01-DA-024759, UL1-DE19586), ABMRF/Association for Alcohol Research Grant, and AACAP Grant.

94

ATS ABUSE ADVERSELY AFFECTS BUPRENORPHINE MAINTENANCE TREATMENT IN MALAYSIA.

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Aims: Abuse of amphetamine type stimulant (ATS) substances has increased dramatically in recent years in Malaysia. A large proportion of opiate dependent individuals, including those in maintenance treatment with buprenorphine (BMT) or methadone (MMT), also abuse ATS.
Methods: We evaluated the relationship between ATS abuse and treatment outcomes in patients treated with BMT for 16 weeks during a previously completed randomized clinical trial evaluating the efficacy adding behavioral counseling to physician management. We also evaluated sex related HIV risk behaviors among ATS abusing patients receiving BMT.
Results: Participants (N=24) were all male, with the mean (SD) age of 40.5 (8.5), and the mean (SD) history of opiate abuse/dependence of 19.3 (8.7) years; 18 (75%) reported lifetime and 7 (29%) current ATS abuse. Current ATS abusers reported the mean (SD) of 4.6 (2.4) days per month of ATS use and the mean (SD) of 1.3 (1.7) years of ATS use. Compared to patients without current ATS abuse, current ATS abusers had higher levels of heroin use during BMT treatment: a lower proportion of opiate negative urine test 65% vs 83% ($p=0.06$) and a shorter duration of opiate abstinence during treatment (8.3 vs 9.4, n.s.). Current ATS abusers also reported significantly higher levels of sex related HIV risk behaviors on their baseline AIDS Risk Inventory Sex Subscale scores (27 vs 13, $p<0.05$).
Conclusions: These findings based on a small sample of patients treated with BMT suggest that current ATS abuse at treatment entry may be associated with adverse treatment outcomes during BMT. The findings raise concerns that ATS abuse, which has become highly prevalent among opiate dependent individuals in Malaysia, may undermine the effectiveness of BMT and MMT and point to the importance of developing effective treatments for co-occurring ATS abuse and opioid dependence.
Financial Support: Supported by NIDA DA014718, DA000445 & CMHC/DMHAS/State of Connecticut

95

USE OF MDMA AND OTHER SYNTHETIC STIMULANTS MONITORED BY WASTEWATER ANALYSES.

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Aims: In recent years there have been reports of both a shortage in 3,4-methylenedioxymethamphetamine (MDMA) supply and an increase in the use of novel stimulants such as mephedrone. The present study was designed to obtain objective data to assess these trends and to determine whether the increase in novel stimulants was temporally related to a decline in MDMA or independent of that trend.
Methods: Wastewater samples from multiple treatment plants in South Australia were collected from 2009 to 2012. A solid-phase extraction/liquid chromatography/tandem mass spectrometry (SPE-LC-MS/MS) method was developed and employed, targeting on MDMA and some of the most reported synthetic cathinones and piperazines. Data were temporally compared throughout the years. Seizure data of the same period were also obtained from state police as reference.
Results: MDMA and 6 other synthetic stimulants, including mephedrone (one of the most reported synthetic cathinones) and BZP (a representative piperazine derivative), were detected and quantified in the samples. While MDMA level decreased 98.3% from 2009 to 2010 and rebounded in 2011, mephedrone level increased in 2010 and dropped back in 2011. BZP level rose from 2009 to 2011 by 50-fold. Seizure data also indicated decreased purity of MDMA in 2010 and increased again in 2011, together with increased level of BZP/TFMPP in "ecstasy" tablets.
Conclusions: In 2010 there was a very marked decline in MDMA use in South Australia, which was associated with increased use of some novel stimulants. However, some other synthetic stimulants showed increasing trends independent of MDMA availability. Wastewater analyses provide important additional information to population surveys that reflects actual rather than believed drug use and has high temporal resolution.
Financial Support: This project was sponsored by the State Government of South Australia.

96

PREDICTORS OF DRUG USE AND BINGE DRINKING OF MIXED-RACE, NATIVE AMERICAN, AND CAUCASIAN GENERAL-POPULATION YOUTHS: TESTING THE EFFECT OF CONTEXTUAL FACTORS.

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Aims: Evidence suggests mixed-race (MR), Native American (NA) youth are at a higher risk for substance abuse. To identify modifiable factors for intervention in these groups, we examined the associations of contextual factors with binge drinking and illicit drug use among youth from these two groups contrasted with Caucasian (C) youth. Contextual factors included four indicators: social bonding, friendships with deviant peers, negative views of substance use and own delinquent behavior. We further assessed relative differences in the levels of associations of these contextual factors with substance abuse.
Methods: We used a dataset combining 2006-2009 National Survey on Drug Use and Health data. SAS 9.2 was used for bivariate analyses and logistic regressions. Sampling weights and standard error adjustments were applied to account for complex survey sampling biases. Logistic coefficients were compared between C and NA and C and MR using two sample Z-tests to identify differences in the effect of each predictor.
Results: Illicit drug use was higher among NA and MR youth than among C youth (31, 24, 20 % respectively). Illicit drug among C youth differed from NA and MR youth ($p<.0001$). Binge drinking differed marginally between C and MR youth ($p=0.06$) and did not differ between C and NA youth ($p=0.34$). Associations of all indicators, except social bonding with substance abuse, were consistent and in the expected directions for the C and MR youth, but not the NA youth. The Z-test results suggested parental attachment differed between C and NA youth for binge drinking ($p=.05$), and parental disapproval of substance use differed between C and NA youth for drug use ($p=.04$); conventional activities differed between C and MR youth for drug use ($p=.05$).
Conclusions: The study suggests common contextual factors across groups. Social bonding factors may affect NA and MR youth differently, or more culturally relevant measures are needed for surveys involving minority youth.
Financial Support: T32DA007313

97

PRENATAL HEALTHCARE UTILIZATION AMONG PREGNANT WOMEN IN THE METHADONE MAINTENANCE TREATMENT PROGRAM IN TAIWAN.

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Aims: Taiwan has launched the National Methadone Maintenance Treatment (MMT) program since 2006. In this study, we retrospectively identified a cohort of heroin-using women and examined their pattern of prenatal healthcare utilization in relation to the methadone treatment.
Methods: Data were first obtained from the 2006-2009 MMT to identify 4300 methadone treated women. We then linked these data to the National Birth Notification database and the National Health Insurance database, 2001-2009, to retrieve 3454 pregnant events, including all live births, still births, and abortions. Poisson regression analyses were used to examine the relationship between sociodemographic characteristics, health condition, and methadone treatment history with prenatal care utilization.
Results: The average prenatal healthcare visit was estimated 1~2 times for heroin-using women, significantly lower than their age-and residence- matched counterparts in the general population. Older ages were associated with reduced visits for prenatal healthcare (20-29 years: relative risk [RR]=0.9, 30 years or above: RR=0.8). With simultaneous adjustment for age, pregnancy complication, educational attainment, prior pregnancy history, we found that the visits of prenatal health care were significantly elevated after the enrollment in MMT program (aRR=1.5, $p<0.001$).
Conclusions: For heroin-using women, utilization of prenatal checkups may be improved by participation in the MMT program. The significance of methadone treatment related increased healthcare utilization through pregnancy reinforces the need to address the well-integrated and-coordinated prenatal care to drug-using population to reduce adverse obstetric and birth outcomes.
Financial Support: National Health Research Institutes

98

ASSESSMENT OF ABUSE-DETERRENT EFFECTS OF NEW DRUGS.

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Aims: This poster is our first attempt to address the assessment of abuse deterrent effects from a regulatory viewpoint. In recent years, we have observed increased interest in development of extended release (ER) Schedule II drug products with abuse deterrent qualities, specifically with crush resistance. In such cases, the crushed extended-release features of the Schedule II drug must be compared with a non-abuse deterrent immediate release Schedule II drug (which serves as the positive control). Results from human abuse potential studies on extracts of the crushed ER drug are compared with results from the immediate release formulation as one of the studies for assessment of abuse deterrent qualities. To date, FDA has not suggested an approach for evaluating abuse deterrent effects.
Methods: We examined methodologies used by the Pharmaceutical Industries for assessing the abuse deterrent effects of new drugs, and summarized subject responses to Schedule II ER opioid drugs and to the placebo in studies in past NDAs. We developed new analytical and graphic methodologies for evaluation of abuse deterrent effects as examples.
Results: We proposed a new definition with an adjustment factor for placebo response in evaluating abuse deterrent effects, and a new responder analysis to test the hypothesis that the new drug has no abuse deterrent effects
Conclusions: The methodologies currently used by the Pharmaceutical Industries for evaluating abuse deterrent effects have serious shortcomings. The proposed new methodologies can take placebo effects into account, and can efficiently assess abuse deterrent effects and may provide more useful language to describe the deterrent effects in drug product labels
Financial Support: N/A

99

GENDER DIFFERENCES IN SUBSTANCE USE AND MENTAL HEALTH SERVICE UTILIZATION AMONG PERSONS WITH SUBSTANCE USE DISORDERS WITH VS. WITHOUT COMORBID MAJOR DEPRESSION.

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Aims: There is evidence that utilization of mental health and substance use treatment differs by gender, but little is known about the role of gender in service use patterns for persons with a SUD as a function of psychiatric comorbidity. We examined gender differences among persons with SUDs with and without a comorbid major depressive episode(MDE).
Methods: Data from 187,864 adults aged 18+ from the National Survey on Drug Use and Health (2005-2009) were used. Gender differences in mental health and substance use patterns among two groups of individuals were examined: those with past-year substance use disorders only (SUD only, N=14,644), and those with past-year substance disorders comorbid with past-year MDE (SUD+MDE, N=1,771). Basic contingency analyses were followed by weighted bivariate and multivariate logistic regression analyses.
Results: Compared to SUD only, those with SUD+MDE were more likely to be female (OR=2.54[2.14, 3.01]), unemployed (OR=1.43 [1.07, 1.90]), divorced/separated (OR=2.56 [1.94, 3.37]); and less likely to be Hispanic (OR=0.77 [0.60, 0.99]), to come from high-income families(OR=0.52 [0.41, 0.66]), and to have Medicare (OR=0.42 [0.20, 0.86]). Females with SUD only were more likely to receive mental health services (OR=2.90 [2.48, 3.38]) compared with males. Similarly, females with SUD+MDE tended to have more mental health service utilization relative to males (OR=2.64 [1.80, 3.87]). Females with SUD only, had significantly lower odds of receiving substance use services (OR=0.72 [0.53, 0.98]); whereas, participants with SUD+MDE showed no significant gender difference with regard to substance disorder service utilization.
Conclusions: Findings indicate that gender is an important factor in service use: females with SUD only or SUD+MDE are more likely to receive mental health services; whereas, males with SUD only are more likely to receive substance use treatment. These analyses can contribute to planning of services and public health campaigns aimed at reducing gender disparity in access to mental health and substance use services.
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100

COMPARING THE EFFECT OF SUCROSE AND COCAINE REINFORCER MAGNITUDE ON RESISTANCE TO EXTINCTION.

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Aims: Drug seeking is assessed in the absence of the drug reinforcer, and thus, in extinction. A treatment that reduces the motivation to seek may therefore affect performance by reducing response rate early in the session, or by increasing the rate of extinction. We used a novel dynamic microscopic model of operant behaviour to examine how reinforcer magnitude during training, a way to manipulate motivation, affected extinction. Sucrose and cocaine were used as the reinforcers. The microscopic model captured the bout-like nature of operant behaviour, and dissociated performance into several baseline behavioural components such as the bout length and bout frequency at extinction onset, and dynamic components such as the time it took for response rate to start extinguishing (latency to decay) and extinction rates.
Methods: Different groups of rats were trained to lever press for a high dose of cocaine (0.75 mg/kg/infusion), a low dose of cocaine (0.375 mg/kg/infusion), a high value food reward (10 sucrose pellets), or a low value food reward (2 sucrose pellets), under a VI 5-min schedule. Reinforcement was then discontinued, and lever pressing during the first extinction session was analysed.
Results: Increasing sucrose amount during training increased extinction baseline bout length and bout frequency, consistent with increased motivation. However, increasing cocaine training dose had no effect on baseline bout length and decreased bout frequency. In contrast, both latency to decay and extinction rates were increased by increasing sucrose amount or cocaine dose.
Conclusions: Increasing cocaine dose decreased baseline bout frequency, suggesting a reduced motivation to seek cocaine at the onset of extinction, possibly due to withdrawal or conditioned aversion. However, sucrose amount and cocaine dose were positively correlated with latency to decay, suggesting that rats were more persistent at seeking before performance began to decline. Latency to decay may therefore be a useful index of degree of motivation during seeking.
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101

PHARMACOKINETIC/PHARMACODYNAMIC MODELING OF COCAINE SELF-ADMINISTRATION BEHAVIOR IN RATS.

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Aims: To develop a predictive pharmacokinetic/pharmacodynamic (PK/PD) model to describe the concentration-effect relationship between cocaine in blood and cocaine-taking behavior in a rat model of self-administration (SA), extinction, and reinstatement.
Methods: Male Long-Evans rats were allowed to self-administer cocaine by snout-poking (0.5 mg/kg/infusion IV) for 3h session over 21 days. Each snout poke into an active (cocaine-paired) hole initiated a cocaine infusion and a cued 25-sec time-out period in which no cocaine infusions were allowed. After 3 wks, snout poking into the active hole was extinguished by 2-4 wks of exposure to the SA procedure without cocaine infusions. After extinction, the effect of a non-contingent cocaine exposure (10 mg/kg IP) on reinstatement of the active snout-poke response was evaluated. Blood cocaine profiles were simulated using a literature PK model, and number of infusions (or "sham" infusions during extinction and testing) was used as a PD biomarker. A linked PK/PD model was developed using Adapt 5 and validated with an external dataset.
Results: The effect of cocaine on infusion (or sham) frequency was described well by a PK/PD model that used an indirect inhibitory structure incorporating a hypothetical dopamine (DA) PD compartment. The PK component was a 2-compartment model with a cocaine elimination rate constant of 331 d^{-1} and a volume of distribution of 1.2 L/kg. In the model, cocaine inhibits apparent DA elimination (IC50=504 ng/mL) which stimulates a behavioral response rate constant (kin). The model predicts that kin decreases with a lag–time (26.1 d) to achieve a new response baseline (2.3 vs 11 infusions/session), which agreed well with an external dataset.
Conclusions: A PK/PD model was developed to describe the behavioral effect of cocaine during three phases: active SA, extinction and reinstatement. The model predicts that repeated exposure to cocaine with extinction leads to a new steady-state in the behavioral response to cocaine.
Financial Support: Supported by NIH Grants R21DA027528 and RO1DA021261

102

EFFECTS OF SUBSTANCE ABUSE ON QUALITY OF CARE AMONG ELDERLY WITH NON-MUSCLE INVASIVE BLADDER CANCER.

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Aims: To analyze the effects of substance abuse on quality of care among elderly with non-muscle invasive bladder cancer.
Methods: A retrospective case control study using SEER-Medicare data. From our cohort of non-muscle invasive bladder cancer patients diagnosed between 2001-2004,we identified those with/without substance abuse diagnosis(ICD-9 codes: Alcohol dependence syndrome-303.xx, Drug dependence 304.xx and Non-dependent abuse of drugs 305.xx). Both groups were retrospectively followed for one year pre and five years post-diagnosis. Effect of substance abuse on quality of care (ER,inpatient and outpatient visits) and cost was analyzed across phases of care. To compute incremental cost, matched cancer free controls were selected from Medicare data. Poisson regression and GLM log-link models were used to analyze the association of substance abuse with health resource utilization and cost.Propensity score approach was used to minimize bias.
Results: We identified 33,396 patients diagnosed for non-muscle invasive bladder between 2001-2004. Mean age of the cohort was 76.7 years (std 7.2), 88% were white and 73% were male. The prevalence of substance abuse was 15.96%. The substance abuse group was associated with higher odds of ER (OR=1.56, CI=1.48-1.63), inpatient (OR=1.17, CI=1.14 - 1.19) and outpatient visits (OR=1.37, CI=1.35 – 1.39) in one year period post-diagnosis, compared to those with no substance abuse. Results were comparable in the five year follow-up period. GLM model showed that compared to non-substance abuse group, the substance abuse group had higher total cost in all phases, after controlling for covariates.
Conclusions: A co-occurring diagnosis of substance abuse appears to affect quality of care and cost among elderly with non-muscle invasive bladder cancer. This highlights the need for further research to study the effects of early diagnosis and treatment of substance abuse to improve quality of care through care coordination.
Financial Support: NIA-NIH #R21AG034870-01A1

103

IMPACT OF REFORMULATED OXYCONTIN® ON RATES OF ABUSE THROUGH ORAL AND NON-ORAL ROUTES AMONG INDIVIDUALS ASSESSED IN SUBSTANCE ABUSE TREATMENT.

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Aims: To reduce abuse through non-oral routes of administration (ROA) that require tampering (e.g., injecting and snorting), OxyContin (oxycodone HCl controlled-release) Tablets were reformulated with physiochemical barriers to crushing and dissolving. Shipments of original OxyContin (OC) stopped on August 5, 2010 and reformulated OxyContin (ORF) started on August 9, 2010. This study compared rates and frequency of abuse through oral and non-oral ROA in the periods before versus after ORF introduction for OxyContin and comparator opioids (ER oxymorphone and ER morphine) among individuals assessed in substance abuse treatment.
Methods: The NAVIPPRO system uses a computer-administered interview (ASI-MV) for adult treatment planning that collects self-report of past 30 day substance abuse, including prescription opioids. Rates of abuse through any route, oral and non-oral routes and continued frequency of use were measured for OC over 14 months before ORF introduction (June 2009-August 8, 2010, n=67,165) and compared to ORF in the 11 months following ORF introduction (August 9, 2010-June 2011, n=37,465).
Results: The rate of abuse of OC, pre-ORF was 4.2%. The rate of abuse of ORF was 2.4%, a 44% difference from that for OC (95% CI=40%-48%). Differences were larger for non-oral versus oral ROA. For non-oral ROA, rates for ORF were 70% lower (95% CI=67%-74%) than for OC pre-ORF, and for oral ROA rates were 22% lower (95% CI=16%-29%). Average frequency of abuse in the past 30 days declined from 11.0 to 7.3 days in the pre- versus post-ORF periods for OC and ORF, respectively. Rates of abuse for ER oxymorphone increased 158% (95% CI=117%-204%) and remained steady for ER morphine.
Conclusions: These findings indicate that rates of abuse of ORF were lower than historical rates of OC abuse, particularly through non-oral ROA that require tampering, in this sample of individuals assessed in substance treatment. Further research is needed to determine the persistence and generalizability of these findings.
Financial Support: Purdue Pharma & Inflexxion, Inc.

104

USING REAL-TIME FMRI TO TRACK "LOSS OF COGNITIVE CONTROL" DUE TO EVOCATIVE (DRUG AND NON-DRUG) CUES.

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Aims: Real-time fMRI feedback offers the potential for training cocaine patients to maintain cognitive control in the face of disruption by cocaine cues, with the therapeutic goal of reducing cue-triggered relapse. As the first step toward this goal, our laboratory recently demonstrated (NeuroImage, 2011) that a whole-brain classifier enabled patients and healthy controls to control a screen cursor by alternating their thoughts between two distinct brain states (e.g., spatial navigation, repetitive motor activity). As the next step, study, we are testing whether evocative (neutral, cocaine, aversive) cues can disrupt cognitive control in an optimized version of our real-time paradigm.
Methods: BOLD fMRI at 3T with a partial least squares (PLS) linear classifier was used to characterize the whole brain response during a cognitive control task that instructed the subjects to alternate their thoughts between active "picture assisted" 6 sec conditions (e.g., scene navigation or repetitive arm sports) v. rest. Neutral, cocaine and aversive pictures were superimposed during the task, and brain perfomance was assessed (n=36 scans, for controls and for patients; ongoing).
Results: The whole-brain classifier robustly distinguished the active v. rest conditions ($p<0.0000$; all $t > 3$). Introduction of the visual cues disrupted cognitive control ($p < .000$) in the task. The degree of disruption and speed of recovery varied substantially across subjects.
Conclusions: This study provides encouraging evidence that our real-time cognitive control task is sensitive to disruption by evocative cues, and that it can detect individual differences in the "loss of cognitive control". These findings are a critical building block toward the goal of using real-time fMRI feedback to improve cognitive control in addiction.
Financial Support: NIDA R21/R33-DA026114 (ARC), NIBIB K25-EB007646 (JM), P50-DA12756, P60-DA005186, VISN 4 MIRECC, Alexander Foundation

105

THE RELATIONSHIP BETWEEN PREGNANCY INTENTION AND PERINATAL CIGARETTE SMOKING BEHAVIOR: AN ANALYSIS OF PRAMS DATA.

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Aims: Many women reduce or quit smoking during pregnancy. Given that half of all pregnancies in the United States are unplanned, we investigated the relationship between pregnancy intention and change in perinatal cigarette smoking behavior.
Methods: Women who self-reported cigarette smoking during the 3 months before pregnancy (n=19,510) were a subset of the Pregnancy Risk Assessment Monitoring System (PRAMS) cohort (N=199,917) for 2004-8 births. PRAMS, a state-specific and population-based surveillance project of the Centers for Disease Control and Prevention and state health departments, collects data from postpartum women on their behaviors and other factors before, during, and shortly after pregnancy. Intended pregnancy was defined by wanting pregnancy "then" or "sooner;" mistimed by "later;" and unwanted by "I didn't want to be pregnant then or any time in the future." Number of cigarettes per day (CPD) smoked before pregnancy was compared to number smoked postpartum. Bivariate analysis using the proper survey and weight functions was performed as was logistic regression. Confounding was assessed via manual backwards elimination with a change-in-estimate criteria of 0.10% being significant.
Results: Forty four percent of the pregnancies were intended, 41.5% mistimed, and 14.7% unwanted. Compared to pre-pregnancy smoking, 25.1% reported reducing the number of CPD but not quitting, 24.3% reported quitting, and 50.6% reported smoking the same number or more postpartum. Change in number of CPD differed between intended/mistimed and unwanted pregnancy groups. Women with unwanted pregnancies had 0.89 times the adjusted odds of quitting or reducing the number of CPD compared to those with intended/mistimed pregnancies (95% CI: 0.80, 0.98).
Conclusions: Among postpartum women who smoked cigarettes prior to pregnancy, those with unwanted pregnancies were significantly less likely to reduce or quit smoking cigarettes compared to women with intended/mistimed pregnancies.
Financial Support: None

106

ANXIETY AND DEPRESSION IN ADULTS WITH LONG HISTORIES OF METHAMPHETAMINE USE.

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Aims: This study examines the association of anxiety and depressive symptoms with stability of abstinence from substance use among adults with long duration methamphetamine (meth) use careers.
Methods: Data are from an 8-year follow-up interview in an intensive natural history study of adults who had used meth regularly (N=393), initiating use an average of 23 years prior to the 2009-11 interview; 41% had not received drug treatment at study recruitment and 25% used meth in the past 30 days. Respondents completed the Beck Depression Inventory and Natural History Interview, which assessed substance use, anxiety and depression in the past month and since the previous interview. To examine stability of abstinence, those with 2 or more years of drug and alcohol abstinence were compared to those who were abstinent for 3-23 months, 1 to 3 months, and less than a month. Bivariate and multivariate regression analyses by gender were conducted.
Results: Preliminary analyses indicate the mean depression score was 10.1 (SD=8.9); serious anxiety was reported by 31% since the last interview and 14% in the past month. Those with 2 or more years of abstinence had significantly lower depression scores (6.9; SD=6.4) compared to those who used in the past month (10.7; SD=9.2), past 3 months (10.6; SD=6.8) or past 2 years (10.6; SD=9.5; $p<.05$). Serious anxiety was related to more days in self-help ($p<.05$). Men with 3-23 months abstinent had a higher rate of anxiety compared to those who continued to use or were abstinent <=2 years ($p<.05$).
Conclusions: These findings suggest that although anxiety and depression are highly correlated, depression remains elevated among meth users of both genders until stable abstinence is achieved, whereas anxiety may be more problematic among men in earlier stages of recovery compared to those who continue to use or have achieved stable abstinence.
Financial Support: NIDA DA025113

107

LONGITUDINAL INVESTIGATION OF ORBITOFRONTAL AND STRIATAL MORPHOLOGY IN ADOLESCENT METHAMPHETAMINE ABUSERS.

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Aims: The presence of abnormal striatal (ST) and orbitofrontal cortical (OFC) structure and function is hypothesized to be associated with loss of self-control and compulsive drug use. However, little is known about how methamphetamine (METH) abuse impacts OFC-ST structure and function during adolescence, a period of increased risk for drug initiation and dependence. Consequently, we examined the relationship between METH abuse during adolescence and the integrity of OFC-STR circuitry.
Methods: Healthy control (HC; N= 8, mean age = 16.0 years) and METH abusing (N= 6, mean age = 14.9) adolescents underwent MRI scans, diagnostic interviews, and assessment with the Eysenck Impulsivity scale. MRI data was acquired using a T1-weighted 3D MPRAGE sequence on a 3T Siemens Trio magnet and volumetric segmentation of ROIs (ST = caudate, putamen, nucleus accumbens; OFC = medial and lateral domains) was performed with Freesurfer.
Results: A significant increase in left putamen volume was observed in METH subjects $t(5) = 2.80$, $p < 0.04$, as well as a significant decrease in left $t(5) = 6.10$, $p < 0.01$ and right $t(5) = 2.64$, $p < 0.05$ lateral OFC volume. No significant changes were observed in either region in HCs. At the second study visit, a significant inverse relationship between impulsivity and right lateral OFC volume was observed in Meth users $r(6) = - 0.85$, $p < 0.02$, whereas left lateral OFC volume inversely correlated with duration of Meth use $r(6) = - 0.79$, $p = .03$.
Conclusions: These preliminary results suggest that there may be a dynamic relationship between OFC and STR development, Meth abuse during adolescence, and impulsivity. Further, this study provides initial evidence that adolescence may be a period of vulnerability during which drug induced changes in the OFC and STR constitute a risk for compulsive drug use.
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108

WHO IS MOST AT RISK FOR HIV IN COMMUNITY CORRECTIONS?

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Aims: The goal of this paper was to identify the HIV risk behaviors and characteristics of individuals who are under criminal justice supervision in the community (community corrections).
Methods: 24,373 individuals under community corrections supervision were assessed for high risk HIV behaviors; 5,139 participants were identified who reported either high risk sexual (n=1,527; 6%), injection drug use, (n=212; 1%) both risk behaviors (n=968; 4%), or no HIV risk behaviors (n=2,432; 10%). Sociodemographic characteristics and drug of choice were then examined through univariate and binary logistic regression.
Results: Historical physical or sexual abuse, a lack of health insurance, and selecting a drug of choice as opposed to no drug were universally associated with higher risk for HIV. Opioids as one's drug of choice was universally associated with the largest effect sizes, while a different pattern emerged between drug of choice and the three categories of HIV risk. For example, cocaine has the strongest association with sexual risk, but only the third strongest associations with the other two groups. Sedatives had the second strongest association with IV drug use, but only the fourth strongest associations with the other two groups. The sexual risk group was associated with being younger, female, black and reporting a history of suicidal ideation. Protective factors for sexual risk included: being divorced/separated/widowed, being unemployed or disabled/retired, and living in a shelter or with relatives/friends. The IV drug use group was associated with being older, male, White, unemployed, and living in a shelter or with relatives or friends. The group with both drug and sexual risk were more likely to be White, report a history of suicidal ideation or attempts, receive government insurance, and report a history of being hospitalized for physical problems.
Conclusions: Distinct sociodemographic characteristics were associated with sexual versus injection drug use risk for individuals under community corrections supervision.
Financial Support: Supported by UAB Psychiatry Departmental Funds.

109

GENDER DIFFERENCES IN SUBSTANCE USE AMONG MONORACIAL/ETHNIC AND BIRACIAL/ETHNIC YOUTH AND YOUNG ADULTS: RESULTS FROM A U.S. POPULATION-BASED SURVEY.

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Aims: The prevalence and correlates of substance use among multiracial and ethnic groups is poorly understood. Even less is known about gender differences in drug use among multiracial youth. This study is among the first to estimate the prevalence of lifetime cigarette, alcohol, and marijuana use in a nationally representative sample of monoracial/ethnic and biracial/ethnic youth and young adults in the US.
Methods: The authors considered a total of 16 racial/ethnic categories and used 4 waves of data from the National Longitudinal Study of Adolescent Health (Add Health). The analysis sample consisted of 20,745 individuals who participated in Wave one. Half of this sample was females (50.6%). Participants responded to 3 binary items that assessed whether they had ever smoked cigarettes, consumed alcohol, or smoked marijuana. The primary statistical methodology used was logistic regression procedures taking into account sample weights.
Results: Participants who self-reported two races/ethnicities had prevalence rates equivalent to the rates of the two monoracial/ethnic groups. There were significant interaction effects between race/ethnicity and gender and race/ethnicity and socioeconomic status.
Conclusions: Significant heterogeneity in drug use is observed between Blacks and biracial Blacks, and there are important gender differences in drug use. The data show the need for further research on patterns and predictors of gender differences in substance use among multiracial populations that may inform interventions.
Financial Support: This work was supported by a Junior Faculty Development Award, Office of the Executive Vice Chancellor and Provost, University of North Carolina at Chapel Hill and a University Research Council Research Grant, Office of the Vice Chancellor for Research and Economic Development, University of North Carolina at Chapel Hill awarded to Trenette T. Clark.

110

EFFECT OF MORPHINE PRETREATMENT ON NALOXONE-INDUCED CONDITIONED TASTE AVERSIONS.

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Aims: Preexposure to morphine sensitizes the discriminative stimulus effects of the opiate antagonists naloxone and naltrexone. To test the relationship between the discriminative stimulus and aversive effects of drugs, the present assessment utilized the conditioned taste aversion design to measure the aversive effects of naloxone following morphine pretreatment. If morphine exposure impacts sensitivity to opiate antagonists in a similar manner to that reported in drug discrimination learning, it would be expected that naloxone would induce more robust taste aversions in animals pretreated with morphine, supporting the position of a common mechanism underlying the two stimulus properties.
Methods: Male Sprague-Dawley rats were preexposed to morphine (10 mg/kg) or saline. One day later, a novel saccharin solution was followed immediately by administration of naloxone (10 mg/kg) or saline. Saccharin consumption in one- and two-bottle tests was measured to assess any differences in consumption by animals pretreated with morphine or saline.
Results: There was no effect of morphine pretreatment on saccharin consumption of animals conditioned with naloxone. Regardless of pretreatment (either morphine or saline), all animals conditioned with naloxone consumed significantly less saccharin on both the one- and two-bottle aversion tests than animals treated with saline during conditioning.
Conclusions: Morphine pretreatment had no effect on saccharin consumption of naloxone-conditioned animals, an effect different from that reported in drug discrimination preparations. These results suggest that the stimulus properties of naloxone following morphine pretreatment are different from those involved in the generation of naloxone-induced taste aversion learning. This dissociation is consistent with the reported weak inverse-relationship between the magnitude of taste aversion learning and the rate of acquisition of discriminative control and the fact that doses of naloxone effective in establishing discriminative control (e.g., 1 mg/kg) do not condition a taste aversion.
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111

RX OPIOID ABUSE: THE ROLE OF PHARMACISTS.

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Aims: Prescription opioid (PO) overdose deaths in the US have increased threefold since 1990. Research suggests screening and brief intervention (SBI) in health care settings can reduce prescription drug misuse. Although pharmacies are the primary sources to obtain POs, SBI for PO misuse has not been tested in that setting. This pilot survey examined pharmacists' attitudes and interests for delivering SBI for PO abuse.
Methods: Utah and Texas pharmacists were invited to participate in an online survey over three months. Pharmacists responded to 35 items using a Likert scale response set (ranging from 1=strongly disagree to 5=strongly agree). Survey items were developed by project investigators or were adapted from previous research questionnaires administered to pharmacists regarding SBI for alcohol. Descriptive, mean, and bivariate statistics were calculated for survey subscales derived from a principal components analysis.
Results: A total of 739 pharmacists completed the survey (19% response rate). Respondents had practiced an average of 18 years and worked in chain (n=206,35%), independent (n=189,33%), or health system (n=186,32%) settings. Subscales indicated pharmacists are interested in addressing PO issues (m=3.7) and believe motivation for SBI engagement would be enhanced with simple/accessible SBI delivery tools (m=3.9). Pharmacists also believe they possess sufficient knowledge and confidence to address PO misuse (m=3.8), with more years of practice being associated with greater knowledge and confidence (B=.17,p=.00). Pharmacists were neutral regarding potential methods of SBI service delivery (m=3.0). Health system (m=2.7) and independent pharmacists (m=2.6) were more confident (F=7.5,p=.01) than chain setting practitioners (m=2.4) that patients would respond favorably to SBI.
Conclusions: Pharmacists may be interested and feel capable addressing PO abuse, but feel tentative about intervention methods and patient response. Tools to facilitate SBI delivery could resolve pharmacist uncertainties. Future research will examine feasibility and strategies for SBI delivery in pharmacy settings.
Financial Support: NA

112

SMOKING BEHAVIORS DURING PREGNANCY: FOCUS GROUP FINDINGS FROM A PUBLIC OBSTETRICS CLINIC.

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Aims: Focus groups of pregnant and postpartum smokers were assembled to determine: smoking rates and patterns; barriers to quitting and triggers to relapse; and openness to and perception of the 5 A's protocol both within clinic and via telephone follow-up postpartum (including scheduling concerns).
Methods: Participants were recruited from a single Medicaid clinic in Baltimore City. Only currently/recently pregnant and current/past-year smokers (Total N=16) were included. Both qualitative and quantitative data were collected, and sessions were digitally recorded and transcribed to determine common themes.
Results: Participants' mean age was 23.6 years. The majority were African-American (87.5%), currently pregnant (87.5%), and currently smoking (93.8%). Mean scores on the Perceived Stress Scale and the Edinburgh Postpartum Depression Scale were 20.7 (SD=6.6) and 11.5 (SD=6.7), respectively, indicating significant stress and possible depression. Themes emerging from the focus group discussions were: (1) decline in smoking rates over the course of pregnancy with marked increase postpartum; (2) satisfaction with the physician's provision of the first two of the 5 A's (Ask, Advise) during pregnancy, but no memory of the last three (Assess, Assist, Arrange); (3) acceptability and usefulness of the 5 A's during pregnancy and postpartum and urine testing for cotinine; (4) strong desire to quit but moderate motivation to do so, (5) health of their unborn child is a primary motivator for quitting during pregnancy and stress is a primary trigger for relapse, (6) positive response to a phone-based postpartum continuing care protocol, and (7) the importance of highlighting social support and mood/stress management in any postpartum protocol.
Conclusions: Focus group findings support the need for continuing care for smoking into the postpartum period, and highlight the acceptability of flexible phone-based intervention that can address triggers to relapse.
Financial Support: The development of this poster was supported by a grant from the National Institute on Drug Abuse (1R37 DA11323-01A2 to Dr. Michael L. Dennis).

113

NEGATIVE AFFECT REDUCTION EXPECTANCIES MEDIATE THE RELATIONSHIP BETWEEN PUBERTY AND ADOLESCENT SUBSTANCE USE.

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Aims: There is an association between puberty and adolescent substance use, but no mechanisms have been identified in this relationship. A paradigm used to explain substance use is negative reinforcement, which conceptualizes the motivational basis of the behavior as efforts to regulate negative emotionality. The model holds particular significance given that using substances to cope with negative emotions represents a risk factor for substance use problems. We examined if adolescents' expectations that substance use reduces negative affect accounts for the relationship.
Methods: 214 adolescents (44% girls; age= 14.00 + .81; 49% White; 35% Black) self-reported their pubertal status using the Pubertal Developmental Scale (Pedersen, 1988) from 1 (have not begun) to 4 (completed). Substance use engagement was measured with a modified version of the YRBSS(CDC, 2002) using a composite risk score that captured adolescents' alcohol use and marijuana and cigarette smoking. We calculated a composite score of negative affective reduction expectancies using the adolescent versions of the Marijuana Effect (Torrealday, 2008), Smoking Consequences (Lewis-Esquerre et al., 2005) and Alcohol Expectancy(Christiansen et al., 1982) questionnaires, which included items such as "[substance] helps a person relax and feel less tense."
Results: Pubertal score predicted substance use (B = .55, SE= .28, sr2=.02, p=.05) and negative affect reduction expectancies (B = 4.73, SE= 1.50, sr2=.04, p=.002). Negative affect reduction expectancies predicted substance use engagement (B=.05, SE=.01, sr2=.07, p=.001). When we entered our two constructs into the model, the expectancies mediated the relationship between puberty and substance use (B=.04, SE=.01, sr2=.06, p<.001).
Conclusions: The findings suggest that adolescents' endorsement of positive beliefs resulting from the use of substances underlies the relationship between pubertal status and substance use, providing an initial step toward examining the mechanisms that underlie the relationship.
Financial Support: R01 DA18647

114

SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF CRUSHED INTRANASAL OXYCODONE TAMPER-RESISTANT TABLETS AND OXYCONTIN® IN HEALTHY ADULTS.

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Aims: Reformulated OxyContin® (oxycodone HCl controlled-release) tablets (ORF) use a polyethylene oxide controlled-release formulation that imparts resistance to physical and chemical manipulations. Original OxyContin® tablets (OC) provided no tamper resistance. Tampering of dosage forms and alternate routes of administration are associated with greater risk of overdose. The safety tolerability and PK of intranasally administered crushed ORF and OC was evaluated.
Methods: Randomized, single-blind, single-dose, 3-treatment, 3-period crossover study. AUC, Cmax, and Tmax were determined. Safety was assessed using AEs, clinical laboratory test results, vital signs, pulse oximetry, physical examinations, and ECGs. Pharmacodynamic measurements included intranasal tolerability (discomfort, itching, burning, pain, runny nose and stuffiness) and endoscopy.
Results: Fine and coarse crushed ORF and fine crushed OC were bioequivalent regarding total exposure (AUC). Cmax for both fine (17.1 ng/mL) and coarse crushed ORF(15.5 ng/mL) were lower than for fine crushed OC (22.2 ng/mL). Tmax for fine crushed OC occurred more rapidly than for fine or coarse crushed ORF (1.1, 2.0 and 3.2 h, respectively). Abuse quotient (AQ=Cmax/Tmax) was computed. Highest AQ values were observed for fine crushed OC (31.7 ng/mL/h).Coarse and fine crushed ORF AQ were approximately 80% and 66% lower, respectively than fine crushed OC. Insufflation of fine and coarse crushed ORF yielded greater nasal discomfort and stuffiness compared to fine crushed OC while fine crushed OC produced greater runny nose compared to fine or coarse crushed ORF. There were no unexpected safety findings.
Conclusions: In contrast to OC crushed ORF retained some control of oxycodone release. Reduced Cmax and increased Tmax for ORF vs. OC produced lower rates of oxycodone absorption. ORF was associated with greater intranasal irritation compared to OC. These data suggest that ORF may have less potential for intranasal abuse compared to OC.
Financial Support: Purdue Pharma LP

115

IN VITRO TAMPER TESTING OF REFORMULATED OXYCONTIN®: AN ITERATIVE AND INCREMENTAL SCIENTIFIC APPROACH.

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Aims: Sponsors are increasing their efforts to develop laboratory-based in vitro assessment protocols for evaluating "tamper-deterrent" properties of products. No standards currently exist describing how these experiments should be conducted. We describe an experimental approach for testing reformulated OxyContin® that was both iterative and incremental in nature.
Conclusions: Given that an exhaustive study of potential tampering methods was impractical, an incremental approach with iterative changes was implemented. The project began with an informational gathering phase. Input was sought from formulators, independent scientific experts, and internet surveys concerning potential tampering methods and preferred routes of administration. Physico-chemical methods were considered that might enhance the speed or amount of drug delivered or allow a change in the route of administration. Because of inherent tablet properties (hardness and formation of viscous aqueous solutions), initial exploratory studies were conducted to identify means of reducing the tablet to small particles and potential extraction methods. After evaluation of initial results, subsequent protocols were developed with scientific rigor to explore a wide range of experimental conditions (particle size, temperature, solvents, pH, reaction time, syringeability, and volatility) and to fully characterize the performance, including failure limits, of the formulation. To the extent possible, each protocol was designed to simulate "real-world" tampering conditions. The study protocols included the use of standardized methods, an appropriate number of replicates to define imprecision, and suitable comparators and controls to insure results were robust and meaningful. Most protocols were executed by third-party vendors to ensure independence. Extensive in vitro testing was conducted to understand the tamper-deterrent properties of reformulated OxyContin.
Financial Support: Pinney Associates provides risk management consulting services for pharmaceutical companies, including tamper testing. This work was funded by Purdue Pharma, Stamford, CT.

116

THE GLOBAL APPRAISAL OF INDIVIDUAL NEEDS: A VALIDATION OF 21 BASELINE MEASURES OF SEVERITY TO THE TRADITIONAL AND THE MORE CONSERVATIVE RASCH MEASUREMENT MODELS.

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Aims: The Global Appraisal of Individual Needs(GAIN)is a standardized biopsychosocial interview that integrates clinical and research assessment for individuals presenting to substance abuse or other behavioral health treatment and is designed to provide support for clinical decision-making related to diagnosis, treatment planning, placement, and outcome monitoring. The aims of this poster are to evaluate the extent to which 21 core baseline "measures" of severity in the GAIN met traditional measures of internal consistency (e.g., Cronbach's alpha) and the more conservative Rasch measurement model (aka 1 parameter item response theory [IRT]).
Methods: Participants were 6,158 to 18,113 adult and adolescent clients entering substance abuse treatment in from 77 to 289 programs around the U.S. For each separate measure, Winsteps was used to place both persons and items on a common, linear, interval "ruler" that enabled examination of: person and item reliability; item hierarchy; item fit statistics; unidimensionality; and item invariance across subgroups based on age, gender, race, and primary drug of choice.
Results: Of the 21 core baseline measures, 9 met the expectations of both the traditional and Rasch model; 8 met the expectations of the traditional model but only some of the more conservative Rasch criteria; and 4 did not meet the expectations of the traditional or Rasch measurement models. All measures had differential item functioning on some symptoms, but not the same symptoms for different subgroups.
Conclusions: The findings suggest that the last three measures are not latent constructs, but they still need to be evaluated further in terms of whether they are at least useful as "indices" that can predict things. Rather than measurement error, the differential item functioning appears to represent real differences in presentation by subgroup. Person misfit also appeared to be useful in identifying atypical but real clinical presentations (e.g., someone who is suicidal but not depressed).
Financial Support: SAMHSA Contract #270-07-0191

117

GETTING MY "LIFE ON TRACK": THE EFFECTS OF LONGTERM PARTNER INCARCERATION ON DRUG USE PATTERNS AMONG AFRICAN-AMERICAN WOMEN.

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Aims: In the US, the incarceration rate for Black men is 6 times that for White men; racial/ethnic differences in drug-related arrest rates help produce this disparity. While research indicates an association between partner incarceration and sexually-transmitted HIV, the impact of partner incarceration on women's drug use has not yet been studied. We seek to understand the effects of long-term incarceration of an intimate partner on drug use patterns among African-American women.
Methods: African-American women whose primary male partner had recently been incarcerated were recruited to participate in this longitudinal study, set in the southeastern United States. The present analysis focuses on the subset of participants who are active crack, heroin, or marijuana users (present N=15). One-on-one semi-structured interviews were conducted with participants. Grounded theory was used to analyze baseline data.
Results: Partner incarceration precipitates reductions in substance use, including cessation, switching from a "stronger" to a "weaker" drug, and less frequent use. During the months after their partners were incarcerated, women prioritized obtaining housing, seeking drug treatment and finding employment. This process was often referred to as getting their "lives on track." Women's drug use patterns changed because of increased difficulty obtaining drugs post partner incarceration. Furthermore, incarcerated partners often asked that women stop using while they were in prison because they associated drug use with intimacy. Most women sought drug treatment during this period due to financial strain. Additionally, many women became homeless during this period, and local homeless shelters prohibit drug use.
Conclusions: In our sample, the period immediately following a partner's incarceration appears to be a pivotal time in women's lives when they need economic and housing services, and are seeking drug treatment and other harm reduction programs.
Financial Support: NIDA:DA026327

118

SEX-DEPENDENT EFFECTS OF MARIJUANA AND NALTREXONE IN DAILY MARIJUANA SMOKERS.

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Aims: Preclinical and clinical data suggest that the effects of cannabinoids and the opioid antagonist naltrexone (NTX) vary according to sex. Given recent findings that NTX enhances marijuana's (MJ) positive subjective effects in a mixed-sex sample, this study sought to determine whether NTX-induced changes in MJ's effects vary as a function of sex.
Methods: Data from two double-blind, within-subject studies measuring NTX's effects (0 & 50 mg) on subjective-effect ratings and cardiovascular effects of MJ (3.27-5.50% THC) relative to inactive MJ (0.00% THC) were used for this analysis. Data obtained from male (M) and female (F) participants matched for frequency of MJ use (days/wk), amount smoked (joints/day), and years of regular MJ use were analyzed according MJ condition (active & inactive), NTX dose, and sex.
Results: Males (n = 17) and females (n = 17) did not differ in MJ smoking frequency (M = 6.7 ± 0.6, F = 6.6 ± 0.6 days/wk), number of joints smoked/day (M = 4.4 ± 2.5, F = 5.3 ± 4.9), or years of regular MJ use (M = 9.6 ± 5.9, females = 7.4 ± 5.3). Relative to inactive MJ, active MJ increased subjective effect ratings including 'High,' 'Good Effect,' 'Stimulated,' 'Liking,' & 'Take Again,' decreased MJ craving, and increased heart rate ($p \leq 0.01$). Females reported higher ratings for 'Good Effect' & 'Stimulated' than males ($p \leq 0.05$). NTX alone produced small but significant increases in ratings of 'High' relative to placebo ($p \leq 0.05$); sex-dependent effects of NTX were not detected. NTX increased MJ-induced effects on ratings of 'High,' 'Good Effect,' & 'Stimulated' relative to placebo ($p \leq 0.05$). A trend towards sex-dependent effects of naltrexone in combination with MJ was observed for ratings of 'Take Again'; NTX increased ratings in males, but decreased them in females ($p \leq 0.10$).
Conclusions: These results demonstrate that when matched for MJ use, females show a greater subjective response to MJ on some measures compared to males. Though males and females did not differ in their response to NTX alone, sex may influence the MJ-NTX interaction in a clinically meaningful manner.
Financial Support: Supported by NIDA Grants DA09236, DA19239, DA027755

119

THE CLINICAL SIGNIFICANCE OF CANNABIS WITHDRAWAL.

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Aims: Quantifying functional impairment during withdrawal from any drug is a neglected area of research. The clinical significance of cannabis withdrawal has been an ongoing debate that has hindered its acceptance into diagnostic measures of cannabis dependence. This study tested the influence of functional impairment from cannabis withdrawal on cannabis use during and after an abstinence attempt. The study also tested which factors predict functional impairment from cannabis withdrawal.
Methods: Functional impairment scores were collected using the Cannabis Withdrawal Scale in 49 non treatment seeking dependent cannabis smokers. Levels of cannabis use were quantified using the Timeline Followback and by urinalysis. The Severity of Dependence Scale and a Structured Clinical Interview for Axis I Disorders measured the severity of cannabis dependence.
Results: Participants who relapsed to cannabis use during the two week abstinence attempt reported elevated functional impairment associated with: restlessness ($p < 0.0001$), physical tension ($p < 0.0001$), mood swings ($p < 0.0001$), headaches ($p=0.006$), nervousness ($p=0.007$) and loss of appetite ($p=0.024$). Higher levels of functional impairment during the abstinence predicted higher levels of cannabis use at follow up ($p = 0.001$). Participants with more severe cannabis dependence ($p = 0.007$) and higher levels of cannabis use ($p = 0.006$) before the abstinence attempt reported greater functional impairment from cannabis withdrawal.
Conclusions: Cannabis withdrawal causes significant functional impairment which is associated with relapse to cannabis use and greater levels of cannabis use following a quit attempt. Functional impairment is predicted by the severity of cannabis dependence and level of cannabis use.
Financial Support: Funding for the work was provided by the Australian Government Department of Health and Ageing.

120

TESTING AN ADAPTED EVIDENCE-BASED HIV PREVENTION INTERVENTION IN A DRUG TREATMENT SETTING.

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Aims: We conducted a randomized controlled trial (RCT) to test the efficacy of the Community-friendly Health Recovery Program (CHRP) intervention among high risk drug users enrolled in an inner-city methadone maintenance program. We hypothesized that patients assigned to the CHRP intervention condition would demonstrate greater HIV risk reduction outcomes compared with those assigned to the active control condition.
Methods: Participants were 280 HIV-negative opioid-dependent patients enrolled in a methadone maintenance program who reported sex- or drug risk behavior. Participants were randomly assigned to the CHRP intervention (n = 136) or the active control condition (n = 144) and were assessed at Pre-intervention, Post-intervention, 3-month, 6-month, and 12-month time points. The analytical strategy was a 5 (Time) x 2 (Group: Intervention vs. Control) x 2 (Gender) mixed effects model. In addition, path analysis was used to examine the theoretical underpinnings of the CHRP intervention.
Results: Significant differences were found between the Intervention and Control groups with regard to key drug-risk reduction (i.e., safer drug use behavior, improved drug-risk reduction skills) and sex-risk reduction (i.e., obtaining condoms, self-efficacy in using condoms) variables. Support was found for the Information-Motivation-Behavioral Skills model of health behavior change.
Conclusions: Our RCT demonstrates the HIV risk reduction efficacy of the CHRP intervention even when implemented in an inner-city drug treatment setting.
Financial Support: This research was supported by a grant from NIH/NIDA (RO1 DA022122; Copenhaver, PI).

121

NATIONAL CHANGES IN OXYCONTIN, OTHER OXYCODONE, AND HEROIN EXPOSURES REPORTED TO POISON CENTERS WITH INTRODUCTION OF REFORMULATED OXYCONTIN®

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Aims: Reformulated OxyContin® (oxycodone HCl controlled-release) Tablets (ORF) have physiochemical barriers to crushing and dissolving intended to deter tampering and reduce abuse and misuse. This study assessed changes in poison center exposure cases for OxyContin, single-entity (SE) oxycodone (excluding OxyContin) and heroin before vs. after introduction of ORF.
Methods: Exposure cases reported to AAPCC's National Poison Data System, a national network of 61 US poison centers, are a proxy measure for adverse events that are classified as intentional exposures (eg, abuse, misuse, suicide), unintentional exposures (eg, therapeutic errors) or other. OxyContin exposures did not differentiate between original OxyContin (OC) and ORF. Shipments of OC stopped on August 5, 2010, and ORF started on August 9, 2010. The pre-period was from July 2009 to June 2010 and the post-period from October 2010 through June 2011.
Results: All OxyContin exposures declined 18% post- vs. pre-ORF (from 693 to 568 cases per quarter), intentional exposures declined 15% (391 to 330 per quarter), unintentional exposures by 20% (243 to 195 per quarter, and therapeutic errors among patients by 13% (161 to 140 per quarter). SE oxycodone exposures (all) increased 13% (1509 to 1705 per quarter) and all heroin exposures increased 17% (587 to 688 per quarter). All exposure rates adjusted for number of prescriptions decreased 11% for OxyContin, and decreased 9% for SE oxycodone. Trends in all exposures one year earlier than the study (July 2008 to June 2010) indicated 8% increase for OxyContin, 11% increase for SE oxycodone and 5% increase for heroin.
Conclusions: SE oxycodone exposures and heroin exposures increased after ORF introduction but were increasing pre-introduction. OxyContin exposures declined for all, intentional, unintentional and therapeutic error exposures after ORF introduction. These results suggest opioid formulations designed to deter tampering may reduce abuse and therapeutic errors among patients. Longer follow up is needed and is ongoing.
Financial Support: Support by Purdue Pharma L.P.

122

THE EFFECTS OF CONTINGENCY MANAGEMENT ON DRUG USE AND HIV RISK BEHAVIORS AMONG HETEROSEXUAL METHAMPHETAMINE USERS.

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Aims: In addition to negative health effects of methamphetamine (meth) use, users are also at increased risk for HIV infection through risky sex and injection behaviors. Reducing meth use is an important addition to HIV prevention programs.
Methods: The current study tested the effects of contingency management and strengths-based case management interventions on reducing meth use and HIV risk behavior in an out-of-treatment, street-recruited population. To date, 114 meth users have completed a baseline interview.
Results: Following the initial interview, subjects were assigned to one of three intervention groups: treatment as usual (HIV testing/counseling; HIV T/C); HIV T/C plus contingency management (CM); and HIV T/C, CM, plus strengths based case management (SBCM). Meth use at the baseline interview was high: clients reported using an average of 20.2 days in the past 30, and used an average of 3.2 times per day. Two-thirds reported lifetime injected meth use, and 12% who injected drugs had used a dirty needle in the past 30 days. Eighty-three percent who had sex in the past 30 days reported not using a condom for some or all sexual encounters. Seventy-one individuals have completed a 6-month follow-up interview. Preliminary results demonstrate decreases in meth use among study participants. Among the 23 individuals who have completed a 6-month follow-up interview, there is an average decrease in meth use of 8.6 days in the past 30 ($p = .005$). This decrease is larger in CM and SBCM interventions than in HIV T/C only.
Conclusions: These results suggest strong effects of CM to reduce meth use. Other updated outcomes such as HIV risk, criminal behaviors and gender differences at follow-up will also be presented.
Financial Support: This study was supported by the National Institute on Drug Abuse, DA026741-02.

123

PATTERNS OF PRESCRIPTION OPIOID USE AND DIVERSION AMONG 18- TO 50-YEAR-OLDS.

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Aims: Only recently have studies of nonmedical use (NMU) of prescription (Rx) drugs included more detailed information on diversion. Friends and relatives are the most common source of diverted medications and diversion is associated with illicit substance use (McCabe et al, 2011). This analysis examines patterns of use and diversion of Rx opioids as reported by past 12 month opioid users in a sample targeted for Rx drugs. We ask: How do opioid users who used as prescribed (Rxed) differ from those who never used as prescribed (Never Rxed)?
Methods: Data come from the Prescription Drug Misuse, Abuse, and Dependence Study of stimulant, sedative and opioid use in adults 18 and older. Participants were recruited via targeted sampling procedures in St. Louis in 2008-2010. People were asked how many days in the past 12 months they used their own Rx just as Rxed; then how many days they used their own Rx more or longer than Rxed; and finally, how many days they used opioids not Rxed to them.
Results: The sample of 258 opioid users 18 to 50 years of age was 58% male and 41% Caucasian. The most common pattern was all use not Rxed to them (31%), followed by a pattern of all 3 types of use (23%). When the Never Rxed (52%) were compared to the Rxed (48%) we found they were more likely to be male (66% vs. 50%, p=.01), unmarried (96% vs. 88%, p=.01) and with an arrest history (83% vs. 71%, p=.02). Rxed were more likely than Never Rxed to obtain pills from a health professional (85% vs. 37%, p<.0001) and take them for pain (94% vs. 77%, p=.0003). Rxed were less likely than the Never Rxed to report obtaining pills from a friend (38% vs. 57%, p<.01) or dealer (14% vs. 25%, p=.03) or to have used illegal drugs (88% vs. 96%; p=.01). Rxed were no different from Never Rxed on diversion (selling, trading or giving away pills) or getting pills from a family member. Reasons for opioid NMU and types of illegal drug use will also be examined.
Conclusions: Learning more about diversion can inform prevention efforts that may reduce the NMU of Rx drugs. These findings suggest Rxed opioid users participate in diversion.
Financial Support: NIDA R01DA03079; LB Cottler, PI

124

MDMA USERS HAVE INCREASED REGIONAL BRAIN ACTIVATION DURING STROOP TASK PERFORMANCE.

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Aims: Recreational MDMA (ecstasy) use is associated with serotonin neurotoxicity and neuropsychiatric consequences. The Stroop color naming task probes brain processes involved in attention, decision making, and cognitive control. We used the Stroop task and fMRI to examine the effects of MDMA use on performance and brain activation in MDMA users.
Methods: Brain activation during a Stroop task was compared in 15 MDMA users (abstinent at least 2 weeks) with 11 non-users using SPM5. Participants identified trials in which the color of the word did not match the text by pressing a button. The main contrast of interest was brain activation in response to incongruent cues greater than congruent cues. Lifetime use of MDMA was correlated with brain activation. Family wise statistical threshold ($p<0.05$) was corrected for multiple comparisons using a voxel level $p=0.05$ with a cluster size of 1301.
Results: There were no differences in reaction time for incongruent trials between MDMA users (668.4±30.5 ms) and controls (697.8±66.3 ms). Brain activation in MDMA users was greater than control participants in 3 large clusters in right and left fronto-parietal regions and posterior cerebellum. Brain activation was positively correlated with lifetime MDMA use in 3 large clusters in a right fronto-parietal region (including cingulate), a right limbic region, and left cerebellum and brainstem. There were no regions of negative correlation.
Conclusions: Despite normal task performance, MDMA use was associated with greater activation in multiple large brain regions. This finding is consistent with other results suggesting reduced brain efficiency in MDMA users in that additional brain regions are recruited to maintain normal task performance. Given the inhibitory role of serotonin in cortical function, the increased activation associated with MDMA use may be secondary to increased cortical excitability caused by MDMA-induced serotonergic neurotoxicity.
Financial Support: Supported by NIDA (R01 DA01537; R21 DA020149) to RLC, AACAP (K12DA000357) to MAB, NIMH (K01 MH083052) to JUB, and Vanderbilt CTSA Grant (UL1 RR024975).

125

OXYTOCIN DECREASES METHAMPHETAMINE SELF-ADMINISTRATION IN FEMALE RATS.

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Aims: Methamphetamine (meth) addiction is a pernicious worldwide problem without any available effective treatments. In clinical populations, females transition faster from casual use to dependence than males. However surprisingly few preclinical studies have examined potential sex differences in meth addiction. The neuropeptide, oxytocin, has been suggested as a potential pharmacotherapeutic agent for drug addiction based on it's behavioral profile. In male rats, oxytocin decreased meth-primed reinstatement of meth seeking. Here, we report on the ability of oxytocin to ameliorate meth-primed reinstatement in female rats.
Methods: Freely cycling, Long Evans female rats (N=9) self-administered i.v. meth (0.0175 mg/50 ul infusion) along an FR1 schedule of reinforcement (14 days) in 2-hr daily sessions. Each infusion was accompanied by a light and tone stimulus complex. Following extinction of lever responding, meth-primed reinstatement was tested in the absence of primary reinforcement or cues. Estrous cycle phase was determined prior to oxytocin (0, 0.3, or 1 mg/kg, ip), and 30 min later, rats received a meth priming injection (1 mg/kg, ip) and meth seeking was assessed.
Results: Female rats showed stable meth self-administration and extinguished their responding in the absence of meth over the extinction period. During reinstatement testing, females showed robust reinstatement, but cycle phase did not impact meth seeking [F<1]. However, oxytocin attenuated meth-induced reinstatement [$F(2,60)=5.42$, $p<0.05$] relative to vehicle control.
Conclusions: Similar to males, oxytocin decreased reinstatement to meth-seeking, regardless of estrous cycle phase. These data suggest that the oxytocin may be a potential treatment for meth addiction in both males and females, perhaps blunting reward processes in regions associated with relapse that receive direct oxytocin input. Further studies will investigate the effect of oxytocin on other forms of reinstatement (e.g., cue-induced) to further characterize oxytocin as a potential treatment for meth addiction.
Financial Support: Supported by NIDA grants DA016511, DA022658, DA7288-20

126

EXAMINING NEUROCOGNITIVE SEX DIFFERENCES IN YOUNG ADULT CANNABIS USERS.

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Aims: Cannabis use is associated with deficits in decision-making and memory. Although sex differences are reported among healthy subjects in these neurocognitive domains, little is known about sex differences in the neurocognitive performance of cannabis users.
Methods: Participants were cannabis users (CU; 55 males & 30 females) and non-users (NU; 40 males & 52 females) aged 17-24 years and free of developmental, psychiatric, and neurological problems, and with minimal history of other drug use (except cannabis, alcohol, & nicotine). They completed the Iowa Gambling Task (IGT; a measure of decision-making) and the Hopkins Verbal Learning Test (HVLT-R; a measure of verbal memory).
Results: We conducted two-way between subjects ANOVA with sex, group, and their interaction as independent variables and IGT net score or HVLT total immediate recall as separate dependent variables. There were no significant predictors of IGT. In contrast, NU recalled more words than CU ($d=.86$, $p=.03$) and females recalled more words than males, $d=.46$, $p=.01$. The interaction did not reach statistical significance for HVLT. When including recent (30 day) alcohol and nicotine use as covariates, recent alcohol use was not associated with HVLT performance, but more recent nicotine use was associated with worse performance, $\beta=-.38$, $p<.0001$. The main effect of sex on HVLT performance remained significant ($d=.37$, $p=.03$), however, the main effect of group was no longer significant, $p=.26$.
Conclusions: CU showed deficits in memory, but not decision-making, compared to NU. However, these differences appeared to be better accounted for by heavier recent nicotine use. This could be due to acute effects of nicotine, nicotine withdrawal, or cannabis/nicotine interactions and will need further investigation. Importantly, we found no evidence of sex by cannabis use interactions. Our results provide preliminary evidence suggesting that cannabis use may not have a differential impact for men and women on neurocognitive measures of decision-making and memory.
Financial Support: K23DA023560

127

IMPROVED CLIENT OUTCOMES WITH THE USE OF VIVITROL IN LOS ANGELES COUNTY.

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Aims: The aims were compare the outcomes of clients who were administered Vivitrol to those who did not receive Vivitrol in the areas of treatment engagement, retention, cravings, and treatment completion.
Methods: Data included the Urge to Drink Scale and the Los Angeles County Participant Reporting System (LACPRS) admission and discharge questions. Clients completed the Urge to Drink every week for the first four weeks and monthly thereafter. The LACPRS was completed at admission and discharge.
Results: Detoxification clients who participated in the Vivitrol pilot completed services at a much higher rate when compared to the County average (91.6% vs 70.1%).
Outpatient counseling:
Engagement was better for the Vivitrol clients compared to the County average (88.2% compared to 79.6%) as were completion rates (46.6% compared to 32.9%). Clients who participated in the Vivitrol pilot also showed greater reductions in primary drug use at discharge when compared to the average for the county - Vivitrol clients at admission reported an average of 11.7 days of primary drug use in the prior 30 which was reduced to 1.3 days. The County average for outpatient counseling went from 6.9 days at admission to 2.4 days at discharge.
Residential treatment:
Length of stay was higher for clients who had taken Vivitrol (121.3 days) compared to the County average (78.2 days). Treatment engagement was better for the Vivitrol clients (94.3% compared to 64.2%) and completion rates were higher (64.1% compared to 39.2%) compared to the County average.
These clients reported greater reductions in primary drug use (13.8 days at admission to 0.9 days at discharge) when compared to the County average for residential treatment (10.4 days at admission to 2.1 days at discharge).
Conclusions: Overall, with the exception of length of stay for outpatient counseling, clients who had at least one dose of Vivitrol had better outcomes, remained in treatment longer and were more likely to complete treatment compared to the County average.
Financial Support: The Los Angeles County Department of Public Health, Substance Abuse Prevention and Control office supported this research.

128

FACTORS ASSOCIATED WITH RETURN TO OPIATE USE AFTER RELEASE FROM JAIL.

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Aims: Opiate use is prevalent among individuals in the criminal justice system, with about a quarter reporting lifetime abuse. Further, return to opiate use following incarceration is a leading cause of death and little is known about the risk factors for return to use. The present study sought to examine contextual factors associated with opiate use after release from jail in a large sample under community supervision.
Methods: 23,854 inmates released from county jail and enrolled in Treatment Alternatives for Safer Communities (TASC) from 2002-2007 were administered a baseline assessment and provided random urine drug screens for opiates during their time under community supervision. Cox Proportional Hazard model analysis was used to examine factors associated with time to opiate use. Given our large and racially diverse sample, we were particularly interested in how race and preferred drug of choice (DOC) would influence relapse rates and included these variables as an interaction term.
Results: During time under TASC supervision, 4,208 (17.6%) participants tested positive for opiates, with a mean time from release from jail to resumption of opiates of 90 days (SD = 151 days). About a third (34%) returned to opiate use within the first 48 hours following release. African Americans with opiate DOC returned to use the quickest (HR = 1.6, [1.3, 1.9]), followed by White individuals with opiate DOC (HR = 1.1, [1.0, 1.3]). All other drug of choice groups were associated with slower resumption of use to opiates compared to the opiate DOC groups.
Conclusions: This study is one of the first to examine racial differences associated with time to opiate resumption in a large jail inmate population following release back to the community. Given the rapid rate for resumption of opiate use following incarceration, it is important to provide interventions prior to the time of release, particularly for African Americans with opiates as their DOC, to prevent return to opiate use in the community.
Financial Support: Supported by UAB Psychiatry Departmental Funds.

129

RISKY AND CAUTIOUS DECISION PROCESSING: GIRLS WITH ANTISOCIAL SUBSTANCE DISORDER.

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Aims: Risky behaviors (e.g., drug use, crimes) may yield big rewards or big losses; cautious behaviors involve few losses, but often smaller rewards. When choosing between the two, youths with antisocial substance disorder (ASD; substance use disorder plus serious conduct problems) often "go risky". Brain pathology may contribute to excessive risky choices. As adolescent boys prepare to perform cautious behaviors, those with ASD (compared with controls) have profound neural hypoactivity in DLPFC, ACC, insula, OFC, cerebellum, and elsewhere; before risky behaviors ASD boys have less severe, but significant, hypoactivity in cerebellum, right frontal pole, and temporal and parietal structures (Crowley et al, CPDD 2011). No studies have similarly examined adolescent girls with ASD (vs. controls) making such decisions, and we hypothesize that ASD girls' brains will show hypoactivity like that of ASD boys.
Methods: Procedures were identical to those in our study of boys. Girls (20 ASD patients, 20 controls; 14-18 years old) had psychological assessments and then played a computer game in a 3T fMRI. In 90 "decision trials" subjects decided between making cautious responses (win 1 cent) or risky responses (win 5 or lose 10 cents; odds of losing increased as the game progressed). We compare neural activation of decision trials with activation in similar no-decision trials.
Results: Data collection ended just 2 weeks ago. As expected, there is no significant age difference between ASD (Mn 16.3 yrs) and control (Mn 16.8 yrs) groups, but DSM-IV all-drug abuse/dependence symptom counts do differ (ASD 22.1 symptoms; control 0.25 symptoms; $p<0.0005$). Image analyses have just begun, and will be completed by the 2012 CPDD meeting.
Conclusions: In ASD both genders take risks, contributing to these youths' substance and antisocial problems, early pregnancies, HIV infections, and premature deaths. This study is the first to examine the neural underpinnings of risky-vs.-cautious decision-making in girls with ASD.
Financial Support: NIDA: DA 009842, 011015

130

TOBACCO USE AND COCA LEAF CHEWING AMONG MALES AND FEMALES IN PERU'S RURAL HIGHLANDS POPULATION, 2008.

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Aims: Motivated by preclinical findings that suggest nicotine modulation of cocaine hydrochloride's reinforcing and discriminative functions, we aim to estimate occurrence of cocaine dependence (CD) among Andean coca leaf chewers, male-female differences in CD prevalence, and to test whether CD is associated with tobacco smoking (TS).
Methods: Data are from the Peruvian National Institute of Mental Health community surveys in Peru's rural highlands in 2008 (n=3,031 adults 18+ years). Standardized MINI neuropsychiatric interviews were used to assess TS and CD, with ICD-10 diagnostic guidelines. Contingency table and regression analyses for complex survey and weighted data produced the study estimates.
Results: CD was rare among these coca leaf chewing adults (0.9%). Among CD clinical features, craving was most prevalent among chewers (1.9%). Nonetheless, tobacco smoking was not associated with CD nor with individual clinical features (all $p>0.05$). Highland males and females of virtually all adult ages chew coca leaf, but CD prevalence did not vary by sex ($p>0.05$).
Conclusions: Perhaps due to micro-doses of cocaine HCl in coca leaf, or for other reasons, TS was not associated with the CD syndrome or its individual clinical features in this sample. CD was found to be quite rare in this population. It affected males and females with equal frequency. Some Peruvian highlanders migrate to metropolitan Lima and to the United States (e.g., New Jersey). In future research we hope to study the natural history of coca chewing and other cocaine self-administration among these migrants.
Financial Support: NIH/FIC/NIDA D43TW05819 (VC) & K05DA015799 (JCA).

131

DISCRIMINATIVE STIMULUS EFFECTS OF MECAMYLAMINE IN NICOTINE-TREATED AND UNTREATED RHESUS MONKEYS.

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Aims: Nicotine withdrawal is one of the challenges associated with quit attempts in cigarette smokers. This study examined mecamylamine-induced nicotine withdrawal using drug discrimination in rhesus monkeys. As a control, the capacity of mecamylamine to serve as a discriminative stimulus in the absence of nicotine treatment was examined.
Methods: Four rhesus monkeys received continuous s.c. infusion of 5.6 mg/kg/day of nicotine base and discriminated 1.78 mg/kg s.c. mecamylamine from saline under a fixed ratio 5 schedule of stimulus-shock termination. The same schedule parameters were used to train mecamylamine (5.6 mg/kg) as a discriminative stimulus in the absence of nicotine treatment in four seperate rhesus monkeys.
Results: Mecamylamine increased drug-lever responding in both nicotine-treated and untreated monkeys; ED50 values of mecamylamine were 0.86 mg/kg and 2.5 mg/kg, respectively. Nicotine, when administered acutely up to a dose of 5.6 mg/kg base in addition to continuous administration of 5.6 mg/kg/day, didn't attenuate the discriminative stimulus effects of mecamylamine in nicotine-treated monkeys. Similar results were obtained in untreated monkeys, i.e., nicotine (up to 10 mg/kg) failed to attenuate the mecamylamine discriminative stimulus. Discontinuation of nicotine treatment resulted in an immediate (i.e., within 24 h) switch from the vehicle to the mecamylamine lever in some but not all monkeys.
Conclusions: Mecamylamine was more potent as a discriminative stimulus in nicotine-treated as compared with untreated monkeys. This might reflect a qualitative difference among the discriminations, with the effects of mecamylamine in nicotine-treated monkeys being due to antagonism of nicotine and perhaps nicotine withdrawal. However, discontinuation of continuous nicotine treatment didn't mimic the effects of mecamylamine in all monkeys and increasing doses of nicotine did not attenuate the effects of mecamylamine. The non-competitive antagonism of nicotine by mecamylamine appears to limit the utility of this approach as a strategy for examining pharmacologic modification of nicotine withdrawal.
Financial Support: USPHS grant DA25267.

132

RESIDENTIAL DRUG TREATMENT CLINICS IN JALISCO, MEXICO: STAFF AND SERVICE CHARACTERISTICS.

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Aims: It has been estimated that Mexico has more than 1800 drug treatment clinics. This study examined the staff and service characteristics of all residential treatment clinics in Mexico's west central state of Jalisco.
Methods: We conducted an on-site survey of all residential clinics in Jalisco that met the criteria for residential treatment according to the Mexican Norm 028 (191 clinics, 5,545 beds). The survey focused on the clinics' organizational structure, resources and characteristics of clinic staff.
Results: The clinics were of three types: Self-Help (78%),combined Medical-Self Help (M-SH)(17%),and Medical (5%). Medical and psychological evaluations were performed more frequently in the Medical and M-SH than in the Self-Help clinics. Of the staff working in the M-SH and Medical clinics, 51% and 89%, respectively, had college degrees. In contrast, only 17% of the staff in the self-help clinics had college degrees. Twenty-five percent of the Self-Help staff and 27 % of the M-SH staff cited their past use of drugs as a reason they had not pursued an educational or college degree. Although college degrees were relatively uncommon among the Self-Help personnel, almost two-thirds (61%) of the Self-Help staff recognized the need for training in the treatment of addictions; and the majority (57%) expressed interest in receiving training.
Conclusions: Most residential treatment in the state of Jalisco is available through Self-Help clinics which are more likely to lack funding, medical-psychological supervision and college educated personnel. Self-Help staff compared with M-SH staff were particularly likely to recognize the need for training and express interest in the possibility of receiving it. As Self-Help clinics predominate in Jalisco, there should be a more focus on support them with funding, supervision and training.
Financial Support: Jalisco State council for addictions

133

THE FEASIBILITY AND ACCEPTABILITY OF USING THE NINTENDO® WII FIT EXERCISE PROGRAM IN PATIENTS RECEIVING METHADONE.

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Aims: Little research has been conducted on physical exercise in patients receiving methadone maintenance treatment (MMT) despite their high levels of sedentary behaviors and elevated rates of medical and psychiatric comorbidity. This pilot study examined the feasibility (i.e., intervention and assessment adherence) and acceptability (i.e., intervention satisfaction) of a novel, popular exercise intervention, the Nintendo® Wii Fit program, in engaging MMT patients in physical exercise.

Methods: Participants were 21 patients receiving MMT with ongoing illicit opioid or cocaine use who entered an 8-week randomized clinical trial involving daily (Mon-Fri) 30-minute sessions of either Nintendo® Wii active game play (AGP) or sedentary game play (SGP). Intervention satisfaction was assessed weekly using quantitative and qualitative measures. Demographic, substance abuse, and treatment information were collected at baseline. AGP and SGP attendance was recorded. Preliminary descriptive analyses on demographics, intervention adherence, and intervention satisfaction were conducted to examine feasibility and acceptability.

Results: Of the 21 participants, 43% were male and 43% were white. Ages ranged from 27 to 59 (M=45, SD=12.6); BMI ranged from 19 to 48 (M=29, SD=7.1). At baseline, patients exhibited past-week substance use (14% opioids only, 57% cocaine only; 29% both opiates and cocaine). Average daily methadone dose was 80.7 mgs. Weekly assessment completion rate was 91% and daily session attendance rate was 64%. Participants reported a high level of satisfaction (M = 6.2 out of a possible 7, SD = 0.2). Qualitative satisfaction data were highly favorable for both AGP and SGP.

Conclusions: The Nintendo® Wii, a highly transportable, affordable, and adaptable exercise-engagement intervention, demonstrated high levels of feasibility and acceptability in MMT. Future research that systematically evaluates its efficacy in opioid-agonist maintained patients is merited.

Financial Support: NIDA P50DA009241, NIDA K23 DA024050, K24 DA00445, R01 DA019511

134

ONE-YEAR RELIABILITY OF THE MARYLAND RESOURCE FOR THE BEHAVIORAL UTILIZATION OF THE REINFORCEMENT OF NEGATIVE STIMULI.

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Aims: The use of laboratory-based behavioral measures of risk-taking provides one strategy to understand problematic alcohol use in early adolescents through emerging adults. We created the Maryland Resource for the Behavioral Utilization of the Reinforcement of Negative Stimuli (MRBURNS), a laboratory analogue designed to measure negative reinforcement-driven risk taking (MacPherson et al., 2011). The present study examines the one-year reliability of the MRBURNS.

Methods: From a full sample of 116 young adults who ever had a period of time in which alcohol was consumed at least once per week (mean age=18.13, 50.3% male, 71.2% White at baseline), 81 returned for a one-year retest of the MRBURNS. At baseline, participants completed the MRBURNS and completed the MRBURNS again at a one-year follow-up. The MRBURNS is comprised of three task phases: 1) Automatic Pump Selection (choice of number of balloon pumps), 2) Aversive Noise (exposure to noise, noise duration is reduced by 0.15 seconds for each pump), and 3) Consequence and Lottery (participant receives a winning lottery ball if balloon is safe and a losing ball if balloon pops). At the end of 30 balloons, 6 lottery drawings occur (one drawing for every successive 5 balloons). For the lottery drawings, potential monetary rewards are $1, $9, $3, $9, $1, $3.

Results: Test-retest reliability between baseline and one-year follow-up was promising with r = .50 (p=.001). Further, reliability within lottery amounts was also acceptable ($1: r= .43, $3: r=.43, $9: r=.51). Individuals who did not return for the one-year follow-up did not differ from those who did return on demographic variables, though participants who did not return for the follow-up pumped significantly less at the $1 monetary amount at baseline than did those who returned.

Conclusions: These results suggest that the MRBURNS exhibits promising one-year reliability and that task mechanisms may differentiate individuals who return for a follow-up from those who do not.

Financial Support: NIAAA 2R21 AA01768 and by NIDA 3K23 DA023143

135

THE EFFECT OF KETAMINE ON USE-RELATED MEASURES IN COCAINE-DEPENDENT VOLUNTEERS.

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Aims: Glutamatergic modulation may have therapeutic implications for cocaine dependence, despite inconclusive findings from human studies. Recent research in other settings indicates that a single sub-anesthetic infusion of ketamine, the NMDA receptor antagonist, has unique and sustained effects on human brain systems. The aim of this 9-day inpatient, randomized, within-subject, controlled trial was to investigate the effects of sub-anesthetic ketamine on use-related measures in non-treatment seeking cocaine dependent volunteers.

Methods: After a 2 day washout, participants were randomized to any of four counter-balanced sequences of three infusions (IV over 50 minutes) separated by 48 hours: 2 mg lorazepam, 0.41 mg/kg ketamine, or 0.71 mg/kg ketamine. Motivation to change use was assessed (by URICA) at baseline, as were cue-induced craving (VAS) and cue reactivity (GSR); these measures were repeated 24 hours following each infusion. Participants were followed for four weeks post-discharge for monitoring and drug use assessments.

Results: Infusions have been well tolerated, with no development of psychosis, drug-liking, or initiation of substance misuse. Thus far (n=6), ketamine significantly increased motivation to change use as compared to lorazepam by a paired-sample t-test (81% gain on URICA vs. -0.4%, $p<0.05$), with a non-significant trend towards reducing cue-induced craving (78% decrease on VAS vs. 44%, p= 0.1). 67% of participants substantially reduced use (by >50% of baseline levels) or maintained abstinence in the follow-up period (by TLFB and urine-toxicology).

Conclusions: This analysis suggests that sub-anesthetic ketamine can be feasibly and safely administered to cocaine users, and that it may have clinical utility in the treatment of cocaine dependence.

Financial Support: This project has been funded by NIDA grants P50-DA009236-17 (Kleber), 1K23DA031771-01 (Dakwar), T32 DA007294-15 (Levin).

136

SEX DIFFERENCES IN AMBULATORY ACTIVITY AFTER ACUTE ADMINISTRATION OF COCAINE, METHAMPHETAMINE, AND CANNABINOIDS.

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Aims: Accumulating evidence suggests that sex-specific differences are present at all stages of the addiction process, including induction, maintenance, and relapse. Our lab has recently shown that female rats' psychomotor responses to cocaine are more robust and longer lasting than male rats. We hypothesized regardless of the drug treatment (cocaine, methamphetamine, or WIN-55, a selective cannabinoid agonist) the behavioral response will be sexually dimorphic.

Methods: Ambulatory activity in male and female Fisher rats was measured after acute administration of cocaine (30 mg/kg, i.p.), methamphetamine (3 mg/kg, i.p.), WIN-55 (0.15 mg/kg i.p.), DMSO or saline.

Results: Preliminary results showed sex differences in behavioral responses only after methamphetamine and cocaine. Specifically, females have more robust behavioral responses than males to both psychostimulants. However, there was no difference in locomotor behavior between males and females in rats administered WIN-55.

Conclusions: This study provides evidence of sex differences in psychomotor activity in response to psychostimulant drugs such as cocaine and methamphetamine, and these sex differences are not observed in response to depressant types of drugs, such as marijuana.

Financial Support: NIH/NIDA R24-012136, RCMI RR03037

137

A WEB-BASED STUDY OF SELF-TREATMENT OF OPIOID WITHDRAWAL SYMPTOMS WITH LOPERAMIDE.

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Aims: Many websites provide a medium for individuals to freely share their experiences and knowledge about different drugs. Such user-generated content can be used as a rich data source to study emerging drug use practices and trends. The study aims to examine web-based reports of loperamide use practices among non-medical opioid users. Loperamide, a piperidine derivative, is an opioid agonist approved for the control of diarrhea symptoms. Because of its general inability to cross the blood-brain barrier, it is considered to have no abuse potential and is available without a prescription.
Methods: A website that allows free discussion of illicit drugs and is accessible for public viewing was selected for analysis. Web-forum posts were retrieved using Web Crawlers and retained in an Informal Text Database. All unique user names were anonymized. The database was queried to extract posts with a mention of loperamide and relevant brand/slang terms. Over 1200 posts were identified and entered into NVivo to assist with consistent application of codes related to the reasons, dosage, and effects of loperamide use.
Results: Since the first post in 2005, there was a substantial rise in discussions related to its use by non-medical opioid users, especially in 2009-2011. Loperamide was primarily discussed as a remedy to alleviate a broad range of opiate withdrawal symptoms, and was sometimes referred to as "poor man's methadone." Typical doses frequently ranged from 100 mg to 200 mg per day, much higher than an indicated dose of 16 mg per day.
Conclusions: This study suggests that loperamide is being used extra-medically by people who are involved with the abuse of opioids to control withdrawal symptoms. There is a growing demand among people who are opioid dependent for drugs to control withdrawal symptoms, and loperamide appears to fit that role. The study also highlights the potential of the Web as a "leading edge" data source in identifying emerging drug use practices.
Financial Support: Financial support was provided by NIDA (R21DA030571; Daniulaityte, PI; Sheth, PI)

138

ISOLATION REARING AS A MODEL OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

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Aims: Rats raised in an isolated condition (IC) are more impulsive compared to rats raised in an enriched condition (EC), and methylphenidate reduces impulsivity in IC rats, suggesting that isolation rearing may model impulsivity, one component of attention-deficit/hyperactivity disorder (ADHD). However, it is not clear if isolation rearing models the hyperactivity associated with ADHD, a facet that is also sensitive to methylphenidate treatment.
The current study determined if methylphenidate (MPH), a dopamine transporter (DAT) blocker and therapeutic agent for ADHD, administered during development in EC and IC rats alters locomotor activity and DAT function in, orbital frontal cortex (OFC) and medial prefrontal cortex (mPFC), two regions involved in inhibitory control.
Methods: From postnatal days (PND) 28-51, EC and IC rats were administered MPH (1.5 mg/kg, p.o., in apple juice) or vehicle. Locomotor activity was assessed on PND 28 and 51. On PND 55, kinetic analysis of [3H]DA uptake was performed using mPFC and OFC synaptosomes from individual rats, and Vmax and Km were obtained.
Results: Greater locomotor activity was observed in IC compared to EC rats on both PND 28 and 51. On PND 28, acute MPH increased activity only in EC rats. On PND 51, MPH did not alter activity in either IC or EC rats. In rats administered vehicle, Vmax for [3H]DA uptake in mPFC was greater in IC compared to EC rats; however, in OFC, Vmax for [3H]DA uptake was lower in IC compared to EC rats. MPH treatment resulted in a decreased Vmax for [3H]DA uptake in mPFC from IC rats only.
Conclusions: Thus, isolation rearing was associated with an increased DAT function in mPFC and this effect was normalized by MPH treatment; however, although isolation rearing resulted in hyperactivity, this effect was not ameliorated by MPH. In summary, isolation rearing models some, but not all, aspects of ADHD.
Financial Support: DA12964 and DA05312

139

ASSESSING ABUSE DETERRENCE STRATEGIES FOR PHARMACEUTICALS USING CROWDSOURCING FOR BLACK MARKET STREET PRICES.

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Aims: Create an online crowdsourcing platform to collect information on street prices of controlled substances. Compare results of crowdsourcing with surveys of law enforcement and regulatory officials. Evaluate 3 abuse deterrence strategies (physical barrier, agonist-antagonist, & prodrug) using real world street prices.
Methods: Launched in Nov. 2010, StreetRx.com allows submission of prices for diverted prescription drugs, search for prices by geography, & rate prices (cheap to overpriced). Data collected were compared to the RADARS® System Drug Diversion Program's Street Price Questionnaire (SPQ) survey, which collects quarterly data from 125 law enforcement and regulatory officials. Street prices for different "abuse deterrent formulations" were compared to corresponding unprotected formulations. Prices were standardized by milligram. Geometric means and 95% confidence intervals were calculated in STATA 11.
Results: There were 15,544 unique site visitors and more than 2000 submissions of street prices in the first year. On StreetRx.com, the mean reported street price for OxyContin® OC (original) was $0.78 per mg, and the more difficult to crush OxyContin OP (reformulation) was $0.56, a 28% difference. Similar results were found using SPQ. Suboxone® (buprenorphine plus antagonist naloxone) had a lower street price than Subutex® (buprenorphine alone): 14% lower in StreetRx and 17% lower in SPQ. Produrg lisdexamfetamine (Vyvanse®) has lower street prices than active metabolite amphetamine: 60% lower in StreetRx and 52% lower in SPQ.
Conclusions: Street prices collected via StreetRx were similar to prices from law enforcement. Of 3 abuse deterrent strategies assessed, prodrugs had greatest difference compared to unprotected formulation, followed by physical barrier and agonist-antagonist. Further work is needed to characterize data collected from online crowdsourcing. StreetRx may be a useful tool for law enforcement.
Financial Support: StreetRx is a Program of the non-profit Researched Abuse Diversion and Addiction-Related Surveillance (RADARS) System.

140

PERCEIVED STRESS AND PATIENT RETENTION OF COCAINE-DEPENDENT MALES IN A DOUBLE-BLIND TREATMENT RESEARCH STUDY.

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Aims: Retention of patients is a major concern facing treatment studies. Stress has been shown to have an effect on a person's use of illicit drugs, including cocaine. The purpose of this study was to examine the relationship between perceived stress of cocaine-dependent treatment seekers and retention in a pharmacological treatment study using Mifepristone as a glucocorticoid receptor antagonist in cocaine-dependent men.
Methods: Sixteen cocaine dependent males were enrolled in a double-blind treatment research study of Mifepristone. Upon enrollment, the participants completed the Perceived Stress Scale (PSS). The PSS is a ten question scale about recent feelings and thoughts pertaining to stress. Participant's scores on the PSS were compared to the ability to complete the nine-week treatment program.
Results: PSS scores at baseline were calculated. There was a significant difference between the PSS score of the treatment completion group (Mdn = 17.5) verse the non-completion group (Mdn = 21.5), $Z = -2.356$, $p = .018$, $r = .589$.
Conclusions: Participants with lower perceived stress scores at baseline were more likely to complete the nine-week treatment study. By gauging a participant's perceived stress level at enrollment in a treatment study, researchers may be able to better understand a participant's needs, therefore proactively gaining higher retention rates for their studies.
Financial Support: NIDA grant: K23DA027044-01

141

DEVELOPMENT, RELIABILITY, AND VALIDITY OF THE ECSTASY CRAVING QUESTIONNAIRE.

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Aims: Although numerous questionnaires have been published to assess craving for a variety of drugs, no such instruments have been developed to assess craving for MDMA/ecstasy. Therefore, this study was designed to develop and evaluate the psychometric properties of such a questionnaire.
Methods: A pool of 19 potential items was developed by modifying items from other craving instruments and writing new items that apply only to MDMA/ecstasy. Using three websites (pillreports.com, facebook.com, & bluelight.ru), I recruited 217 regular users of MDMA/ecstasy. Participants rated their craving on these 19 items and were then showed one of two 3-minute cue-exposure videos: (a) dancing + music + interspersed photos of pills or (b) marching band + music
+ interspersed photos of peanuts. Following cue-exposure, subjects re-rated their craving on the same items, and completed questionnaires to assess motivations for use, refusal self-efficacy, obsessive/harmonious engagement in ecstasy use, substance use/problems, and demographic information.
Results: Based on a conceptualization of craving that emphasized current desire, use intention, and loss of control, 11 potential items were removed to comprise the final 8-item ECQ. None of these 8 were "unbalanced" (i.e., 80+% agreed or disagreed) nor were they highly inter-correlated ($r > 0.70$). Internal reliability consistency across the 8 items was high ($\alpha = 0.93$). The criterion validity of the ECQ was supported by significant positive correlations of craving scores with motives for use, problems related to drug use, frequency of ecstasy use, and obsessive/harmonious engagement in ecstasy use, and a significant negative correlation with self-efficacy to refuse ecstasy. As one element of construct validity, we also found a statistically significant interaction on ECQ scores as a function of time (pre vs. post cue exposure) X condition (rave/pills video vs. band/peanuts video, $F=5.276$, $p < .05$).
Conclusions: This evaluation supports several aspects of reliability and validity of this measure, but further testing of drug takers is required to evaluate the generalizability of initial findings.
Financial Support: None

142

SURVEILLANCE OF VOLATILE CONSTITUENTS IN ELECTRONIC CIGARETTES.

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Aims: To promote consumer appeal, e-cig manufacturers must ensure that product nicotine delivery, flavor and other chemosensory characteristics are sufficient to promote and maintain nicotine dependence. The aim of this study was to characterize two different brands of e-cigs, each at 3 different nicotine levels, to determine the nature of additives and tobacco-related constituents used in e-cig cartridges. We tested NJOY (0%, 1.2% and 1.8% nicotine) and Intellicig (low, medium and high nicotine) and characterized the cartridge contents using headspace-solid phase microextraction (SPME)-gas chromatography. Select components were quantitated, and compared to selected popular tobacco cigarette brands.
Methods: The entire e-cig cartridge was sampled using a carboxen/ polydimethylsiloxane SPME fiber and desorbed onto a DB-WAX capillary column. Analytes were detected and identified using mass spectrometry. A modified Coresta method was used to determine nicotine, menthol, and minor alkaloids content.
Results: Consistent with the package label, nicotine was identified and quantitated in the e-cigs. Tobacco related compounds, and some flavorants (menthol, methyl salicylate) were identified in products that were not sold as flavored e-cigs. Pyrazines were also identified in some products. The composition of e-cigs as determined by volatile constituents was less complex and less strong than that of tobacco cigarettes.
Conclusions: The presence of tobacco-related products in e-cigs could be attributed to the use of nicotine extracted from tobacco plant material. The identification of other flavorants suggests that tobacco companies may be adding them to enhance the chemosensory properties of e-cigs, including, flavor, impact and smoothness-harshness balance. E-cigs are under the regulatory purview of the FDA, but final regulatory guidelines have not been issued. Surveillance of the design features of e-cigs, and an understanding of their influence on human use and dependence, is essential for the development of effective regulatory policy.
Financial Support: National Cancer Institute grant # R01CA125224

143

PREVALENCE OF DRUG USE AMONG DRIVERS WHO DRANK ON ALCOHOL OUTLETS OF PORTO ALEGRE, BRAZIL.

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Aims: Traffic crashes (TC) are a public health problem, and the use of multiple drugs increases its risk. The aim of this study is to estimate the prevalence of driving under influence of alcohol and other drugs among drivers who drank at alcohol outlets (AO) of a Brazilian state capital.
Methods: A survey was conducted with a probabilistic three-stage cluster sample, and 3018 individuals who were leaving AO were approached. Drivers who had drunk alcohol answered a structured interview, were breathalized and had saliva collected for the screening of benzodiazepines, THC, cocaine and ecstasy. Data analysis was conducted in R considering sample design and post-stratification calibration weights.
Results: 683 drivers were interviewed, leading to an estimate of 151,573 drivers who drank at the AOs. More than a half (56.3%, SE 3.5%) intended to drive in the 60 minutes after the interview. Among drivers who were going to drive, 11% had used one other drug, 0.4% had use two and 0.1% had use three drugs in addition to alcohol. THC and benzodiazepines were the most frequent drugs (4.3% each), followed by cocaine (3.0%).
Conclusions: It is important to emphasize that every driver had use alcohol and the frequencies presented for drug use indicates that this population has a huge risk for TC. Since Brazil is still struggling with the control of alcohol use among drivers, the high prevalence of other drugs represents a challenge for policies and enforcement in the country. Data about drivers who had not drunk was not collected, and future studies should address this question.
Financial Support: National Secretariat for Alcohol and Drug Policies (SENAD) and
FIPE- HCPA

144

MATERNAL ALCOHOL USE AND EARLY TEENAGE PREGNANCY IN THE OFFSPRING OF TEENAGE MOTHERS.

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Aims: Although most children of teenage mothers break the inter-generational cycle of teenage parenthood (Furstenberg, 2007), they remain significantly more likely to become pregnant during adolescence than the children of adult mothers. Previous research indicates that teenage mothers have different patterns of substance use than other mothers, maintaining higher levels of substance use a decade after giving birth (De Genna, Cornelius, & Donovan, 2009; Gillmore et al., 2006). However, it is not clear if maternal substance use is associated with behavior in offspring that promotes inter-generational continuity in teenage pregnancy.
Methods: Mothers were recruited as pregnant teenagers (n = 416; age range = 12-18 years; 68% African-American) from an outpatient prenatal clinic. Data were collected on maternal substance use (alcohol, tobacco, marijuana) twice during pregnancy, at delivery, and at postnatal ages 6, 10, 14 and 16. Offspring were also assessed at these time points, providing information about their substance use, sexual behavior and pregnancy at ages 14 and 16 years (n = 332 seen at age 16; 51% girls).
Results: Maternal alcohol use at the 10-year follow-up predicted more casual first sexual experiences (one-night stands and casual partners compared to serious romantic partners or abstinence) when the offspring were 16 years old. Maternal prenatal alcohol use and alcohol use at the 10-year follow-up predicted 2 or more sex partners in the past year when the offspring were 16 years old. Nine percent of the offspring had experienced a pregnancy by age 16, more than expected in the general population. Twenty percent of offspring whose mothers were heavy drinkers at the 14-year follow-up had gotten pregnant or gotten someone pregnant by age 16 years, compared to 6% whose mothers were not heavy drinkers at this follow-up.
Conclusions: Maternal substance use, specifically alcohol use, may contribute to inter-generational continuity in teenage pregnancy via its association with adolescent behaviors such as early and casual sex and multiple sex partners.
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145

CRIMINAL JUSTICE REFERRAL AND INCENTIVES IN OUTPATIENT SUBSTANCE ABUSE TREATMENT.

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Aims: Stimulant users who sought treatment in a psychosocial outpatient treatment program participated in a multi-site 12- week randomized controlled trial (n = 415) of a prize-based abstinence incentive intervention. Primary study outcomes were published previously (Petry et al., 2005). The present analysis examined the influence of criminal justice referral on treatment retention and stimulant use.
Methods: In this Clinical Trials Network study, participants were categorized based on study condition (incentives vs. usual care) and whether they were referred to treatment by the criminal justice system (yes/no). Analyses that assessed the separate and interactive effects of these factors on retention and stimulant use were conducted.
Results: Participants referred from the criminal justice system (N = 138) were more likely to be retained in treatment (p = .025) and to provide stimulant negative urine samples (p = .017) than those not referred from criminal justice (N = 277). There was a significant interaction of criminal justice referral and incentives on treatment retention. Among voluntary referrals, those receiving abstinence incentives submitted 11.2 negative urines on average vs 7.8 submitted by those in usual care (p =.001). Among criminal justice referrals, mean number of negative urines submitted was 12.5 in those who received abstinence incentives vs 10.3 in usual care (NS).
Conclusions: Abstinence incentives significantly improved outcomes in voluntary but not in criminal justice referred admissions to outpatient treatment, probably due to higher base rates of retention and abstinence in the CJ referrals. Nevertheless, an additive effect of external motivation sources was seen with best outcomes in those exposed to both positive (abstinence incentives) and negative (CJ monitoring and sanctions) motivators and worst outcomes in those with neither source of external motivation.
Financial Support: U10DA13034 from the NIDA Clinical Trials Network.

146

ROUTES OF ADMINISTRATION AND FREQUENCY OF ABUSE OF OXYCONTIN® AND IMMEDIATE-RELEASE OXYCODONE IN A RURAL KENTUCKY COUNTY FOLLOWING INTRODUCTION OF REFORMULATED OXYCONTIN.

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Aims: In August 2010, shipments of original OxyContin® (oxycodone HCl controlled-release; OC) stopped and reformulated OxyContin (ORF) started. ORF is more difficult to crush and forms a gel when dissolved. This study describes changes in routes of administration (ROA) and frequency of abuse of OxyContin and immediate-release (IR) oxycodone following the introduction of ORF in a sample of OxyContin abusers.
Methods: Structured interviews assessing opioid abuse, including past 30-day ROA and frequency, were completed by 192 OC abusers in rural Kentucky. Participants reported retrospectively about their abuse in the pre-ORF period in July 2010, and concurrently about their abuse in the post-ORF period in interviews conducted December 2010 through September 2011.
Results: After its introduction, ORF abuse was lower than for IR oxycodone, and was mainly limited to oral ROA, with 21% reporting oral abuse (average 6.8 days per month), 5% snorting (4.2 days), and only one participant injecting (1.0 day). Prevalence of IR oxycodone abuse increased pre- to post-ORF from 57% to 70% for snorting and 45% to 51% for injecting; oral abuse remained stable at 30-32%. In addition, frequency of IR oxycodone abuse increased for all ROA (oral: 4.1 to 12.3 days; snorting: 13.3 to 14.6 days; injecting: 12.6 to 20.3 days). Before introduction of ORF, prevalence of OC abuse in the sample was 25% for oral, 50% for snorting, and 51% for injecting ROA. Before ORF, average days per month of OC abuse were 0.3 for oral, 11.6 for snorting, and 16.6 for injecting ROA.
Conclusions: After its introduction, the prevalence of ORF abuse was lower than that of OxyContin before ORF introduction, especially by non-oral ROA. After introduction of ORF, there was an increase in the prevalence and frequency of IR oxycodone abuse, particularly through snorting and injecting ROA.
Financial Support: Supported By Purdue Pharma L.P.

147

SEX DIFFERENCES, DECISION-MAKING AND THE NEURAL CORRELATES OF COGNITIVE CONTROL IN COCAINE DEPENDENCE.

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Aims: Sex differences have been widely demonstrated in the clinical presentation of addiction. Growing evidence supports sex differences in brain structure and function and in aspects of impulsivity and impaired decision-making which may contribute to the development or maintenance of addiction. Despite substantial literature on functional magnetic resonance imaging (fMRI) in addiction, very few studies have directly assessed sex differences. To our knowledge, this is the first study of sex differences in the neural correlates of cognitive control in cocaine dependent and healthy control groups.
Methods: Twenty-three individuals meeting DSM-IV criteria for current or past Cocaine Dependence (CD; 11 females) and 24 age-matched Healthy Controls (HC; 12 females) completed an event-related fMRI Stroop task, neurocognitive decision-making and risk-taking measures, and impulsivity questionnaires. FMRI analyses assessed sex and diagnostic group differences in 'Stroop effect,' (i.e., Incongruent>Congruent) and were whole-brain family-wise-error-corrected ($p<.05$). Impulsivity and decision-making measures were included in fMRI correlation analyses.
Results: The CD group scored higher on self-reported impulsivity while main and interactive effects of sex and diagnosis were observed on different decision-making measures. FMRI data showed that, relative to the HC group, the CD group demonstrated greater Stroop-related deactivation in the ventromedial prefrontal cortex. Activation in this cluster correlated with measures of risky decision-making. Within the CD group, females demonstrated greater Stroop activity than males in regions including right inferior frontal gyrus, ventral striatum and orbitofrontal cortex.
Conclusions: Sex differences in cocaine addiction may in part arise from sex differences in the neural underpinnings of cognitive control and decision-making.
Financial Support: T32-AA015496, K12-DA031050, R01-DA019039, P50-DA09241, K12-DA00167

148

REVERSAL OF FENTANYL-INDUCED RESPIRATORY DEPRESSION WITH A NOVEL OPIOID RECEPTOR ANTAGONIST ALKS 33 IN DOGS.

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Aims: Naloxone is an opioid antagonist used clinically to counter CNS and respiratory depression resulting from opioid overdose, but because of its short half life, may result in renarcotization. ALKS 33 is a μ-opioid antagonist with δ and κ partial agonist activity and a longer half-life. The purpose of this study was to establish a non-rodent model of opioid overdose and evaluate the effects of ALKS 33 to reverse the actions of a continuous intravenous (IV) infusion of fentanyl (FEN) as measured by behavioral, cardiovascular and respiratory function.
Methods: Naïve male Beagle dogs (N=6) were surgically implanted with telemetry devices to continuously monitor several physiological functions. Each animal was administered an IV FEN infusion (0.36-0.48 mg/kg) for up to 12 hours to induce and maintain significant sedation and respiratory depression (pCO_2 and breaths per minute). Dogs received a single intramuscular (IM) injection of ALKS 33 (0.1 or 0.2 mg/kg) approximately 1.5 hours after the initiation of the FEN infusion. Data was collected for clinical observations, systemic arterial blood pressure, core body temperature, pulmonary function (respiratory rate, tidal and minute volumes) and blood gasses.
Results: All animals reached a heavily sedated state ($pCO2 = 58.7 \pm 1.4$) within 1 hour of FEN administration. Within 5 minutes of dosing with ALKS 33, all animals were moderately to fully awake and remained so for the remainder of the 12 hour FEN infusion. Blood pressures were elevated and heart rates, pulmonary functions and body temperatures were decreased during the initial FEN infusion. These measures returned to baseline levels soon after the ALKS 33 injection. Respiratory depression (decreased pO_2 and increased pCO_2) with continuous FEN infusion was ameliorated within minutes following ALKS 33.
Conclusions: ALKS 33 rapidly reversed FEN-induced CNS and respiratory depression and maintained this reversal of FEN's actions for up to 10 hours following a single IM administration.
Financial Support: Alkermes, Inc.

149

THE IMPORTANCE TO MONITOR ALL SUBSTANCE AND NON-SUBSTANCE ADDICTIVE BEHAVIORS IN THERAPEUTIC COMMUNITY SETTINGS.

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Aims: Most studies evaluating Therapeutic Communities (TC) report a decrease of substance use during time in TC. However, these studies focused on illegal drugs and alcohol but not tobacco and non-substance addictive behaviors.
Objective: To assess change in substance and non-substance addictive behaviors during 18-month treatment in TC.
Methods: Residents were assessed at entry in TC and at 6-, 12-, 18-months after intake. Substance use (including alcohol and tobacco) and non-substance addictive behaviors (including gambling and eating disorders) were assessed with the French modified version of the Addiction Severity Index. ANOVA's repeated measures were performed to evaluate the change in substance use and non-substance addictive behaviors over time.
Results: Residents (n= 98) presented at least one substance-related addiction disorder and reported alcohol, cocaine and opiates as main problem drug. During time in TC, alcohol, cocaine and opiate use significantly decreased. However, there was a trend for an increase of tobacco use, benzodiazepine use, gambling and eating disorders during the same time.
Conclusions: Although illegal drug use and alcohol dramatically decreased while in TC, it is possible that the addictive disorder might still be active and residents switched their addictive behaviors to tobacco, gambling and eating disorders. Treatment programs focused on promoting abstinence from substance use might consider monitoring all possible addictive behaviors such as gambling and eating disorders.
Financial Support: OFDT 2008

150

COMPARATIVE STUDY OF SUBSTANCE DISORDER SYMPTOM HIERARCHY BY TYPE OF SUBSTANCE AND AGE.

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Aims: While there have been several studies looking at the structure and validity of substance use disorder symptoms for individual substances, there have been few examinations that have directly compared the results across the type of substance or examined how the interact with age. 1) Do the severity hierarchies of substance use symptoms vary depending on the type of substance (i.e. amphetamines, alcohol, cannabis, cocaine, and opiates)? 2)Do the substance severities differ for adolescents vs. adults? 3)Do the severity hierarchies for a given substance differ for adolescents vs. adults?
Methods: Eleven symptoms of abuse/dependence from the Substance Problems Scale of the Global Appraisal of Individual Need (GAIN; Dennis et al., 2003)were collected on a sample of 51,840 adolescents and adults from 292 sites around the U.S. Rasch (1 parameter Item Response Theory or IRT) model was used to place symptoms, substances and persons on a common, linear, interval measure that enabled examination of the relationships of these three facets.
Results: Symptom severity hierarchies varied by substance, age, and age within each type of substance use. The order of presentation was almost perfectly reversed for opioids vs cannabis with other substances falling in between. Adolescents and adults differed in terms of the drugs they used and in the differential severity of their symptoms. One of the rarer adult symptoms proposed for deletion from DSM-V (repeated problems with the law) was actually a relatively common adolescent symptom. Severity was more strongly influenced by drug of choice than by age.
Conclusions: The current 11 symptoms of abuse and dependence worked across substances and age, but varied in different ways. The findings reiterate the importance of knowing how the substance use and age impacts the course of expected order of symptom presentation. The tight range of presentation for several substances reinforces the Langenbucher et al(2004) recommendation to use more symptoms at the high and low ends of the hierarchy to improve the reliability and validity of diagnosis.
Financial Support: SAMHSA contract #270-07-0191

151

RACIAL/ETHNIC DISPARITIES IN HIV INFECTION AMONG PEOPLE WHO INJECT DRUGS: AN INTERNATIONAL SYSTEMATIC REVIEW.

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Aims: The Ethnic Minority Meta-Analysis (EMMA) aims to assess racial/ethnic disparities in HIV infection among people who inject drugs (PWID) in different countries. This is the first report of the international data.
Methods: Standard systematic review/meta-analysis methods were utilized, including searching for, screening, and coding published and unpublished reports, and meta-analytic statistical techniques.
Results: Racial/ethnic disparities in HIV prevalence among PWID were examined in 72 prevalence reports, with 144 racial/ethnic minority to majority comparisons. Overall, the pooled OR indicates a strongly increased likelihood of higher HIV prevalence among racial/ethnic minority compared to racial/ethnic majority PWID (OR=2.06, 95% CI 1.86-2.28). Among 144 comparisons, 75 produced a statistically significant higher OR for minority group members; in 66 comparisons the OR was not significantly different from 1.0; only 3 comparisons produced a statistically significant OR for majority group members. Disparities were particularly large in the US, pooled OR = 2.36 (95% CI 2.10 - 2.64) and China, pooled OR = 2.49 (95% CI 1.71 - 3.64). There was substantial variation in the ORs (I squared = 78.8%; IQR = 1.25 - 3.28). There were statistically significant disparities even at low prevalence levels, with a pooled OR = 1.53 (95% CI 1.18 - 1.98) for studies with HIV prevalence between 0.014 and 0.123.
Conclusions: Among PWID, ethnic minorities are approximately twice as likely to be HIV seropositive than ethnic majority group members. Significant disparities at low prevalence levels suggest the conditions producing disparities may exist prior to the introduction of HIV into a local population.
Financial Support: Funding for this research study was provided by the National Institute on Drug Abuse through grant 5R01DA024612.

152

BREAKDOWN OF CONTROL TOWARD SMOKING CUES IN EMERGING ADULT LIGHT NON-DEPENDENT SMOKERS.

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Aims: Hypothesis: Many studies suggest that dependent smokers have a preference or attentional bias toward smoking-related stimuli. The purpose of this study was to test the ability of very light non-dependent smokers to control their eye movements toward smoking-related stimuli. We hypothesized that poor control in these smokers would indicate behavior driven by smoking cues even prior to nicotine dependency as measured by daily smoking.
Methods: Participants: 17 (11 males and 6 females) emerging adult (M=20.12 yrs. Old) light non-dependent smokers (Fagerström: M= 0.35) and 17 (6 males and 11 females) lifetime non-smoking emerging adults (M= 19.76) participated. The smokers were recruited intentionally to be non-dependent.
Procedure: Each trial began with a central fixation flanked by two boxes 7.2° on the left and right. After fixation offset, an image (nicotine-related, alcohol-related, neutral or a simple dot) appeared in the left or right box. Participants were instructed to move their eyes (saccade) to the box opposite the suddenly appearing image. This instruction to make a saccade away from the image was repeatedly stressed throughout the experiment. A saccade in the direction of the image was a breakdown of control; and one away from the image was successful control.
Results: Results: Non-dependent light smokers were significantly impaired at controlling their eye movements toward smoking-related cues ($t(16)= 2.36$, $p < .04$). This breakdown in control was specific to smoking-related images and not other drug types (alcohol; $t<1$), and was found in light smokers but not non-smokers ($F(3, 96)= 7.04$, $p< .0001$).
Conclusions: Conclusions: These non-dependent smokers demonstrated a smoking cue-elicited breakdown in control over behavior that was specific to nicotine, and not other drugs. In short, even the lightest of smokers without nicotine dependence have a specific smoking cue-elicited breakdown in control.
Financial Support: This research was supported by a Fisher Grant from the College of the Holy Cross.

153

COCAINE AFFECTS OPTOGENETICALLY INDUCED GAMMA OSCILLATIONS IN THE MEDIAL PREFRONTAL CORTEX: AN ANESTHETIZED RECORDING STUDY.

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Aims: Local gamma oscillations in the prefrontal cortex (PFC) are thought to underlie higher cognitive functions (e.g. decision making). An understudied area of addiction is how these cognitive functions are affected by drugs of abuse. Recently it was shown that in mice expressing channel rhodopsin (ChR2), optical stimulation in the gamma frequency range (20-80 Hz) effectively induced gamma oscillation rhythms (Cardin et al., 2009). This was specific to animals expressing ChR2 in parvalbumin-positive (PV+), fast-spiking interneurons.
Methods: In the present study we used male B6 PV-cre knock-in mice injected with AAV-YFP-ChR2 in the mPFC to test the hypothesis that cocaine treatment will alter gamma oscillations in the mPFC. Expression of ChR2 in PV+ neurons was confirmed by immunohistochemistry and confocal microscopy. Light stimulation elicited spiking activity in fast-spiking interneurons and suppression of spontaneous activity in pyramidal neurons as observed with single–unit recordings.
Results: In field recordings, 40 Hz light stimulation (1 ms pulses) produced an increase in power over baseline around 40 Hz, while 8 Hz stimulation was ineffective, confirming that PV-cre mice can be used to induce gamma oscillations specifically. Acute cocaine injection (15 mg/Kg i.p.) produced a further increase in power at 40 Hz and sharpened the peak of the induced oscillation (4 of 6). The remaining two animals showed a decrease in power at 40 Hz. D1-like antagonist (SCH-23390, 1 mg/Kg) administration partially restored the oscillation to pre-drug state in all cases (n=6).
Conclusions: The different actions of cocaine might be layer-specific as interneurons are thought to be differently involved in gamma production (i.e. PING vs. ING models). These data demonstrate that acute cocaine modulates properties of local oscillatory circuitry in the mPFC. These changes may underlie the disruption of decision making processes in cocaine users. Future experiments will test the role of D2-like receptors, and the effects of long-term exposure to cocaine.
Financial Support: DA007288-19

154

NICOTINE WITHDRAWAL AND HEART-RATE PARASYMPATHETICS DURING SMOKING CESSATION: PROSPECTIVE RELATIONS AND SELF-REGULATORY IMPLICATIONS.

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Aims: Smoking is widely recognized as a major preventable cause of mortality and disability worldwide, yet quit attempts often fail within the first week due in part to rapidly developing withdrawal symptoms. One factor likely to affect smoking cessation outcome is variation in the self-regulation processes important for overcoming withdrawal. These regulatory processes can be measured via heart-rate variability (HRV), which is associated with self-regulation in various health domains. Our aims are to determine (1) whether smokers experience phasic changes in resting HRV during nicotine deprivation, owing to the stresses associated with withdrawal; and (2) whether baseline HRV and changes in resting HRV among smokers are predictive of smoking cessation outcome.
Methods: Participants were nicotine-dependent adults (n=106) from Greater St. Louis who smoked regularly over the preceding 12 months. Measures were obtained during an ongoing smoking cessation treatment at (i) baseline (smoking); (ii) 24-hour nicotine abstinence; (iii) one-week follow-up; and (iv) two-week follow-up. Longitudinal physiological data and relevant covariates were analyzed via Mixed ANCOVA and multinomial logistic regression.
Results: After 24-hours of nicotine abstention, participants showed phasic increases in resting HRV and cortisol, a proxy stress measure. These phasic HRV increases were temporary, however, as resting HRV decreased to near baseline at follow-up assessments. By contrast, cortisol remained elevated. Both characteristics of the deprivation response were more pronounced among relapsed smokers than among those who remained abstinent or "slipped". Baseline HRV did not predict cessation outcome.
Conclusions: Participants expectedly demonstrated phasic HRV changes that were predictive of smoking cessation outcome. This suggests that phasic HRV changes following nicotine deprivation have the potential to be considered biomarkers of predictive utility for smoking cessation.
Financial Support: RC1 DA028271 NIDA Neurocognitive Predictors of Smoking Cessation

155

CRITICAL REVIEW OF SUBSTANCE USE AND SEXUAL RISK BEHAVIORS AMONG MSM IN NYC BATHHOUSES.

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Aims: The HIV prevalence in New York City (NYC) is particularly high among men who have sex with men (MSM), where 43% of all diagnoses in 2009 (57% among males) were attributed to this population (NYC HIV/AIDS Annual Surveillance Statistics, 2009). Substance use and sexual behaviors of MSM that occur in commercial sex venues (i.e., bathhouses) are a target for research and intervention due to concerns about the role these venues may have in the transmission of HIV and other sexually transmitted infections. This presentation will provide a systematic review of recent literature investigating substance use and sexual risk among men in bathhouses, with a renewed focus on NYC.
Methods: Medline, Web of Science, and Google Scholar search using the following criteria: (1) quantitative studies published 2006 – 2011 (journal articles, conference abstracts); (2) required keywords—bathhouse, MSM—in the title and/or abstract; and, (3) at least one additional keyword (substance use, drug use, sex). Abstracts were sorted by sample (NYC, other U.S. cities) and reviewed for assessments of substance use and sexual behavior (both in general and in the context of venue use).
Conclusions: New evidence from a national online survey suggests that men who met their most recent sex partner at a bathhouse had a higher prevalence of methamphetamine use and were more likely to report using alcohol in the context of their sexual encounter compared to those who met their most recent partner online or at a public sex venue (Grov et al., 2011). Further, men recruited in NYC bathhouses reported more recent use of methamphetamines and erectile dysfunction drugs without a prescription than men recruited online or in bars/clubs (Grov, 2011). These findings are particularly concerning as researchers have found that bathhouse attendees who feel the effects of drugs during attendance, compared to those who do not, are more likely to report unprotected anal sex (Woods et al., 2007).
Financial Support: NIDA (T32 DA007233)

156

EFFECT OF CIRCADIAN RHYTHM DISRUPTION ON METHAMPHETAMINE PREFERENCE IN RATS.

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Aims: A substantial number of clinical studies suggest an association between circadian rhythm abnormalities and drug abuse. Drug abuse is more prevalent in subjects with sleep and circadian rhythm disturbances, and sleep disruption is a significant factor predicting relapse. The goal of this study was to examine the effect of experimentally induced circadian disruption on oral methamphetamine consumption in rats.
Methods: Adult male Sprague-Dawley rats (n=32) were housed in individual running wheel cages in light-tight, temperature and humidity controlled boxes in a 12 hour light: 12-hour dark cycle (LD12:12; lights on 05:00, off 17:00). Feeding, drinking, and locomotor activity were continuously recorded. After assessing baseline feeding, drinking, and activity for 7-10 days, one group of rats (n=16) underwent two weeks of forced methamphetamine consumption (0.01% methamphetamine in drinking water) while a second group (n=16, drug naïve) received water only. This was followed by a two week abstinence period during which half of the animals from both groups were exposed to 4 consecutive 6-hr phase shifts of the light:dark cycle, and half remained on the original light:dark cycle. Changes in methamphetamine consumption were assessed using a two-bottle choice paradigm following the deprivation period (a model of relapse).
Results: Under these conditions, methamphetamine consumption was decreased in rats previously exposed to methamphetamine as compared to drug naïve rats, as predicted due to the development of sensitization during the deprivation period. We also found that preference for methamphetamine was significantly higher in shifted versus non-shifted rats that were previously exposed to methamphetamine, while drug-naïve rats showed no differences in preference.
Conclusions: These data suggest an association between circadian rhythm disturbance and relapse vulnerability, and further suggest that treatment of circadian disorders may be of therapeutic value in methamphetamine addiction.
Financial Support: Supported by NIDA grant R01DA024716(WJL)

157

THE COGNITIVE EFFECTS OF METHADONE AND BUPRENORPHINE IN MAINTENANCE PATIENTS.

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Aims: To determine if methadone or buprenorphine produce impairment in cognitive function in patients maintained on these drugs. Using a within subjects design, participants were tested at time of trough and peak concentration. We hypothesised greater impairment at peak concentration for each of the drugs, but that this may be less with buprenorphine. The effects of varying concentrations of alcohol were also initially evaluated for comparison.
Methods: All 3 studies compared control (no drug) and experimental (i.e. alcohol in Study 1, methadone in Study 2, and buprenophine in Study 3) groups across multiple time points. In Study 1 (N = 56) participants were tested pre-dose, and at subsequent time-points corresponding to experimental group blood alcohol concentrations of 0.05, 0.08, and 0.10%. In Study 2 (N = 55) the participants were tested pre-dose, and at subsequent time-points corresponding to pre-peak, peak, and post-peak methadone blood concentrations (90,180 and 480 minutes respectively). In Study 3 (projected N = 28) participants were tested pre-dose and at peak blood concentration (+90 minutes).
Results: ANOVA indicated alcohol produced significant effects across the majority of tasks. In contrast, the effects of methadone were not significant, with the exception of Inspection Time a measure of information processing speed, where peak effects of methadone were equivalent to those of the highest blood alcohol concentration. Preliminary results suggest that buprenorphine may have a lesser effect compared to methadone, but a full data set will be presented.
Conclusions: Cognitive impairment in tolerant opioid maintenance patients has been an area of controversy. The present results suggest that methadone produces significant impairment that is reflected in speed of information processing. This appears to be a more sensitive measure of sedation than previously employed tests. Conclusions regarding buprenorphine will be presented.
Financial Support: This research was funded by NHMRC grant NP09565410.

158

A MIXED METHODS APPROACH TO IDENTIFYING FACTORS RELATED TO VOLUNTARY HIV TESTING AMONG INJECTION DRUG USERS IN SHANGHAI, CHINA.

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Aims: Injection drug use is a major route of HIV transmission in China yet relatively little is known about why so few injection drug users utilize free HIV testing services. This study aim to examine barriers to HIV testing/ VCT service utilization among injection drug users in Shanghai, China.
Methods: Utilizing mixed methods, we analyzed data from a survey of 540 compulsory drug abuse treatment patients and data from focus groups with 70 service providers and patients.
Results: Only 24.4% of patients expressed willingness to be tested for HIV. Willingness to be tested was associated with younger age and more positive attitudes toward condom use. Patients reported several barriers to utilization of voluntary HIV testing services, including lack of information about this services, perceptions of no- or low-risk for HIV infection, fear of positive results, and the stigma or discrimination that may be experienced by oneself or family. Having limited skills related to HIV counseling was reported by service providers as the primary barrier to encouraging patients to utilize HIV testing/VCT services.
Conclusions: Special intervention programs targeting injection drug users, their family members, and service providers may increase HIV testing in China.
Financial Support: supported by NIH/NIDA(R01DA027195)

159

CRF DOSE-RESPONSE IN COCAINE-DEPENDENT VS. NORMAL VOLUNTEER SUBJECTS.

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Aims: To determine whether administration of two doses of corticotropin releasing factor (CRF) would elicit differences in stress responsivity between cocaine dependent subjects and normal healthy controls.
Methods: Subjects were admitted to the stress-minimized inpatient unit at the Rockefeller University Hospital the evening prior to neuroendocrine testing. On separate days, a saline placebo, low dose CRF (0.5mcg/kg) and high dose CRF (2.0mcg/kg) were administered intravenously to both cocaine dependent (n= 18) and healthy, normal volunteer subjects (n=36). Blood was sampled from 10 minutes prior to placebo or CRF, up to 6 hrs afterward and assayed for plasma levels of ACTH and cortisol. Area under the curve (AUC) for ACTH and cortisol from 0-90 min on the placebo day, and after each dose of CRF was calculated for each subject at each dose. The dose response effect for both hormones was examined in each group by one-way ANOVA with repeated measures, followed by Newman-Keuls post hoc tests.
Results: There was a significant dose response effect of CRF on plasma ACTH AUC: $F(2,100)=38.15$, $p<0.000001$, but no difference between cocaine dependent and normal volunteer subjects, $F(1,50) <1.00$. Mean AUCs after the low dose were greater than placebo ($p<0.0002$), and mean AUCs after the high dose were greater than after the low dose ($p<0.002$). A similar pattern was found in cortisol AUCs with a significant dose response effect, $F(2,104)=48.53$, $p<0.000001$, with no significant difference between groups.
Conclusions: These results contrast with our previously published report of a hyperresponsive HPA axis in former severe heroin addicts in stable methadone maintenance following the higher CRF dose as compared to normal volunteers. The current findings underscore the need to examine specific components of the HPA-axis in subjects according to their respective addictive disease diagnostic group.
Financial Support: NIH-NIDA P60-DA005130 (M.J.K.) and The Adelson Medical Research Foundation

160

IMPROVING THE ETHICS OF CONSENT: REFINEMENT OF THE COERCION ASSESSMENT SCALE.

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Aims: The development of interventions for substance abusing offenders has led to a proliferation of RCTs to establish their efficacy, raising concerns about how to ensure autonomy of this doubly vulnerable population. Despite federal requirements to ensure the autonomy of research participants, there is no reliable and valid way of measuring perceived coercion to participate in research. In response to this need, we developed the Coercion Assessment Scale (CAS), a tool focusing on coercive pressures that substance abusing offenders may experience when asked to participate in research. In this study, we expanded the content domain of the CAS, ensured its appropriateness for the population, and examined the reliability of the items over time.
Methods: In Phase 1, we conducted focus groups with prisoners, drug court clients, and prison and drug court staff. The discussions focused on pressures that substance-involved offenders may perceive related to research participation. Using this qualitative data, we identified additional CAS items. In Phase 2, we conducted cognitive interviews with drug court clients. Clients rated the comprehensibility and relevance of each of the items. In Phase 3, we administered the CAS to drug court clients at intake into a host study and 3 days later (N = 94). Item responses were evaluated, and test-retest reliability was assessed using percent exact agreement.
Results: Analysis of focus group data resulted in the identification of 8 additional items. Protocol analysis indicated that all 15 items were correctly interpreted and relevant to clients. Average percent exact agreement for the items was .80 (range = .64 - .99).
Conclusions: Like consent quizzes and cognitive tests, the CAS may be useful in identifying individuals who may need enhanced consent procedures or who may not be appropriate for research because of their perceived coercion. In this context, the CAS may be useful to research staff, research intermediaries, and IRBs. The CAS may be useful for researchers as they develop and evaluate the efficacy of new consent strategies.
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161

THE CONTEXTS OF SUBSTANCE USE AMONG YOUTH LIVING WITH HIV/AIDS.

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Aims: This study seeks to understand the relationship between the physical and social environments of substance use and sexual risk in order to improve the effectiveness of substance abuse treatment and HIV "prevention with positives" interventions for youth living with HIV/AIDS. This qualitative study, examining the environments where youth living with HIV/AIDS use alcohol and illegal drugs, is part of a larger qualitative study which examined the life experiences, developmental characteristics, and illness-related adaptive tasks of youth living with HIV/AIDS.
Methods: The investigative team conducted semi-structured, in-depth interviews with 59 African American and Latino youth (16-24 years) living with HIV/AIDS in the New York metropolitan area. Content analysis was conducted to identify themes related to the environments where substance use took place.
Results: The results show that more than 70% of the sample used alcohol and/or illegal drugs post HIV diagnosis. Half of youth using alcohol or illegal drugs reported doing so in isolation (social environment) to cope with their HIV diagnosis, HIV-related stress, or a mental disorder. Few youth (less than 10%) reported increased sexual risk and unprotected sex solely due to substance use. However, those who did reported alcohol and illegal drug use in physical environments such as bars and clubs.
Conclusions: The findings suggest the need for youth-focused HIV primary care providers to discuss substance use and possible treatment with their young clients. Further, substance use and HIV "prevention with positives" interventions should target the physical and social environments where youth gather to educate them on ways, other than substance use, to cope with stress and/or mental disorders and the possible increased sexual risk behaviors that may result from alcohol intoxication and/or illegal drug use.
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162

ASSOCIATION OF PRETREATMENT DRINKING GOAL WITH TREATMENT OUTCOME: A SECONDARY ANALYSIS OF THE COMBINE DATA.

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Aims: In the U.S., approximately 2.8 million people seek alcohol dependence treatment each year. Few studies have evaluated whether self-defined pretreatment drinking goal (e.g., abstinence vs. nonabstinence) is associated with treatment outcomes. This secondary analysis of the COMBINE study data evaluated the association between pretreatment drinking goal and outcome.
Methods: The COMBINE study assessed the efficacy of acamprosate, naltrexone and behavioral treatment among 1,305 alcohol dependent patients. For the present analyses, subjects were dichotomized into abstinent (n=959) and nonabstinent (n=346) goal groups. Analysis of demographic variables revealed no significant between-group effect size differences. Subjects were [Mean (SD)] 44.9 (10.4) years old, 70% male, and 77% Caucasian. 44%, 44% and 56% of subjects received acamprosate, naltrexone, and behavioral treatment, respectively. The primary outcome for these analyses was the % of subjects meeting treatment goal, defined for the abstinent goal group as no drinking and for the nonabstinent goal group as having a >50% decrease from baseline drinking levels, during the final 7 days of treatment.
Results: Logistic regression controlling for medication and behavioral treatment group found that subjects who identified a nonabstinent treatment goal were significantly more likely to achieve that goal when compared to the abstinent goal group (67% vs. 61%; $\chi 2$ (1)= 4.08, P <.05, CI=1.005-1.202). Linear regressions controlling for medication and behavioral treatment indicated that pretreatment goal was also significantly associated with % change in drinks per day from intake (46% vs. 67%; P<.001), total number of abstinent days (154 vs. 135; P<.05) and total number of heavy drinking days (108 vs. 92; P<.05) among nonabstinent and abstinent groups, respectively.
Conclusions: These data suggest that categorizing subjects based upon their self-reported pretreatment goal may be a clinically relevant and empirically advantageous method for assessing efficacy of an intervention, and may represent an important stratification variable for future studies.
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163

UNDERSTANDING ASSESSMENT PROCESSES FOR RE-ENTERING OFFENDERS IN KENTUCKY.

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Aims: In the correctional system, the continuum of substance abuse assessment, service planning, and service delivery for offenders is not well defined, developed, or implemented in general(Taxman, et al., 2007; Taxman, Perdoni & Harrison, 2007; Belenko & Peugh, 2005). The purpose of this study was to conduct a needs assessment to better understand the processes by which different providers within the Department of Corrections of one rural state collect information used to identify offenders strengths and needs, and how that information is used to guide service planning and service delivery.
Methods: The CJ-DATS Assessment of Needs (ICAN) Survey was administered to 27 Kentucky Department of Corrections employees by the University of Kentucky Center on Drug and Alcohol Research. Of those individuals sampled, 52% reported working primarily in a prison setting while 48% reported working primarily in a community correctional setting.
Results: Results of the survey indicated that substance use (79%) and related treatment history (64%) were consistently assessed by providers in the correctional system. Information regarding criminal risk (43%), readiness to change (39%), employment (39%), HIV/AIDS (25%) and appropriateness of pharmacological treatment (11%) were also collected. Assessment of substance use tended to be more consistent at intake (13%) with less emphasis placed on the collection of information either during custody (4%) or at discharge/release (5%).
Conclusions: Overall, both the limited amount of detailed assessment information and the inconsistent sharing of that information between correctional and community agencies were identified as the primary impediment to more effective offender service planning and service delivery. Implications for enhancing the continuum of care for offenders with substance abuse problems at community re-entry are discussed.
Financial Support: This research is funded by the National Institute on Drug Abuse (U01-DA016205, PI: Leukefeld).

164

EFFECTS OF MONOAMINE REUPTAKE INHIBITORS ON DECISION-MAKING IN THE RAT GAMBLING TASK.

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Aims: Aims: Dysfunctional decision-making is characteristic of numerous psychiatric disorders including schizophrenia, mood disorders, ADHD, eating disorders, pathological gambling and substance abuse. The rodent Gambling Task (rGT) is analogous to the Iowa Gambling Task (IGT) and models risky decision-making in rodents. The goals of this study were two fold: validate the rGT model and examine how acute doses of monoamine transport inhibitors (methylphenidate, cocaine, and bupropion) impact risk-based decision-making.
Methods: Methods: Adult male Long Evans rats (n=11) were trained to nose poke for sucrose pellet reinforcement in operant chambers. The reward/penalty contingencies were distributed across four unique response options (P1, P2, P3, P4) such that as the reward magnitude increased (1-4 pellets) the reward probability decreased (p=0.9-0.4), while penalty magnitude (5-40-sec timeout) and probability also increased (p=0.1-0.6). In a 20-min testing session, exclusive choice of an intermediate response (P2) was the optimal strategy for maximizing pellet deliveries. Once stable behavior was established, we examined acute administration of d-amphetamine HCl (0.3-1.5 mg/kg), eticlopride HCl (0.003-0.01 mg/kg), bupropion HCl (10-30 mg/kg), methylphenidate HCl (1.0-5.7 mg/kg), cocaine HCl (5-15 mg/kg), or vehicle on responding in the rGT.
Results: Results: Behavior following d-amphetamine administration was similar to previous reports (Zeeb et al. 2009). Intermediate and high doses of all drugs, except eticlopride, significantly decreased optimal responses (P2). However, differences existed in the corresponding increases of suboptimal responses. Methylphenidate and d-amphetamine increased both "low risk" (P1) and "high risk" responses (P4), whereas cocaine increased only P1 responding. Bupropion administration decreased P2 choice without impacting suboptimal responding.
Conclusions: Conclusions: Acute administration of monoamine reuptake inhibitors disrupted the ability to optimize responding behavior in the rGT.
Financial Support: Financial Support: Florida State University

165

ABUSE LIABILITY EVALUATION OF THE MGLU5 ANTAGONISTS MPEP AND MTEP.

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Aims: Metabotropic glutamate receptor 5 (mGlu5) antagonists are investigated for a range of indications including analgesia, anxiety, depression and addiction. We have previously shown that the mGlu5 antagonists 3-((2-methyl-1,3-thiazol-4-yl)ethynyl)-pyridine (MTEP), 2-methyl-6-(phenylethynyl)-pyridine (MPEP) and fenobam did not produce PCP-appropriate responding in the drug discrimination model. However, rats were readily trained to discriminate MTEP from no drug and MPEP as well as fenobam, but not PCP, produced full MTEP-appropriate responding. Here we evaluate the abuse liability of MPEP and MTEP in a rat self-administration model validated to detect reinforcing properties of a diverse range of drugs. For comparison, PCP was also tested in an identical setup.
Methods: Intravenously catheterized Wistar rats maintained on a cocaine base-line (0.5 mg/kg/infusion) were allowed to self-administer MPEP (0, 0.1, 0.3, 1 and 3 mg/kg/infusion), MTEP (0, 0.01, 0.03, 0.1, 0.3, 1 and 3 mg/kg/infusion) and PCP (0, 0.01, 0.03, 0.1, 0.3 and 1 mg/kg/infusion) on an FR5 schedule of reinforcement in 3 hour sessions. One dose each of MPEP (1 mg/kg/infusion) and MTEP (0.1 mg/kg/infusion) was also tested on an FR1 schedule of reinforcement.
Results: MPEP and MTEP were not self-administered at higher levels than vehicle alone, regardless of dose and FR schedule tested. PCP was self-administered in a dose-dependent manner and the number of PCP infusions/hour (mean±SEM) peaked at 0.1 mg/kg/infusion (10.3±2.2 compared to 1.6±0.2 on vehicle alone).
Conclusions: The lack of self-administration of MPEP and MTEP indicates that mGlu5 antagonists are not likely to have abuse liability. However, the fact that rats were easily trained to discriminate MTEP from no drug suggests that mGluR5 antagonists may produce idiosyncratic effects and caution may be warranted.
Financial Support: AstraZeneca R&D, Södertälje, Sweden

166

AN EVENT-BASED ANALYSIS OF DATING VIOLENCE AND SUBSTANCE USE AMONG FEMALE YOUTH IN AN URBAN EMERGENCY DEPARTMENT.

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Aims: Dating violence has been linked to substance use and can lead to injuries, psychological disorders, and death. The Emergency Department (ED) provides an opportunity for screening and interventions to prevent youth dating violence (DV). Additional data is needed regarding characteristics of DV in order to develop ED-based interventions.
Methods: The sample included 247 female patients who screened positive in an urban ED for drug use in the past 6 months (ages 14-24; 58% presenting for violent injury and an age matched comparison group; 59% African-American). Participants completed a timeline follow-back semi-structured interview with substance use and violence modules (past 30 days). Analyses examined demographics and substance use on days that DV occurred and correlates of DV severity (Moderate/Severe Victimization; Moderate/Severe Aggression).
Results: 30.8% of the sample reported a total of 212 incidents of victimization and 23.5% reported 112 total incidents of aggression (past 30 days). Youth reported reasons for DV that included angry/bad mood, jealousy/rumors, and personal belongings. Bivariately, victimization was associated with any alcohol use/binge drinking, marijuana, cocaine, and sedative/opiate use. Aggression was associated with any alcohol use/binge drinking, marijuana, and sedative/opiate use. Multilevel, multinomial regression analyses showed that cocaine and sedative/opiate use were associated with severe victimization, whereas alcohol and sedative/opiate use were associated with severe aggression. Demographic factors associated with DV severity included age, race, and ED visit for violent injury.
Conclusions: Findings suggest that alcohol and drug use (cocaine, sedatives, opiates) should be addressed in ED-based DV interventions for urban female youth, and that interventions should also target a number of psychosocial factors (e.g. personal belongings, jealousy, coping with negative emotions).
Financial Support: NIDA R01 024646; T32 DA007267

167

PHARMACOLOGY OF PSYCHOACTIVE DESIGNER "BATH SALTS".

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Aims: The use of "bath salts" is a growing health concern. To determine mechanisms for psychiatric consequences of drug use, we determined the affinity, potency, and efficacy of the substituted cathinone "bath salts" butylone, 4-fluoromethcathinone (4-FMC), mephedrone, methylone, MDPV, and naphyrone at the biogenic amine and vesicular monoamine (VMAT2) transporters and at 4 dopamine (DA) and 3 serotonin receptors.
Methods: HEK cell lines individually expressing recombinant human DA (DAT), serotonin (SERT) and norephinephrine (NET) transporters, VMAT2, 5HT1A, 5HT2A and 5HT2C receptors and the DA D4.4 receptor were used. In addition, CHO cell lines individually expressing recombinant human DA D2 and D3 receptors and L cells expressing recombinant human DA D1 receptor were used. Selective radioligands were used in the binding assays, and [^{3}H]neurotransmitters were used for uptake and release assays.
Results: Butylone, 4-FMC, mephedrone and methylone may be substrates, like methamphetamine and methylenedioxymethamphetamine (MDMA) at the DAT, SERT and NET because potency at blocking uptake is higher than affinity for the radioligand binding site. In contrast, naphyrone and MDPV may be transporter inhibitors, like cocaine, because potencies at blocking uptake are similar to affinities for the radioligand binding site. Preliminary data support this idea, as some, but not all, of the compounds are efficacious at releasing [^{3}H]DA and [^{3}H]serotonin from preloaded DAT and SERT cells, respectively. Methamphetamine and MDMA also elicited robust release. All 6 compounds had very low potency at VMAT2 and very low to no measurable affinity for the DA and serotonin receptors tested.
Conclusions: Substituted cathinones (i.e. "bath salts") may be either inhibitors or substrates at biogenic amine transporters. In general, the compounds had higher potency at inhibition of uptake at DAT and NET compared to SERT. In addition, overdose effects of these compounds do not appear to be due to direct interactions with the VMAT2, DA or serotonin receptors.
Financial Support: NIDA Y1-DA-0101-01 (AJ)

168

PERCEIVED NEIGHBORHOOD SAFETY, SOCIAL CAPITAL, AND DRUG USE ABSTINENCE AMONG MOTHERS 10 YEARS AFTER SUBSTANCE ABUSE TREATMENT.

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Aims: Neighborhood characteristics may explain variations in drug use behaviors beyond what can be explained by aggregated individual-level characteristics alone. We examine drug use outcomes among mothers approximately 10 years after admission to drug abuse treatment.
Methods: Participants (n=713) were recruited at admission to 44 treatment programs in 13 California counties during 2000-2002 and completed a 10-year follow-up interview in 2010-2011. The addiction severity index was administered at both intake and follow-up. Perceived neighborhood safety and social capital were measured using a standardized neighborhood questionnaire.
Results: At baseline, mothers' mean age was 31.7 + 7.3. Race/ethnicity was 53% white, 23% Hispanic, 16% African American, and 7% other. Few were married and most had one or more dependent children. Most reported methamphetamine (43%) as the primary drug problem, followed by heroin (19%), alcohol (17%), cocaine (11%), and marijuana (9%). At follow-up, about half were drug abstinent and perceived neighborhood safety was moderate. Preliminary logistic regression analysis indicated that neighborhood safety increased the odds of drug use abstinence, even after controlling for individual-level characteristics. Future analyses will explore whether social capital mediates the effect of neighborhood safety on drug use abstinence.
Conclusions: Mothers living in neighborhoods that are perceived to be safe are more likely to be drug abstinent. More research is needed to understand associations between neighborhood climate, social capital, and treatment outcomes.
Financial Support: Supported by NIDA R01DA021183, P30DA016383, & K05DA017648 (PI: Hser)

169

EARLY LIFE PREDICTORS OF OBTAINING HELP FOR SUBSTANCE USE AMONG SUBSTANCE USERS IN AN URBAN AFRICAN-AMERICAN COHORT.

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Aims: Most research on predictors of obtaining help for substance use has been cross-sectional and focused on adult predictors. This study, using a life course perspective, extends this research by examining how contextual and substance use-related factors in early childhood and adolescence influence obtaining help for substance use in adulthood.
Methods: 632 drug and alcohol users (53% male) were selected from a community cohort of urban African Americans followed from childhood to mid-adulthood (assessed at age 6, 16, 32, 42). Obtaining help for substance use was determined by 3 questions asked at age 32: ever 1) talking to a doctor, 2) attending a self-help group, or 3) staying overnight in a facility for a drug or alcohol problem. Logistic regression was used to examine first grade social and family predictors of obtaining help for substance use as well as adolescent substance use mediators.
Results: 25% (n=148) of individuals reported ever obtaining help for substance use by age 32. Childhood factors are related to obtaining help via adolescent substance use and severity of use. For example, maladaptive social functioning in first grade predicted obtaining help for substance use in adulthood (OR: 1.25; CI: 1.02, 1.53). However, once early onset of drug use (by age 16) was added to the model, childhood social adaptation fell to non-significance with early onset of drug use almost doubling the odds of obtaining help for substance use (OR:1.69; CI: 1.12, 2.54).
Conclusions: Factors early in childhood such as social adaptation may set someone on a pathway to early and more serious substance use in adolescence which in turns predicts obtaining help for adult substance use. Further investigation into these pathways is needed, such as potential moderators. Understanding paths leading to obtaining help for substance use are vital for improving rates of help seeking and treatment entry among substance users.
Financial Support: NIDA RO1 DA 022366 (PI: Ensminger) and NIDA 2T32DA007292

170

FACTORS THAT CONTRIBUTE TO SUCCESSFUL PRISON-BASED HIV RISK-REDUCTION INTERVENTIONS.

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Aims: A literature review was conducted to determine the characteristics of successful prison-based HIV risk-reduction interventions. HIV risk behaviors are very common in incarcerated populations and the prevalence of HIV is much higher in this group compared to the general population. A significant proportion of incarcerated individuals have a positive history of drug use and drug offenses are a leading cause of incarceration in the United States. The transition period from incarceration to community re-entry has been identified as an opportunity to intervene in this high risk group for their benefit and also the benefit of the communities to which they will return.
Conclusions: The nature of correctional settings make it very challenging to conduct randomized clinical trials and there are very few published studies on interventions of any kind targeting HIV prevention among incarcerated subjects. As a result, it is difficult to draw definite conclusions as to what makes a successful prison-based HIV risk reduction intervention. Given the variability in intervention design, variables assessed, and reported efficacy of prison-based interventions, other important characteristics such as the timing, content, and delivery method of an intervention as well the duration of follow up, may be useful to study to determine whether or not an intervention is feasible and/or efficacious. Another important factor is whether an HIV risk reduction intervention that is an integral part of a larger program such as transitional management is more efficacious. Current evidence suggests that social factors such as housing and employment are major issues faced by recently released prisoners and can greatly influence their subsequent health risk behaviors.
Financial Support: No financial support was provided for this review.

171

DOES QUITTING NICOTINE REDUCE COCAINE INVOLVEMENT?

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Aims: Among mice, cocaine-taking is enhanced by nicotine pre-treatment followed by concurrent cocaine and nicotine. In humans, tobacco cigarette smoking (CS) often starts before cocaine; new cocaine users often are current smokers. We posited that, comparatively, recent CS quitters might be less likely to persist and might have lower cocaine use rates, once cocaine starts. Our aim was to produce novel estimates that test these ideas, with data from a nationally representative sample of newly-incident cocaine users (NICU; onset <24 months before survey).
Methods: Data are from US National Surveys of Drug Use & Health (2004-9) with representative samples of US residents. Standardized assessments of CS, cocaine, and other drug use yielded 4,211 NICUs. Cocaine persistence and rates can be derived from each NICU's number of cocaine-using days during 30 days prior to survey. Becoming a NICU, cocaine persistence, and usage rates were compared via a generalized linear model, with adjustment for background covariates (e.g., drinking alcohol).
Results: Risk of NICU was associated with current smoking ($p<0.05$). As time since last CS increased, risk of becoming a NICU decreased, and remained moderate for ex-smokers of 3 years or more ($p<0.05$). Most NICUs were current smokers (76%), and being a recent CS quitter (< 30 days; < 12 months) predicted reduced odds of cocaine persistence (vs. current smokers, at $p<0.05$). Conditional on cocaine persistence, never smokers had a lower rate of cocaine use ($p<0.05$), but contrary to expectations, the rates did not differ appreciably in contrasts of current smokers versus recent quitters. Covariate adjustments did not affect the conclusions.
Conclusions: Cigarette smoking history now predicts risk of becoming a newly incident cocaine user. Recent CS quitters may be at a reduced risk for starting NICU and persisting, but may not show reduced cocaine use rates. This novel evidence is generally supportive of the prior lines of preclinical and human research on nicotine and cocaine. We will highlight some unanswered questions and puzzles.
Financial Support: Supported in part by NIDA K05DA015799 (JCA); T32DA021129.

172

RELATIONSHIPS BETWEEN SLEEP DISTURBANCES AND VARIATIONS OF CRAVING INTENSITY IN PATIENTS BEGINNING TREATMENT FOR ADDICTION: A COMPUTERIZED AMBULATORY MONITORING STUDY.

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Aims: Many studies have reported sleep disturbances among substance use disorder patients. However, few studies has explored the relation between drug craving and sleep impairment. This study used Experience Sampling Method (ESM) in patients beginning treatment for addiction, to assess the relationship between craving and sleep disturbances.
Methods: Participants were recruited from an outpatient addiction treatment center. Craving was assessed in real time with four daily assessments during a two weeks period. Sleep characteristics were assessed each morning during the same period. Data were submitted to Hierarchical Linear Model (HLM) analysis to test the effect of sleep on craving intensity. Predictors of craving intensity were both inter-individual variables (age and gender) and intra-individual variables (day in treatment, number of sleeping hours).
Results: 109 participants were recruited and main substance-problem was alcohol (n=38), opiates (n=27), tobacco (n=23) and cannabis (n=21). Multi-level models indicated that having shorter sleep duration than usual was associated with increased craving intensity the subsequent day ($\beta = 0.844$, T-ratio=2.35, df = 3040, $p= 0.019$). Variation in craving intensity was also predictive of variation in sleep duration ($\beta = -0.175$, T-ratio=2.57, df :3488, $p=0.011$) and numbers of sleep problems experienced by patients the subsequent night ($\beta =0.069$, T-ratio=2.07, df :3495, $p=0.038$).
Conclusions: Based on these results, we hypothesize a link between sleep-related disorders and craving. The nature of this link has to be further studied as craving might cause sleep disorders as well as sleep disorder might generate craving.
Financial Support: PHRC 2006, MILDT 2010, CRA 2009, PRA-CNRS-CHU 2008

173

STRUCTURAL LEVEL INTERVENTIONS TO INCREASE NEEDLE/SYRINGE ACCESS FOR PREVENTING HIV AND HEPATITIS C AMONG PEOPLE WHO INJECT DRUGS IN LOW- AND MIDDLE-INCOME COUNTRIES: AN INTERNATIONAL SYSTEMATIC REVIEW.

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Aims: Persons who inject drugs (PWID) are at an elevated risk for HIV and Hepatitis C (HCV) infection. In many high income countries, needle and syringe exchange programs (NSP) have been associated with reductions in blood borne infections, when implemented at a level that reaches at least 50% of the PWID community. However, we do not have a good understanding of the effectiveness of NSP in low and middle income countries.
Methods: Systematic literature reviews based on the PRISMA guidelines were utilized to collect primary study data on coverage of NSP programs and changes in HIV and HCV prevalence over time among PWID in low/middle countries. Inclusion criteria were laboratory measures of either HIV or HCV over time and at least 50% coverage of the local injecting population (using the program either directly or through secondary exchange).
Results: Countries with large scale-structural level interventions for PWID in this review include Bangladesh, Brazil, China, Estonia, Iran, Lithuania, Taiwan, and Thailand. Decreases in HIV prevalence ranged from 3% to 42.4% in six studies while decreases in HCV prevalence ranged from 4.2% to 10.2% in three studies. Moderate increases in HIV ranged from 5.6% to 14.8% in two studies.
Conclusions: While not fully consistent, the data generally support the effectiveness of NSP in reducing HIV and HCV prevalence in low/middle income countries. Additional research on contextual factors, such as stage of the local epidemic and law enforcement support versus interference, is needed to explain the variation in the results.
Financial Support: The funding for this research study was provided by the National Institutes of Health through grant R01AI083035

174

DIFFERENCES BETWEEN DSM-IV DIAGNOSTIC ORPHANS AND ABUSERS AMONG ADOLESCENT ALCOHOL AND CANNABIS USERS.

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Aims: Use of DSM-IV criteria for substance use disorders with adolescents is widespread. However, its use with this population presents some limitations and causes high rates of "diagnostic orphans (DO)" (one or two symptoms of dependence and none of abuse). The aim of this study was to assess clinical significance of differences between alcohol and cannabis DO and abusers.
Methods: Information was obtained by a self-reported questionnaire from 796 students aged 15-20 years (M = 16.99; SD = 1.24; 57.8% girls) from the Principality of Asturias (Spain). T tests were undertaken to determine statistically significant differences between cannabis DO and abusers, and alcohol DO and abusers in: prevalence and age of onset of drugs use, patterns of heavy use, associated problems (assessed with the Cannabis Problems Questionnaire-Adolescents and the Rutgers Alcohol Problems Index), and psychopathological symptoms, assessed with the Brief Symptom Inventory. Characteristics of DO were thoroughly analyzed.
Results: 18.0% of last-year cannabis users were DO for cannabis and 29.4% were abusers. 28.3% of last-year alcohol users were alcohol DO and 24.8% were abusers. Significant differences were found between alcohol abusers and DO in all variables assessed except lifetime prevalence of alcohol use, with more severe use and consequences among abusers. Cannabis abusers and DO did not differ in their prevalence of cannabis use neither in their age of onset, but abusers showed higher scores in CPQ-A and more severe symptomatology in two global scales of BSI. Dependence symptoms reported by Alcohol and Cannabis DO were mostly related to tolerance and loss of control.
Conclusions: Alcohol abusers showed more severe patterns of use and consequences than DO. Among cannabis users, patterns of drug use were similar between DO and abusers, but consequences and mental health were worse for the latest. Limitations of DSM-IV criteria and reasons for high rates of DO are discussed.
Financial Support: Spanish Ministry of Science and Innovation. Project No: MICINN-08-PSI2008-00309

175

ASSESSING DUI OFFENDERS' NEEDS AND RISKS TO IMPROVE TREATMENT AND SUPERVISION.

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Aims: A critical challenge for our field is to devise an evidence based tool for assessing DUI offenders at the point of arrest to help inform their dispositions and to target them into the most effective and cost-efficient programs. To date most decisions of this type have relied solely on Blood Alcohol Concentration (BAC) and number of prior offenses. The current study sought to develop a brief triage tool that incorporates markers of alcohol abuse/dependence (need) and predictors of DUI recidivism (risk). The triage is designed to help inform DUI dispositions in a way that links offenders to the optimal level of treatment and criminal justice supervision.
Methods: In Phase I of the study, our research team conducted a systematic literature review to identify robust predictors of DUI recidivism (risk) and markers of alcohol dependence (need). In Phase II an expert panel reviewed and finalized the list. In Phase III we created a web-based beta version of the triage. Finally, in Phase IV we administered the completed triage assessment to 30 first time DUI offenders and 30 repeat DUI offenders (>1 offense). First-time offenders completed items using the time of their current DUI arrest as a reference point, and repeat offenders completed items using the time of their first DUI arrest as a reference point. A series of Chi-square analyses were then conducted to determine the degree to which each item discriminated between first-time and repeat DUI offenders.
Results: Findings revealed a total of 10 risk and 4 need items that discriminated between first time and repeat DUI offenders. Importantly, BAC was not found to discriminate between the two groups.
Conclusions: The utility of these items in the development of the triage and their implications for policy change will be discussed. These findings represent the first step in developing and validating a point of arrest DUI triage tool that can be used to inform decisions about the most appropriate and effective criminal justice and treatment responses for DUI offenders.
Financial Support: Commonwealth of Pennsylvania SAP #4100050911

176

DRUG USE FOLLOWING BRIEF MOTIVATIONAL INTERVENTION FOR AT-RISK DRINKERS IN THE TRAUMA DEPARTMENT.

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Aims: There is increased interest in the application of brief interventions in medical settings to address illicit drug use. To advance our understanding, this study examines the potential effects of brief intervention for at risk drinking on subsequent drug use and changes in drug use following injury.
Methods: The MARIA Project screened trauma patients for at risk drinking and acute intoxication in Level I trauma centers. Of 1,279 trauma patients who screened positive, 603 were randomized to brief advice (n=203), brief motivational intervention (n=205), or brief motivational intervention with telephone booster (n=195). A total of 512 participants (85%) completed the 12 month follow-up. This study examines the effects of brief intervention for at risk drinking on drug use and percent days of drug use using generalized estimating equations (GEE) and multivariate analysis of variance (MANOVA), respectively.
Results: A series of GEEs indicated significant time effects on reducing any drug use (OR=.74, 95% CI=.66-.83), poly substance use (OR=.70, 95% CI=.59-.84), marijuana use (OR=.73, 95% CI=.65-.82), and cocaine use (OR=.66, 95% CI=.48-.91). With respect to percent days of drug use, MANOVAs revealed significant main effect of time on reducing percent days of marijuana use [(F (3, 264)=23.684, p<.001]. No significant treatment effects were observed.
Conclusions: Results of this study indicated that there was an overall decrease in drug use following admission to a level I trauma center for an alcohol related injury. Thus, traumatic injury may constitute a unique opportunity to provide brief intervention targeting substance abuse. Brief interventions specifically designed to identify and address may significantly influence illicit drug use and should be evaluated in randomized clinical trials.
Financial Support: This study was supported by the National Institute on Alcohol Abuse and Alcoholism (R01-AA-01543; PI: Field)

177

EARLY CANNABIS USE AND EDUCATIONAL TRAJECTORIES: EPIDEMIOLOGICAL EVIDENCE FROM 16 COUNTRIES OF THE WORLD MENTAL HEALTH SURVEYS CONSORTIUM.

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Aims: In some prior research, early-onset cannabis use (before 17 years; EOCU) has predicted failure to complete secondary school, but there rarely has been thorough control over environmental processes and conditions of the locally shared social environment (e.g., social norms and expectations with respect to school success and dropout). This study's aim extends the research to other educational milestones such as failure to enter primary school, and holds constant socially shared aspects of local area environment, as well as sex and birth cohort.
Methods: Data are from the World Mental Health Surveys Initiative, with community survey probability samples from 16 countries in the Americas, Middle East and Africa and Asia (n=41,695 adults). A standardized interview schedule was used to assess cannabis use, covariates, and education, with transnational calibration of educational milestones and other variables. Estimates are from conditional logistic regression for local area matched sets.
Results: The initial estimate indicated an association between EOCU and having failed to enter primary school, but covariate adjustment rendered a null association ($p>0.05$). There were similar findings for the other educational milestones such as failing to enter and to complete college, with robust associations and $p<0.05$ prior to covariate adjustment, but with much attenuated associations and $p>0.05$ after covariate adjustment.
Conclusions: If early-onset cannabis smoking truly accounts for disruption of educational trajectories and failure to achieve educational milestones, it has not been disclosed in this multi-country study of suspected hazards attributed to cannabis smoking, despite rigorous community sampling and assessment. Potential limitations of approach are noted. Future directions for more probing multi-national research on suspected hazards of cannabis and other drug use are sketched.
Financial Support: D43TW05819, R01DA016558, K05DA015799 (JCA). FF is in the MSU NIDA Drug Dependence Epidemiology Training Program.

178

PROVIDING BRIEF ADDICTIONS TREATMENT IN AN EMERGENCY DEPARTMENT: EXPERIENCES OF UNIVERSITY OF NEW MEXICO HOSPITAL RESEARCH INTERVENTIONISTS IN THE SMART-ED TRIAL.

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Aims: Hospital emergency departments (EDs) are receiving increased attention as venues for addiction treatment (Cherpitel et al., 2010; Vaca et al., 2011). Brief interventions in the ED may be effective and economical and reach those who might not seek treatment in traditional addiction treatment settings. However, provision of brief intervention in the ED requires consideration of several factors in order to be implemented successfully. Here we offer the interventionists' perspectives on the complexities of providing a brief intervention in a medical ED setting.
Methods: The University of New Mexico Hospital Emergency Department served as one of six sites in the National Institute on Drug Abuse (NIDA) Clinical Trials Network (CTN) Screening, Motivational Assessment, Referral and Treatment (SMART-ED). Following completion of the active phase of treatment, the interventionists described the unique challenges and lessons learned.
Results: Three themes emerged in our exploration of the challenges involved in conducting screening, assessment, and brief intervention using motivational interviewing (MI). (1) Challenges inherent in the nature of the emergency department including patient flow, availability of space, frequent interruptions, privacy and confidentiality, and patient acuity. (2) Maintaining focus on addictions in the face of competing priorities, including medical reasons for ED visit and other psychosocial/mental health needs. (3) Using MI techniques appropriately during intervention, and not using them during screening and assessment.
Conclusions: There are many complexities involved in providing brief addiction intervention in the ED. Understanding and preparing for these challenges is critical to the successful implementation of addiction treatment programs or research aiming to implement brief interventions in this environment.
Financial Support: U01DA015833

179

ANTISOCIAL PERSONALITY DISORDER PREDICTS TREATMENT EFFECTIVENESS IN HOMELESS, SUBSTANCE-DEPENDENT MEN WHO HAVE SEX WITH MEN.

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Aims: Contingency management (CM) interventions have produced better substance use outcomes in participants diagnosed with ASPD. No study to date, however, has tested the efficacy of CM in improving healthy behaviors in participants with and without ASPD. This secondary analysis sought to test the efficacy of a CM intervention for reducing methamphetamine use and increasing health-promoting and prosocial behaviors in participants both with and without ASPD.
Methods: 131 homeless, substance-dependent MSM were randomized into a CM (n=64) or control (n=67) condition; targeted behaviors were reinforced using vouchers redeemable at an onsite store. Participants in both conditions received voucher points for study visits and participating in activities; participants in the CM condition also earned voucher points for substance abstinence and engaging in health-promoting and prosocial behavior.
Results: 34.4% (n=45) of participants were diagnosed with ASPD at baseline. ASPD status showed no significant association with methamphetamine use at baseline. However, by intervention completion, ASPD diagnosis was significantly positively associated with methamphetamine abstinence ($\beta=0.1$ [0.05]; $p<.05$) for participants in both conditions. Analysis of the voucher earnings for health-promoting and prosocial behaviors revealed that participants with ASPD earned significantly fewer vouchers for these behaviors ($\beta=-7.8$ [3.2]; $p<.05$).
Conclusions: Given that both conditions produced significantly greater reductions in methamphetamine use for participants diagnosed with ASPD, it appears that providing positive reinforcement with incentives, even if only for study visits and participation, is efficacious in reducing methamphetamine use with these dually-diagnosed individuals. However, the same intervention failed to produce corresponding increases in health-promoting and prosocial behaviors among participants with ASPD and, thus, the CM intervention had insufficient magnitude to overcome the nature of the disorder itself.
Financial Support: This study is supported by NIDA grant #1 R01 DA 015990.

180

IMPLEMENTING ADDICTION TREATMENT TRIALS IN MEDICAL SETTINGS IN THE NATIONAL INSTITUTE ON DRUG ABUSE CLINICAL TRIALS NETWORK.

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Aims: Many people with addictions receive health care but never receive specialty addictions treatment. With movement toward integrating addiction treatment into medical care, the CTN began conducting protocols in medical settings such as primary care and emergency departments. Here we describe the implementation process of the first CTN trial conducted in medical emergency departments.
Methods: The NIDA CTN six-site Screening, Motivational Assessment, Referral and Treatment in the Emergency Department (SMART-ED) trial presented unique challenges because of the ED setting. The factors necessary for successful implementation include site selection, staff selection, RA and interventionist training, site preparation, and data collection.
Results: Several implementation components were particularly important in the SMART-ED trial. 1. Site selection. ED Department and staff buy-in was central to decisions on which sites were chosen to participate. 2. Staff selection. Interventionists/RAs needed to possess the empathy necessary to deliver an MI based intervention, research abilities necessary for protocol adherence and the ability to navigate busy EDs. 3. RA and interventionist training and ongoing coaching. In-person and webinar trainings ensured that research staff understood and were able to follow protocol procedures and be certified to deliver the intervention. Ongoing telephone coaching is successfully preventing drift. 4. Site preparation. Prior to beginning the main trial, each site also had real-world practice conducting study procedures through standardized patient visits. 5. Data collection. The screening data is collected using direct entry into tablet computers to facilitate rapid screening and mobility within the ED setting.
Conclusions: Some of the procedures used in this clinical trial may be useful in the successful implementation of future addiction trials conducted in medical settings.
Financial Support: U01DA015833

181

RELAPSE TO SUBSTANCE USE IN POSTPARTUM WOMEN.

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Aims: To assess relapse to substance use in postpartum women who achieved abstinence in pregnancy.
Methods: We evaluated 153 pregnant women drawn from a randomized controlled trial comparing brief advice to a psychological treatment for substance abuse. To evaluate relapse we selected women who met minimum criteria for use in the 6 months before pregnancy and were abstinent in their last month of pregnancy. We examined cigarette, alcohol, marijuana, and cocaine use separately. We defined minimum pre-pregnancy baseline use as 7 drinks per week or 3 or more drinks per day for alcohol, 2 days of use per month for marijuana and cocaine, or 3 cigarettes per day. We calculated rates of use in the 3 months post delivery for women who met criteria for each substance individually.
Results: Of the 153 women in our sample, 94 (61%) met the baseline use cutoff for cigarettes, 69 (46%) for alcohol, 60 (39%) for marijuana, and 18 (12%) for cocaine. In the last month of pregnancy 35 (37%) of cigarette users, 67 (97%) of alcohol users, 42 (70%) of marijuana users and 13 (72%) of cocaine users achieved abstinence. Clean cigarette users relapsed at a rate of 49% (95% CI: 31%, 66%), which was similar to clean alcohol users (46%, 95% CI: 34%, 59%) and clean marijuana users (50%, 95% CI: 34%, 66%). Clean cocaine users, however, relapsed at a somewhat lower rate, 23% (95% CI: 5%, 54%).
Conclusions: Pregnancy-related abstinence rates were high among alcohol, marijuana and cocaine users, but not smokers. Unfortunately, postpartum relapse was common. Our findings speak to the need for interventions that can capitalize upon a period of naturally occurring abstinence from substances of abuse.
Financial Support: R01 DA019135-03 PI:Yonkers

182

"BATH SALTS": DISCRIMINATIVE STIMULUS EFFECTS OF SEVERAL CATHINONE COMPOUNDS.

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Aims: A number of psychostimulant-like cathinone compounds are being sold as "legal" alternatives to methamphetamine or cocaine. The purpose of these experiments was to determine whether cathinone compounds stimulate motor activity and have similar discriminative stimulus effects with cocaine and/or methamphetamine.
Methods: 3,4-Methylenedioxypyrovalerone (MDPV), methylone, mephedrine, and naphyrone, were tested for locomotor stimulant effects in mice and subsequently for substitution in rats trained to discriminate cocaine (10 mg/kg, i.p.) or methamphetamine (1 mg/kg, i.p.) from saline.
Results: All compounds had locomotor stimulant effects with efficacy ranging from 75% to 100% of cocaine or methamphetamine. MDPV and methylone fully substituted for the discriminative stimulus effects of cocaine and methamphetamine, whereas mephedrine, and naphyrone each produced at least partial substitution.
Conclusions: Several commonly marketed products produce discriminative stimulus effects comparable to those of cocaine and methamphetamine, which suggests that these compounds are likely to have similar abuse liability.
Financial Support: Supported by NIH N01DA-7-8872.

183

NEW EVIDENCE: DAT GENOTYPE MODULATES BOTH WITHDRAWAL-DRIVEN AND CUE-DRIVEN PHENOTYPES IN SMOKERS.

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Aims: Smoking cue (SC)- and withdrawal (WD)-induced "cravings" are two major motivators for continued smoking and relapse. Previously, we evaluated the impact of variation in the gene that encodes the dopamine transporter (DAT) on the brain during smoking cue (SC) exposure in Sated smokers (i.e., just having smoked). We found, and confirmed that smokers carrying a 9-repeat allele (9-Rs) of the VNTR polymorphism in the 3' un-translated region of the DAT gene had greater responses than homozygotes for the 10-repeat allele (10/10-Rs) in the ventral striatum and medial orbitofrontal cortex (VS/mOFC), providing evidence that genetic variation in the DAT contributes to neural responses elicited by SCs and supporting the existence of a 9-R "SC-driven" phenotype. Given the low SC responses in the Sated state in 10/10-Rs, we hypothesize that this group represents a "WD-driven" phenotype. Thus, in a third cohort, we imaged genotyped smokers during SC exposure in both Sated and WD conditions.
Methods: In a within subjects design (N=20), perfusion fMRI data were acquired both in the brain 'at rest' and during 10-minute audio/videos that contained SCs (vs non-SCs) in smokers who were Sated or in WD.
Results: In the brain at rest, activity in the VS/mOFC was elevated in WD vs Sated conditions in both 9- and 10/10-Rs. During SC exposure when Sated, we replicated our earlier findings; 9-Rs had greater activity in the VS/mOFC than 10/10-Rs. During SC exposure when in WD, bilateral amygdala were recruited in 10/10-repeats, but not in 9-Rs. fMRI data are reported FWE cor (0.32–.036).
Conclusions: The recruitment of the amygdala in 10/10-Rs during SC exposure may demonstrate the neural correlate of heightened cue vulnerabilities during nicotine deprivation to distinguish DAT genotype modulated SC- and WD-driven endophenotypes. The use of neurogenetics to identify relapse predictors should accelerate personalized approaches for the treatment of nicotine dependence, substantially improving treatment outcomes.
Financial Support: 5-P60-DA-005186-18, 1R21 DA025882-01A1

184

DISCOUNTING BY MONKEYS IN AN ALLOMORPHIC CHOICE PARADIGM: IMMEDIATE DRUG VS. DELAYED FOOD.

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Aims: We recently reported that delayed cocaine is discounted less steeply than delayed saccharin and sucrose, suggesting that delay to reinforcement reduces the value of cocaine at a relatively slow rate. These results, however, were obtained using isomorphic choice paradigms in which the immediate and delayed reinforcers were qualitatively the same, and it was unclear whether the same results would hold in an allomorphic paradigm in which the choice was between immediate cocaine and a delayed nondrug reinforcer.
Methods: Using a two-option toggle lever, 4 male rhesus monkeys chose between an immediate cocaine injection (0.006-0.40 mg/kg/inj) and a fixed number (4 or 8 in different conditions) of delayed 1-g food pellets. In different conditions, delays to food reinforcement ranged from 0 to 120 sec. Daily sessions consisted of 2 forced-choice trials on each lever followed by 16 free-choice trials, with a 30-min ITI.
Results: Choice of immediate cocaine increased as a function of dose in all 4 monkeys, and choice of food decreased as a function of delay, such that cocaine dose-response functions shifted to the left with increasing delay to food. In the one monkey who to date has completed all of the planned delay conditions, choice of cocaine was well described by the hyperbolic discounting function, and food was discounted at a rate comparable to that in isomorphic choice paradigms using other nondrug reinforcers (i.e., saccharin and sucrose).
Conclusions: These data indicate that choice of cocaine self-administration increases with delay to a non-drug alternative reinforcer. Further, our initial data suggest that the hyperbolic model describes discounting in allomorphic as well as isomorphic choice paradigms. This finding may have important implications for a behavioral analysis of substance abuse because experimental paradigms involving allomorphic choice (i.e., drug vs. nondrug) are more ecologically valid than paradigms involving isomorphic choice.
Financial Support: This research was supported by grant R01-DA-027666 to WLW from the National Institute on Drug Abuse.

185

WORKFORCE DEVELOPMENT IN VIETNAM: HVATTC.

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Aims: UCLA ISAP through the support of a cooperative agreement with SAMHSA will work to develop a HIV-Addiction Technology Transfer Center (VHATTC) in Vietnam. The purpose of the VHATTC is to reduce the individual and societal harm due to HIV and substance use disorders in Vietnam. Based at Hanoi Medical University (HMU), the VHATTC will organize training programs for counselors and medical professionals, develop partnerships between HMU leaders, policymakers, and health professionals, and promote the principles of recovery-oriented systems of care.
Methods: Planned activities include an ongoing multi-stage work force training needs assessment. Conferences will be conducted in Hanoi and Ho Chi Minh, Vietnam. Broad dissemination of evidence-based information, however, will reach many regions in Vietnam. One method for rapidly disseminating the information from the VHATTC will be by creating partnerships with other training groups: the government Ministries, Family Health International (FHI) and UNODC. Overall, in year 1, the VHATTC will, at a minimum, provide information dissemination, intensive skills-building and a variety of SUD, HIV and mental health training events with 400 individuals. In addition, 10 health educators will participate in a train-the-trainer program on screening, brief intervention, and referral to treatment.
Conclusions: There is an urgent need for workforce development in the area of HIV and SUD. Vietnam is experiencing an HIV epidemic due, in large part, to the persistent problem of injection drug use. While heroin use is highly prevalent throughout Vietnam, there is evidence of increasing amphetamine-type stimulant use in the southern part of Vietnam, particularly among sex workers. The VHATTC will build on a tremendous amount of training and advocacy work conducted by HMU, FHI, the WHO, and the UNODC. In addition, the VHATTC will draw upon the expertise of ATTC leaders in the U.S. to develop a counselor education curriculum and to train Vietnamese providers in clinical supervision.
Financial Support: SAMHSA #TI023603

186

ROLE OF NEURONAL NITRIC OXIDE SYNTHASE-CONTAINING STRIATAL INTERNEURONS IN METHAMPHETAMINE-INDUCED DOPAMINE NEUROTOXICITY.

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Aims: Production of nitric oxide (NO) has been implicated in methamphetamine (METH)-induced dopamine (DA) neurotoxicity. The source of this NO has not been clearly delineated, but recent evidence suggests that it arises from activation of neuronal nitric oxide synthase (nNOS), which is selectively expressed in a subpopulation of striatal interneurons. Thus, we hypothesized that DA-mediated activation of these nNOS-containing striatal interneurons is necessary for METH-induced neurotoxicity. Our aim was to determine whether inhibiting activation of nNOS-containing interneurons in the striatum blocks METH-induced neurotoxicity.
Methods: nNOS-containing striatal interneurons selectively express the neurokinin 1 (NK-1) receptor, which is activated by substance P. One particular toxin, a conjugate of substance P to the ribosome inactivating protein saporin (SSP-SAP), selectively destroys neurons expressing the NK-1 receptor. Here, male Sprague Dawley rats (N=12) received four unilateral intrastriatal infusions of either targeted toxin (SSP-SAP) or control toxin (Blank-SAP). Three weeks later, animals were treated with a neurotoxic regimen of (±)-METH (4 x 10 mg/kg, s.c. at 2-hr intervals) or saline. Animals were sacrificed 1 week after exposure to METH and DA depletions were determined.
Results: SSP-SAP lesions resulted in a significant and selective loss of nNOS-containing interneurons throughout the striatum. Surprisingly, this deletion did not confer resistance to METH-induced DA neurotoxicity. Quantification of DAT levels in the intact vs. lesioned hemisphere showed no difference between hemispheres in any treatment group.
Conclusions: These results suggest that activation of the nNOS-containing striatal interneurons is not necessary for METH-induced neurotoxicity, suggesting that another source of NO may contribute to the toxicity or that there is no involvement of NO in METH-induced monoamine neuron toxicity.
Financial Support: DA013367 (KAK), and DA031523 (AFG)

187

TECHNOLOGY-BASED INTERVENTIONS FOR SUBSTANCE USE DISORDER TREATMENT.

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Aims: The Richmond Behavioral Health Authority (RBHA), a behavioral health services provider serving residents in the city of Richmond, Virginia is implementing a Health Information Technology (HIT) Project (Tech-Connect Project) that will enhance existing recovery and wellness services through the use of technology, including web-based services and mobile devices. This will enhance the ability of the RBHA to make innovative "connections" between individuals receiving services, RBHA services provider staff and other community-based service providers. The target population for the Tech-Connect Project is adults with a diagnosed substance use disorder (SUD), and with co-occurring mental health disorders, who are in or seeking recovery at RBHA. The aims of the project are to: 1) Improve consumer outcomes by enhancing the continuum of care by using technology to enhance existing treatment and recovery support services; 2) Create necessary infrastructure at RBHA and key partner organizations that promotes a broader adoption of and use of HIT by both consumers and service providers; and 3) Expand RBHA's electronic footprint by adopting and implementing social media enhancements. Specific objectives to be achieved within these broad aims include: 1) Increased consumer empowerment and involvement in directing and evaluating their treatment and recovery services; 2) Expanded electronic training of consumers, partners and staff to enhance knowledge and skills specific to HIT; 3) Increasing access to and use of technology enhancements for both consumers and staff; and 4) Increasing staff-to-consumer and consumer-to-consumer communication about recovery through the use of social media. Each element of the Tech-Connect project is being evaluated
Conclusions: The technology improvements and infrastructure to be established through this project will address multiple strategic priorities of the agency, establish a broader system of recovery support for consumers and help prepare the RBHA for healthcare reform.
Financial Support: This project is supported by SAMHSA TI-23824.

188

VARIATIONS OF SMOKING TRAJECTORIES FROM EARLY ADOLESCENCE INTO ADULTHOOD: THE ROLE OF SINGLE NUCLEOTIDE POLYMORPHISMS OF NICOTINIC RECEPTOR AND ADHD SYMPTOMS.

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Aims: To examine the association of single nucleotide polymorphisms of the CHRNB3 (rs4950 and rs13280604) and CHRNA6 (rs892413, rs2304297) nicotinic acetylcholine receptors and symptoms of attention deficit hyperactivity disorder (ADHD) symptoms in predicting smoking patterns from early adolescence to adulthood.
Methods: The study sample consisted of a longitudinal cohort of 1469 unrelated youth from the National Longitudinal Study of Adolescent Health who provided responses on four surveys from Wave I to IV and a genetic sample in Wave III. To examine smoking behavior from ages 13 to 32 years a cohort sequential design was employed. Zero-inflated Poisson growth mixture modeling was applied to identify smoking patterns based on use and to assess the effects of the four SNPs and ADHD symptoms on cigarette use over time.
Results: No main effect of the four SNPs was observed, whereas main effects of ADHD symptoms were found in either the binary or count components of the smoking trajectory. The two SNPs of CHRNB3 interacted with inattentive symptoms in predicting the change of smoking levels. The GG combination of rs4950 and rs13280604 had relatively lower levels of cigarette use over time, especially among those who had 2 or more inattentive symptoms. The SNPs of CHRNA6 interacted with hyperactive symptoms in predicting smoking initiation over time. Having 2 or more hyperactive symptoms increased the risk of smoking initiation among adolescents who had the AA combination of rs892413 or who had the GG combination of rs2304297.
Conclusions: These findings demonstrate for the first time that SNPs of nicotinic receptors interact with ADHD symptoms to contribute to cigarette use across adolescence and young adulthood. Importantly, the findings show unique associations between specific genotypes and patterns of ADHD symptoms. These data could be useful to identify those individuals at greatest risk for cigarette smoking and may help target prevention efforts.
Financial Support: R01DA030487(BFF)

189

ACTIVATION OF THE BRAIN NORADRENERGIC SYSTEM DURING CANNABINOID WITHDRAWAL IN MICE.

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Aims: The present study investigates the behavioral and neurochemical changes in mice during cannabinoid receptor agonist CP 55,490 (CP55) withdrawal.
Methods: Mice were chronically treated with CP55 for five days. Behavioral and neurochemical changes precipitated by cannabinoid receptor antagonist AM251 were examined in CP55-treated mice. The concentrations of monoamines in the brain tissue were assessed using an HPLC system.
Results: Cannabinoid receptor antagonist AM251 precipitated jumping and rearing behavior in CP55 treated mice. In addition, 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG) and noradrenaline turnover (MHPG/noradrenaline) levels in the cerebral cortex were increased following AM251 challenge in CP55-treated mice. However, 5-hydroxytriptamine turnover did not alter the increase following AM251 challenge in CP55-treated mice. Pretreatment with CRF1 receptor antagonist CRA1000 decreased the incidence of AM251-precipitated jumping and rearing behavior.
Conclusions: Our findings demonstrated that the cannabinoid receptor antagonist could precipitate withdrawal signs in CP55-treated mice. These findings suggest that CP55 might have a physical dependence liability. Furthermore, elevation of noradrenaline transmission in the cerebral cortex through CRF1 receptors but not in 5-hydroxytriptamine transmission may play an important role in the incidence of cannabinoid withdrawal signs. Analysis of cannabinoid receptor antagonist-precipitated withdrawal signs is a useful method for studying physical dependence on the cannabinoid receptor agonist.
Financial Support: This work was supported by a Research Grant for Regulatory Science of Pharmaceuticals and Medical Devices, Health and Labour Sciences Research Grants from the Ministry of Health, Labour and Welfare of Japan (to M.F).

190

DESCRIPTIVE STUDY OF SPIRITUALITY IN A SAMPLE OF SPANISH ADDICTS.

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Aims: To describe spirituality levels in a sample of drug addicts and its relationship with sociodemographic factors, drug of abuse, addiction severity and psychiatric comorbidity.
Methods: 248 patients attended as first visits at Hospital Vall d'Hebron's Outpatient Drug Clinic were included (January 2009-June 2011) in an observational, cross-sectional study. Patients were >18 years and had a diagnosis of at least one drug dependence other than nicotine according to DSM-IV-TR criteria. Methods used to measure addiction severity, psychiatric comorbidity and spirituality were the Europ-ASI, SCID-I and SCID-II, and the Spirituality Self-Rating Scale (SSRS) respectively.
Results: The mean age of patients was 35.69 (SD 9,678) y.o. 78% were male. 88% were born in Spain, 6% in the European Union and 5% in Africa. The distribution by educational level was: higher education 9%, secondary education 37%, primary studies 37% and incomplete studies 17%. The distribuition by drug of abuse was: polidrug use in 26%, cocaine and alcohol in 15%, alcohol only in 14%, cocaine only in 13%,only cannabis in 7%, opiates and cocaine in 7%, cocaine and cannabis in 6%, and opiates alone 4%. The mean SSRS's score was 14,38 (SD 6,8). No statistically significant differencies in spirituality were found depending neither on drug of abuse nor severity of addiction mesured by the score of the subscales of the EUROP-ASI. The Psychiatric comorbidity model explained a 11.7% of the variance (F=6,150, p=0.003). Relationships were found between spirituality scores and having suffered from Substance-induced psychotic disorder (β 0.282, Sig. 0,005).
Conclusions: Spirituality has been related to recovery in previous studies. Spirituality scores in our sample were lower than expected and than found in other similar samples (Gallanter, 2007). No relationship was found neither with drug of abuse nor severity of addiction.
Financial Support: No external support

191

LIFETIME ALCOHOL USE AND LIVER FIBROSIS IN A COHORT OF HIV-INFECTED ADULTS WITH ALCOHOL PROBLEMS.

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Aims: To characterize the effect of alcohol on liver disease in HIV infection.
Methods: We performed a multivariable analysis of the association between lifetime alcohol use and liver fibrosis in a cross-sectional study of HIV-infected patients with current or past alcohol problems (CAGE≥2 or physician investigator diagnosis). Liver fibrosis was estimated with FIB-4, an index which includes platelets, liver function tests (ALT, AST) and age. FIB-4 score ≥1.45 defined fibrosis and FIB-4 >3.25 defined advanced fibrosis. The main independent variable was lifetime alcohol consumption (<150 kg, 150-600kg, >600 kg). Possible patterns corresponding to these amounts are: for <150 kg, <2 standard drinks (28 gr)/day for 15 years; for >600 kg, >4 drinks/day for 28 years. We examined years of heavy episodic drinking and current risky drinking(past 30 days)in secondary analyses .
Results: Participants (n=308) were 73% male, mean age 43 years, 49% with detectable HCV-RNA, 60% on antiretroviral therapy, 49% with an HIV RNA load <1000 copies/mL, 26% with a CD4 count <250 cells/mm3, 45% had lifetime alcohol consumption >600 kg, 30% drank current risky amounts and 69% had >9 years of heavy episodic drinking. Based on FIB-4, 39% had liver fibrosis and 10% had advanced fibrosis. In logistic regression analyses controlling for age, gender, HCV infection, and CD4 count, no association was detected for lifetime alcohol consumption and liver fibrosis (AOR=0.90 for >600 kg vs.<150 kg; AOR=0.92 for 150-600 kg vs. <150 kg; global p=0.97). No associations were observed for years of heavy episodic drinking or current risky alcohol use and liver fibrosis. Factors associated with liver fibrosis were HCV co-infection, low CD4 cell count, and age.
Conclusions: In HIV-infected patients with alcohol problems, lifetime alcohol consumption did not appear to be associated with liver fibrosis, suggesting that it may be less potent relative to other known liver fibrosis promoting factors.
Financial Support: This study was supported by R01AA13216 and K24AA015674. Dr. Fuster is a postdoctoral Grantee from the Spanish Ministry of Education (EDU/3495/2010).

192

ILLICIT DRUG USE AMONG PREGNANT WOMEN ENROLLED IN TREATMENT FOR CIGARETTE SMOKING CESSATION.

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Aims: Smoking during pregnancy is the leading preventable cause of poor pregnancy outcomes in the U.S. Cessation rates are low and one potential barrier to quitting is illicit drug use. Drug use is known to interfere with cessation attempts in other populations and pregnant cigarette smokers are more likely to report illicit drug use than pregnant nonsmokers. The purpose of the present study was to examine the prevalence of illicit drug use among pregnant women enrolled in clinical trials on smoking-cessation.
Methods: Urine specimens from 115 pregnant women in smoking cessation treatment were tested for illicit drug use during a study intake visit (~10th week of pregnancy) and during the final antpartum smoking-status assessment (~28th week of pregnancy). Participants were recruited from the greater Burlington, Vermont area, were smoking about 18 cigarettes per day pre-pregnancy, were largely young (<25 yrs), Caucasian, had a high school education and no private insurance.
Results: 34% of samples collected at the intake visit and 25% of those from the final antepartum assessment tested positive for an illicit drug. The most common drug detected was marijuana (90% of positive samples), followed by opioids (18%), cocaine (5%), benzodiazepines (3%), and methadone (3%). None tested positive for amphetamines. The majority of women (55%) who tested positive for an illicit substance at intake also tested positive at the final antepartum assessment.
Conclusions: Approximately a quarter to a third of pregnant women enrolled in this smoking-cessation trial were determined to also be using illicit drugs, with marijuana being the most prevalent but with opioid and cocaine use being detected as well. Those providing smoking-cessation services to pregnant women may want to be prepared to assist with obtaining services for other drug use as well.
Financial Support: NIDA R01DA14028 and T32DA007242

193

CHRONIC DISEASE MANAGEMENT FOR HOMELESS VETERANS: THE ROLE OF SUBSTANCE USE AND PEER SUPPORT.

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Aims: The Department of Housing and Urban Development and VA Supported Housing Program (VASH) offers housing and case management for chronically homeless veterans. At the VA Greater Los Angeles, the 1800 veterans in VASH have profound substance use, mental health and medical treatment needs. We developed a pilot program to decrease service utilization by using peer support and Care Coordination Home TeleHealth (CCHT), a phone-based chronic disease management program for persons with severe hypertension, diabetes, COPD, CHF and/or depression. A team of 2 veteran peers in recovery from substance use disorders (SUD) and/or serious mental illness served as health coaches for veterans with CCHT in VASH housing, providing ongoing contact and exploring barriers and facilitators to CCHT use.
Methods: We used successive Plan-Do-Study-Act cycles to facilitate data collection, interpretation and improvement of this program. We conducted medical record review to identify baseline health conditions, service use (prior and subsequent 12 months) and the content of peer sessions.
Results: The 16 veterans in VASH housing with CCHT have serious SUD, mental illness and chronic medical conditions. They are high utilizers of VA services, with a mean of 19 primary care and 19 specialty visits over the past year and no change in service use with the pilot study of peer support and CCHT. Social isolation is a salient problem for veterans in the intervention group and many veterans describe particular reluctance to disclose substance use to providers/case managers. The health coaches provided social support and clarified the common misconception that VASH housing is dependent on sobriety.
Conclusions: Substance use is closely related to chronic disease management for homeless veterans. Though peer support did not impact VA clinical service use, this pilot elucidates the potential role for peer-delivered motivational enhancement therapy to manage chronic disease for homeless veterans.
Financial Support: V22 VA Assessment and Improvement Lab for Patient Centered Care.

194

A PHARMACOGENETIC TRIAL OF NALTREXONE FOR METHAMPHETAMINE DEPENDENCE.

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Aims: Small trials have shown beneficial effects for oral naltrexone (NTX) in amphetamine dependence. NTX has shown efficacy in alcohol dependence, with better response in persons hetero- or homozygous for the A118G single nucleotide polymorphism (SNP) of the μ-opioid receptor (OPRM1). We conducted a pharmacogenetic trial of sustained release intramuscular (IM) NTX to examine the role of the A118G SNP in methamphetamine (MA) dependence.
Methods: Subjects seeking entry into the study were screened for the presence of the A118G SNP. 11 consecutive subjects with the A118G SNP were admitted to the trial. 11 subjects without the A118G SNP (wild-type; WT) were randomly selected as blinded controls. All subjects received a single 380 mg IM injection of sustained release NTX, and weekly psychotherapy. Adverse events, self-report of MA use, and urine toxicology for MA were assessed twice weekly for 4 weeks. Urine samples with <1,000 ng/mL of MA were classified as negative.
Results: There were no serious adverse events. There were no differences between A118G and WT groups in days of abstinence from MA use (18.3 ± 13.3 v. 18.5 ± 12.7, respectively, $p = 0.97$) or number of MA-negative urine samples (2.7 ± 3.4 v. 3.0 ± 4.3, respectively, $p = 0.57$).
Conclusions: Despite trials in alcohol dependence showing that A118G hetero- and homozygous persons who received NTX had lower rates of relapse and longer time to return to heavy drinking when compared to WT, in this study A118G and WT groups of MA dependent persons did not differ in MA use outcomes. While the trial in alcohol dependence showed A118G/WT differences in time to relapse to drinking at one month, that difference increased over time; therefore extended NTX treatment might yet reveal differences in A118G vs WT MA users. However, our findings suggest that the release of endogenous opioids and OPRM1 genetics may be less a factor in reward, reinforcement, or other aspects of the experience of MA use compared to alcohol use.
Financial Support: Supported by NIH R01 DA027161

195

EVALUATION OF THE QUALITY OF LIFE (WHOQOL-BREF) AMONG METHADONE AND SUBOXONE SUBSTITUTION STATE PROGRAM PATIENTS AND HEALTHY VOLUNTEERS IN THE REPUBLIC OF GEORGIA.

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Aims: Background: Quality-of-life improvement is an extremely important goal and commonly used diagnostic and outcome measure in chronic illnesses, particularly Substance use disorders.
The aim of this pilot study was to evaluate QOL patients being treated with methadone and Suboxone in State-sponsored programs in Georgia.
Methods: Methods: The WHOQOL-BREF (26 questions) version was administered to patients in State substitution program and healthy volunteers to assess their overall function and life satisfaction in physical, mental, social health, and environment domains. Domain scores were calculated and converted to 4-20 and 0-100 scales, identical to the WHOQOL-100. Data analyses were carried out using SPSS (Windows) Version 11.5.
Results: Results: Patients (485; 309 from 6 Tbilisi, 176 from 5 regional centers; 2 females) and 50 healthy controls (13 male, 37 female) were surveyed. Significant differences were observed between new admitted patients (0-3 month) and healthy controls by mean physical (47.5 vs. 51.94; CI 95%); psychological (55.0 vs. 60.50; CI 95%) and environmental (46.2 vs. 52.2; CI 95%) domains, but not by social relationships or regions. The Social domain scores were raised in accordance with time spent in treatment reaching a maximum improvement within 1-3 years (social-72.8 vs. 67.7; CI 95%), further with few descending tends round the healthy people's scores.
Conclusions: Conclusions: These pilot data show decrements in QOL among patients entering maintenance treatment with improvements in the course of maintenance treatment. Additional studies with larger numbers of patients and controls are needed to confirm these findings.
Financial Support: GRIA- Georgian Research Institute on Addiction

196

INCENTIVES ARE EFFECTIVE ACROSS COCAINE-DEPENDENT OUTPATIENTS WITH DIFFERENT ECONOMIC RESOURCES.

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Aims: Voucher-based contingency management (CM) has demonstrated efficacy for treating cocaine addiction but few studies have assessed the impact of individual characteristics and response to CM and most research has been conducted in the USA. The strength of the reinforcers may vary across individuals and geographic regions. The aim of this study is to examine the impact of socioeconomic variables of clients on the effectiveness of CM in a European clinical setting.
Methods: Cocaine-dependent outpatients (n = 118) were randomized to Community Reinforcement Approach (CRA) treatment or CRA plus a CM program (CRA plus vouchers) in Spain. At the initial assessment participants provided past month income, sociodemographic characteristics, addiction severity variables and EuropASI measurements. Urine specimens were collected throughout the 24-week treatment to monitor abstinence. The impact of baseline economic variables, alone and in combination with treatment conditions, was assessed on abstinence and retention outcomes after six months of treatment. Four regression analysis were conducted to examine the effect of economic variables on response to treatments.
Results: Combining CRA with vouchers improves treatment outcomes in cocaine-dependent outpatients. Income did not predict retention and abstinence outcomes after six months of treatment in either treatment condition. Further, income did not impact the effectiveness of CRA plus vouchers compared to CRA.
Conclusions: The addition of CM component to CRA is beneficial for clients with various economic resources. These results support the generalizability of the use of CM strategies in community outpatient settings. This is important for the dissemination of efficacious cocaine-addiction treatment elements in different cultural contexts.
Financial Support: Spanish National Plan on Drugs (MSC-06-01) and the University of Oviedo (UNOV-08-PF).

197

THE TEMPORAL RELATIONSHIP BETWEEN PSYCHOLOGICAL CLIMATE, WORK ATTITUDE, AND THERAPIST TURNOVER.

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Aims: This study examined the extent to which a latent measure of work attitude (e.g., job satisfaction, intentions-to-quit) temporally mediated the relationship between latent measures of psychological climate (e.g., supervisor support, coworker support) and therapist turnover.
Methods: Therapists (N = 105), who were providing evidence-based treatment to adolescents with substance use disorders, completed organizational surveys at both study recruitment and three months post-recruitment. Additionally, each participant's turnover status was tracked throughout the study, including whether turnovers were voluntary or involuntary.
Results: Overall, 24% of therapists voluntary turned over during the course of the study. In addition to revealing that none of the participant background characteristics were significant predictors of staff turnover, multilevel discrete-time survival analyses supported our hypothesis that work attitude fully mediated the temporal relationship between psychological climate and staff turnover.
Conclusions: This study provides empirical evidence that therapist turnover is more than simply correlated with an individual's work attitude or perception of the work environment, which has been a primary conclusion of much of the existing therapist turnover research.
Financial Support: Financial support for this study was provided by the Substance Abuse and Mental Health Service Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT; contract 270200700004C) and the National Institute on Drug Abuse (NIDA; R01-DA030462).

198

PREFERENCES FOR REINFORCEMENT TYPE AND ANCILLARY SERVICES: A COMPARISON OF EMERGING ADULTS AND OLDER CHEMICAL DEPENDENCY TREATMENT CLIENTS.

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Aims: Emerging adults (18-24 year olds) have been characterized as being more difficult to engage in substance abuse (SA) treatment and have poorer treatment outcomes than their older counterparts. Use of contingency management along with the provision of ancillary services may improve treatment outcomes; however reinforcement preferences and service needs may differ from what is typically offered. This study sought to elucidate reinforcement and ancillary service preferences of emerging adults compared to older clients in SA treatment.
Methods: Clients (n=388, 56% female) of 3 treatment programs in Western Washington completed an anonymous survey to rate 14 incentives and 11 ancillary services on a 0-4 Likert scale. Ratings of older and younger clients were compared utilizing MANOVA.
Results: Emerging adults (n=80, 20%) rated "non-essential" incentives such as electronics store vouchers, iTunes vouchers, restaurant vouchers, and movie tickets more highly than older adults [$F(6, 342)=2.4$, $p<.05$]. There were no significant age group differences in ratings of more practical incentives such as vouchers for food or clothing. Emerging adults reported a greater need for ancillary services related to meeting basic needs, such as finding a job, job training, housing, legal aid, and completing school [$F(6, 344)=2.45$, $p<.05$], but did not differ from adults in their perceived need for other services, such as improving relationships or increasing parenting skills.
Conclusions: An understanding of incentives and ancillary services that are relevant to emerging adults may help to inform interventions tailored for this group. Emerging adults may have an increased need for a variety of services, and be appreciative of reinforcement options that reflect their developmental stage.
Financial Support: National Institute on Drug Abuse, U10 DA13714

199

Δ9-THC-LIKE DISCRIMINATIVE STIMULUS EFFECTS OF COMPOUNDS COMMONLY FOUND IN K2/SPICE.

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Aims: A number of cannabinoid compounds are being sold as "legal" alternatives to marijuana in the form of incense. The purpose of these experiments was to determine whether the most common of these compounds have discriminative stimulus effects similar to Δ9-tetrahydrocannabinol, which is thought to be the main active component in marijuana.
Methods: The compounds JWH-018, JWH-073, and JWH-200 were tested for substitution in rats trained to discriminate Δ9-tetrahydrocannabinol (3 mg/kg, i.p.).
Results: JWH-018, JWH, 073, and JWH-200 each fully substituted for the discriminative stimulus effects of Δ9-tetrahydrocannabinol at doses that produced only marginal amounts of rate suppression (decreases to 79 to 84% of vehicle control).
Conclusions: Several of the most commonly used ingredients of K2 or Spice products produce discriminative stimulus effects comparable to those of Δ9-tetrahydrocannabinol, which suggests that these compounds may indeed mimic the psychoactive effects of marijuana responsible for abuse liability.
Financial Support: Supported by NIH N01DA-7-8872.

200

CLIENT ATTITUDES TOWARD, AND SATISFACTION WITH, GENERAL MEDICAL PRACTITIONERS' APPROACH TO CANNABIS USE INTERVENTIONS.

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Aims: The specific aims of the study were to identify: 1) cannabis user's expectations regarding the GPs' approach; 2) aspects of their actual experience; and 3) their reactions to that experience and its impact on future help-seeking.
Methods: An online survey of adult cannabis users available from the Australian National Cannabis Prevention and Information Centre's website from March to December 2011. The survey asked a range of questions regarding their demographic characteristics, experiences of discussing their cannabis use with their GP, and a range of satisfaction questions using the Client Satisfaction Questionnaire (CSQ-8).
Results: Of the first 43 respondents, the majority (61%) were male and believed that they no problems with alcohol or other drugs besides cannabis (56%). They reported that their GP rarely (12%) raised the issue of their cannabis use despite them consulting regularly. The most common concerns regarding their cannabis use was the impact on their mental health (58%), physical health (47%), and wanting to reduce their use (42%). The top 3 expected responses were supportive listening (61%); withdrawal medication (29%) or referral to counseling (29%). The top 3 actual responses were referral to counseling/supportive listening (34%), withdrawal medication (17%) and "just stop" blanket message or do nothing and ignore the issue (15% each). Overall, the majority did not believe that they received the service they wanted or that it helped them deal with their concern.
Conclusions: While GPs are seen as a credible and preferred source of assistance in the management of cannabis-related concerns, including management of withdrawal and craving, the experiences of cannabis users suggest that there is a need for improved training in the screening and assessment of cannabis use and related problems and in the delivery of brief advice and referral for ongoing treatment.
Financial Support: The National Cannabis Prevention and Information Centre is supported by the Australian Government's Department of Health & Ageing.

201

UNHEALED WOUNDS: CHRONIC COCAINE USERS WITH PRIOR TRAUMA EXHIBIT DIFFERENT RESTING STATE FUNCTIONAL CONNECTIVITY FROM THOSE WITHOUT PRIOR TRAUMA.

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Aims: Abnormalities in amygdala functional connectivity during resting state distinguish individuals with posttraumatic stress disorder (PTSD) from healthy controls. Among chronic cocaine users, prior history of self-reported trauma is associated with greater limbic response to both "seen" and "unseen" aversive and appetitive cues. We hypothesized that amygdalar functional connectivity *during the resting state* may also differ in cocaine-addicted individuals with, vs. those without, self-reported trauma history.
Methods: Stabilized, detoxified male cocaine patients (n=17, ongoing) were divided into two groups based on prior trauma history (TRAUMA n=8; NO TRAUMA, n=9), using the related question from the Addiction Severity Index. Arterial spin labeled (ASL) perfusion fMRI was used to measure resting rCBF. Perfusion data were pre-processed within SPM8, using functional connectivity analyses with amygdala (AMYG) as the reference region.
Results: Trauma group evidenced robust bilateral insula-AMYG connectivity ($p<.001_{(uncorr.)}$, t=16.59), a finding consistent with individuals suffering from PTSD and notably absent in the no trauma group. Unique to the no-trauma group was a positive anterior cingulate-AMYG connectivity ($p<.001_{(uncorr.)}$, t=8.49).
Conclusions: Our data provide additional evidence that trauma history is associated with abnormal functional connectivity. The enhanced amygdala-insula connectivity at rest may reflect an underlying dysfunction that manifests more fully during functional tasks as exaggerated brain response to both conscious and unconscious processing of evocative cues. Ongoing studies will test whether the compromised connectivity can predict poor treatment response or greater relapse risk.
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202

THE ASSOCIATION BETWEEN ALCOHOL CONSUMPTION AND DOMESTIC VIOLENCE AMONG WOMEN: PRELIMINARY ANALYSES.

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Aims: The aim of this study was to investigate the association between patterns of alcohol consumption and episodes of domestic violence (between the couple and also directed to children) among women in a Brazilian low-income neighborhood.
Methods: A household survey was performed, using a probabilistic sample of adult women in the city of Juiz de Fora, countryside of Brazil. A sample of 480 women aged between 18 and 60 years were interviewed, using the following instruments: a sociodemographic questionnaire, a screening instrument for alcohol consumption, AUDIT, and two scales of domestic violence: CTS2 and CTSPC. Data was analyzed using the SPSS statistical software. Pearson's chi-square test was used to verify association between violence and alcohol use.
Results: Preliminary analyses indicate a prevalence of risky alcohol consumption among women of 7.8%. Statistically significant associations between alcohol consumption of women and violence were observed in severe physical violence behaviors: abuse directed at children (p=0.049), women's physical victimization by their partners (p=0.039) and injury situations (p=0.020). There was no association between woman's alcohol consumption and violence against her partner.
Conclusions: Despite the clear association between alcohol consumption and domestic violence episodes, both phenomena are complex and require research on how they are associated. The data showed how these two major public health problems are distributed in the community context studied. Together with other information, they can contribute to develop prevention and treatment strategies for such events.
Financial Support: FAPESP (Process n° 2010/ 51094-7; 2010/51837-0); CNPq (Process n°400675/2010-2) and AFIP.

203

SBIRT FOR RISKY STIMULANT USE IN A SKID ROW COMMUNITY HEALTH CENTER.

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Aims: The NIDA-funded UCLA Quit Using Drugs Intervention Trial (QUIT) conducted a small RCT of a federally qualified health center (FQHC)-based very brief intervention for reducing risky stimulant use and drug-related harm in low-income, racially-diverse primary care patients in Los Angeles. The design emphasizes screening, very brief clinician advice (2-3 minutes), and two telephone drug-use health education sessions vs usual care control (240 per condition).We present findings on recruitment in a Skid Row FQHC.
Methods: Pre-visit screening of all adults in the waiting room is conducted using a touchscreen Tablet PC. At-risk drug use is defined as casual, frequent, or binge use without the physiological or psychological manifestations of dependence, that is a score of 4 to 26 on the WHO ASSIST.
Results: Between February 25 to April 28, 2011, 1060 adult patients were approached: 86% were 40+ yo; 70% male; 64% Black, 21% Latino, 13% white; 70% homeless. 80% were excluded prior to the ASSIST (non primary care visit, refusal, in substance use treatment, no stimulant use past 3 mos). Among the 210 who completed the ASSIST, 23% were dependent on drugs or alcohol. ASSIST score rates were (no/low risk, moderate risk, dependence, respectively): tobacco (24, 48, 28), alcohol (28, 46, 26), cannabis (43, 36, 21), cocaine (42, 34, 24), opioids (60, 26, 14), sedatives (66, 22, 12), methamphetamine/amphetamine type stimulants (69, 20, 11), hallucinogens (81, 14, 5), inhalants (86, 10, 4). Excluding low risk stimulant users or dependent substance users, 56 patients (5.3% of those observed in waiting room) met study criteria of past 3 mo "risky" stimulant use.
Conclusions: Integrating SBIRT into FQHCs is feasible. In Skid Row, only 5% of patients qualified for the study based on rates of risky stimulant use, as study eligible patients were generally low-users or had levels of use that approached dependence. Stimulant use rates observed are higher than in the general population (NSDUH).
Financial Support: NIDA DA 022445

204

METHAMPHETAMINE-INDUCED HYPERTHERMIA, METHYLPHENIDATE NEUROPROTECTION AND THE VESICULAR MONOAMINE TRANSPORTER-2.

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Aims: Hyperthermia and reduced vesicular monoamine transporter-2 (VMAT2) function both contribute to persistent striatal dopaminergic deficits caused by repeated methamphetamine (METH) injections. Methylphenidate (MPD) post-treatment attenuates this METH-induced damage, likely through changes in VMAT2 synaptic vesicle localization. This study investigated the associations between METH-induced hyperthermia, VMAT2 function and localization, and MPD protection.
Methods: Male Sprague-Dawley rats received 4 injections (s.c., 2-h intervals) of METH (7.5 mg/kg/injection) or saline (1 ml/kg/injection) and were sacrificed 1 h later. In other studies, rats received the same METH or saline regimen followed by 3 injections (s.c., 2-h intervals) of MPD (15 mg/kg/injection) or saline (1 ml/kg/injection) beginning 1 h after the final METH injection.
Results: MPD post-treatment attenuated both acute (1 h) and persistent (7 d) decreases in VMAT-2 immunoreactivity and function when core body temperature was maintained ≤ 40°C during METH treatment. In contrast, MPD did not protect if METH-induced core body temperature was > 40°C during METH treatment.
Conclusions: These data indicate that the degree of METH-induced hyperthermia impacts the ability of MPD to afford neuroprotection, which is closely tied to the localization of VMAT2 synaptic vesicles within striatal dopaminergic terminals.
Financial Support: DA00869, DA04222, DA13367, DA11389, DA019447 and DA09407

205

DIVERGENCE IN BEHAVIORAL MEASURES OF NEGATIVE AFFECT IN ACUTE OPIATE AND NICOTINE DEPENDENCE IN RATS.

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Aims: The emergence of negative affective states is a common and persistent feature of withdrawal from addictive drugs. Although most animal models of drug dependence examine withdrawal after long-term drug exposure, similar emotional signs are manifested during withdrawal even after acute exposure to opiates and nicotine. These signs can broadly be characterized as reflecting underlying states of either anxiety or anhedonia/dysphoria. Anxiety and mood disorders are clinically differentiable and have distinct, albeit overlapping, neurobiological substrates. Thus, one might expect there to be systematic differences in expression of one state versus the other in preclinical models of drug dependence.
Methods: To address this possibility, we have begun to examine the effects of acute and repeated opiate or nicotine exposure using three different measures of negative affect: increases in current thresholds necessary to maintain intra-cranial self-stimulation (ICSS), conditioned place aversion (CPA) and potentiated startle (PS). ICSS and, to a lesser extent, CPA are closely associated with anhedonia, whereas PS provides a measure of anxiety.
Results: Naloxone-precipitated withdrawal from morphine induces negative affect, indexed by all three measures. In contrast, the time course of spontaneous withdrawal from morphine is much more rapid as assessed by PS than by ICSS or CPA. Mecamylamine precipitates signs of withdrawal measured using ICSS, but not PS. Finally, the anxiogenic drug yohimbine, which potently reinstates drug-seeking, induces PS but has no effect on ICSS thresholds.
Conclusions: These data suggest systematic differences in expression of anxiety- versus anhedonia-related signs in early drug dependence. Future research will investigate differences in neural substrates of these states and the role that each may play in vulnerability to the development of habitual drug use.
Financial Support: DA018784, MMRF Translational Addiction Research Program.

206

INVESTIGATING GAMBLING AND SUBSTANCE USE BEHAVIORS: DOES ONE'S RELIGIOUS FAITH PLAY A DIFFERENTIAL ROLE?

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Aims: Gambling data from the Arab world, across different religious denominations is limited. This study investigated the link between gambling and use of various substances in youth from Lebanon, exploring the differential role of belonging to the Christian or Muslim faith.
Methods: A cross-sectional representative sample of 570 undergraduate and graduate American University of Beirut (AUB) students were surveyed in 2010 using a self-filled anonymous English questionnaire, including the South Oaks Gambling Screen.
Results: Slightly more than half (55%) of the university students had engaged in one or more gambling activities. About 7% were identified as possible problem/pathological gamblers (PG); the majority was social non-problem gamblers. Lifetime gambling was statistically significantly associated with all substance use measures ($p<0.05$), except nonmedical prescription drug use NMPDU; significantly stronger associations were observed in Muslim students (e.g., lifetime illegal drug use: odds ratio (OR)= 6.26, 95% confidence interval (CI)=3.17,12.35 in Muslim vs. OR=1.94, 95% CI=0.87,4.35 in Christian students, interaction term p-value=0.03). Lifetime strategic (e.g., card games) vs. nonstrategic (e.g., lottery) gamblers had statistically significantly higher odds of using all substances, except NMPDU; associations were equally strong, or stronger in Christian students. Past year NMPDU was statistically significantly higher in PGs than non-gamblers (NGs), in students of both religious faiths. Past-year alcohol abuse was strongly associated with PG in the overall sample, but only in Christians once adjusted for demographics and other substances; conversely, PGs were more likely to report illegal drug use (vs. NGs) but only in Muslims upon adjustment.
Conclusions: Gambling among youth seems ubiquitous to non-Western cultures, and its links to the use of various substances is differentially present in both Christian and Muslim students (whose faith prohibits the act).
Financial Support: Study funded by University Research Board at AUB.

207

THE ROLE OF THE LATERAL HABENULA IN THE REINSTATEMENT OF COCAINE-SEEKING.

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Aims: Recent studies have focused on a previously overlooked pathway from the lateral habenula (LHb) that innervates the rostromedial tegmental nucleus (RMTg), and regulates dopamine neurons in the ventral tegmental area (VTA). These projections from the LHb to the RMTg and VTA have been characterized for their role in both appetitive and aversive responses (Hong et al., 2011). The current study examined whether temporary inactivation of the LHb alters reinstatement of cocaine-seeking in a rat model of relapse.
Methods: Male Sprague-Dawley rats self-administered cocaine (0.2 mg/50-µl infusion) on an FR1 schedule of reinforcement (14 days). Following self-administration, rats underwent a minimum of 7 daily extinction sessions, followed by reinstatement tests. Immediately prior to the first extinction session and each reinstatement session, rats received bilateral LHb infusions (0.3 µl/side) of the GABA agonists, baclofen and muscimol (1.0/0.1 mM), or phosphate-buffered saline. Reinstatement tests consisted of cocaine primed (10 mg/kg, IP), cue induced (tone+light), and yohimbine (2.5 mg/kg) + cue reinstatement. Yohimbine was used as a model of stress-induced potentiation of cocaine-seeking.
Results: Rats showed stable cocaine self-administration and subsequent robust cocaine seeking under all forms of reinstatement. Temporary LHb inactivation prior to yohimbine + cue-induced reinstatement attenuated cocaine seeking compared to vehicle control infusions ($p<0.05$). LHb inactivation failed to affect responding during the first extinction session, cue-induced, and cocaine-primed reinstatement.
Conclusions: LHb inactivation failed to alter cocaine seeking under standard conditions of reinstatement (cue and cocaine-primed). However, intact LHb function is necessary for responding in the presence of cocaine-associated cues during a state of heightened anxiety (yohimbine pretreatment). These findings suggest that the LHb may be recruited during high anxiety but not low anxiety drug seeking.
Financial Support: NIDA DA10462, DA15369, T32007288.

208

NICOTINE-DEPENDENT RATS EXHIBIT INCREASES IN ALCOHOL SELF-ADMINISTRATION AND ALTERED SENSITIVITY TO VARENICLINE.

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Aims: Alcohol-dependent individuals are 3 times more likely to be smokers, and smokers are 4-10 times more likely to be alcohol-dependent. The aim of this study was to examine alcohol self-administration in rats made dependent on nicotine via chronic intermittent vapor inhalation.
Methods: Male Wistar rats (n=17) were trained to self-administer 10% w/v ethanol vs. water on an FR1 schedule in 30-min 2-lever operant sessions. Five rats were exposed to increasing doses (1.0, 2.0, 5.0 lpm) of nicotine vapor for several weeks on an intermittent (14 hrs ON/10 hrs OFF) daily schedule. Rats were tested for operant alcohol self-administration (SA) at the end of 14-hr nicotine exposure and also 8 hrs into withdrawal (WD) from nicotine vapor. Rats were repeatedly tested for somatic signs of WD from nicotine vapor. Near the end of the experiment, half of the control rats (n=6) were exposed to 5.0 lpm nicotine vapor for several weeks. The final 6 control rats were always exposed to ambient air. After 1 week of abstinence from nicotine vapor, all rats were tested for effects of varenicline (2 mg/kg s.c.) on operant alcohol SA. Results were analyzed with ANOVA and SNK post-hoc tests.
Results: Rats exhibited somatic WD from 2.0 and 5.0 lpm nicotine vapor, suggesting rats were physically dependent on nicotine. At the 5.0 lpm dose of nicotine vapor, rats exhibited increases in alcohol SA when tested during intoxication and also 8 hrs into WD. Nicotine-dependent rats exhibited reduced sensitivity to the suppressive effects of varenicline on alcohol SA when tested 1 week into abstinence.
Conclusions: This study suggests that chronic intermittent nicotine vapor inhalation produces nicotine dependence, excessive alcohol consumption, and changes in nAchR sensitivity in rat brain. This rat model will be useful for examining the neurobiology of nicotine and alcohol co-abuse and co-dependence.
Financial Support: Supported by NIAAA grant AA018400 and NIDA grant DA023597.

209

NARROWING OF THE GENERALIZATION GRADIENT OCCASIONING ETHANOL-SEEKING WITH PROLONGED RECOVERY.

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Aims: Stimuli signaling drug-availability occasion drug-seeking, and the breadth of such stimulus control may expand as addiction develops. Conversely, the longer a person remains in recovery, the less likely is relapse. This may be due to a reduction in the ability of stimuli to occasion drug-seeking. Stimulus generalization gradients allow exploration of the breadth of stimulus control over behavior. Here we conducted experiments examining whether extended exposure to a stimulus and contingencies reducing ethanol-seeking alters the stimulus generalization gradient of ethanol-seeking.
Methods: Rats responded under a multiple concurrent schedule of food and ethanol reinforcement comprised of components where food responding predominated (8kHz tone, food FR5, ethanol FR5) or ethanol responding predominated (16 kHz tone, food FR150, ethanol FR5) . For nine consecutive sessions, components either alternated between food-predominant and ethanol-predominant conditions or were only food-predominate conditions. On the 10th session, a stimulus generalization gradient was established by inserting components into the same multiple schedule where the tone presented varied from 6 kHz to 18 kHz. During these components, five responses on either lever ended the test component, and no reinforcement was delivered.
Results: Following the alternating condition, the proportion of ethanol/total responses increased in a graded manner as the tone increased from 6 kHz to 18 kHz. After nine consecutive sessions where ethanol choice was reduced and rats were only exposed to the 8 kHz tone, the stimulus generalization gradient was significantly shifted downwards.
Conclusions: Recent contingencies can reduce and narrow the stimulus control exerted by stimuli that occasion drug-seeking. These results suggest that the reduction in relapse likelihood with extended periods of recovery may be due, in part, to a reduction in the stimulus control that occasion-setting stimuli exert over drug-seeking.
Financial Support: This work was supported by PHS grant AA016987

210

ASSOCIATION OF POST-TRAUMATIC STRESS DISORDER WITH POST-TREATMENT OUTCOMES OF METHAMPHETAMINE-DEPENDENT ADULTS.

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Aims: Although trauma is a well established risk factor for substance use disorders, little is known about the association between post traumatic stress disorder (PTSD) and treatment outcomes among methamphetamine (MA) users. Using data from 526 adults in the largest psychosocial clinical trial of MA users conducted to date, this study examined (1) treatment outcomes of MA users with concomitant PTSD three years after treatment; and (2) PTSD symptom clusters as risk factors for post-treatment relapse to MA use.
Methods: Participants received psychosocial treatment for MA dependence as part of the Methamphetamine Treatment Project and were reassessed for substance use at a mean of 3 years after treatment initiation. DSM-IV psychiatric diagnoses were assessed at follow-up using the Mini-International Neuropsychiatric Interview.
Results: The odds of receiving a PTSD diagnosis were significantly elevated among those with a history of physical (OR=2.5, 95% C.I., 1.1-5.5) and/or emotional (OR=2.8, 95% C.I., 1.1-6.9) abuse. Relative to those without an PTSD, the presence of PTSD was associated with poorer MA use outcomes over the 3-year follow-up period, increased risk of suicide attempts (OR= 3.8, 95% C.I., 1.8-8.3), and higher levels of psychopathology. Avoidance and arousal symptoms predicted post-treatment MA use.
Conclusions: Addressing these high risk PTSD symptoms and syndromes in MA users may be helpful as a means of improving treatment outcomes in this population.
Financial Support: The research presented herein was supported by NIDA Grant 1K23DA020085 awarded to S. Glasner-Edwards and by the Methamphetamine Abuse Treatment – Special Studies (MAT-SS) contract 270-01-7089 and grants numbers TI 11440–01, TI 11427–01, TI 11425–01, TI 11443–01, TI 11484–01, TI 11441–01, TI 11410–01 and TI 11411–01, provided by the Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration (SAMHSA), US Department of Heath and Human Services.

211

ENDOCRINE STATUS: NOVEL IMPLICATIONS FOR UNDERSTANDING SEX-RELATED DIFFERENCES IN SELF-MEDICATION AND TREATMENT RESPONSE.

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Aims: Aim: To identify the influence of endocrine status on the inflammatory response in order to better understand the etiology of disease in men and women and to guide the selection of the most favorable treatments.
Methods: Evidence: Current literature suggests that sexual dimorphism plays a far greater role in human function than previously thought. In fact, a "sexual brain model" may have driven gonadally modulated meta-hormonal regulation as humans evolved. For example, one of the crucial features of a mammalian species' survival is to be able to generate an appropriate and adequate inflammatory response in order to combat a variety of disease states. There is now emerging evidence that this protective, yet potentially damaging, response of the human body is sex-specific as it is influenced by gonadal hormones such as testosterone, estradiol, and progesterone.One of the hallmarks of the inflammatory response is the production of pain, which seems to be differentially modulated by sex hormones. For example in a setting of temporomandibular joint inflammation, estradiol may "exacerbate" while testosterone "mitigates" the pain response. Similar correlations are reported for other fundamental signs of inflammation, such as swelling and increased blood flow (heat and redness).
Results: Several key elements have been proposed to play a critical role in differential hormone-specific inflammatory response. For instance, cytokines like CD16, TNF-alpha, substance P, galanin, NPY and majority of the neurotransmitter systems, such as GABA, glutamine, dopamine and opioid are differentially modulated by gonadal hormones.
Conclusions: Conclusion: Understanding the underlying impact that endocrine status has on the inflammatory response may be valuable for identifying individuals who are at risk for self-medicating their pain and ultimately may help identify a more appropriate and selective treatment for individuals who are afflicted with these disorders.
Financial Support: Sundry fund #400474

212

UNMET NEED FOR TREATMENT OF SUBSTANCE USE DISORDERS AND SERIOUS PSYCHOLOGICAL DISTRESS AMONG VETERANS: A NATIONWIDE ANALYSIS USING THE NSDUH.

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Aims: To measure the extent of unmet need for treatment of substance use disorders (SUDs) and serious psychological distress (SPD) among young veterans in the general population.
Methods: The 2004-2009 National Survey on Drug Use and Health (NSDUH) data are used to estimate the prevalence of SUD (based on the DSM-IV criteria) and SPD (based on the K6) among veterans and to examine the prevalence of unmet mental health needs among veterans age 21-34 and a comparable nonveteran population matched on gender and age. Logistic regression is used to examine the covariates of SUD and SPD as well as the likelihood of treatment.
Results: The prevalence of untreated SUD (15%) among veterans was almost twice as high as untreated SPD (8%). Similar rates of untreated SUD and SPD were found in the nonveteran comparison sample. Overall, veterans were more likely to have received treatment for SPD than were nonveterans, but not for SUD. Treatment rates for SUD were lower for participants that were non-white, younger, more educated, employed, married, and had higher income. Treatment rates for SPD were lower for participants that were male, non-white, younger, less educated, employed full time, and had low income.
Conclusions: The Department of Defense (DOD) and Department of Veterans Affairs (VA) provide extensive mental health screening, outreach, and treatment services. These findings suggest that overall the DOD and VA screening and outreach programs are very effective. Indeed, reducing unmet need for mental health treatment for veterans in the general population may require improving outreach to all Americans and creating greater acceptance for mental health treatment.
Financial Support: This research was supported by a grant from the National Institute on Alcohol Abuse and Alcoholism (NIAAA R01 AA020178). Points of view expressed in this paper do not necessarily represent the official position of the U.S. Government, NIAAA, or NDRI.

213

DIMINISHED BRAIN ACTIVATION IN METHAMPHETAMINE USERS DURING A GO-NO-GO TASK.

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Aims: Methamphetamine (METH) is a major stimulant abused in the United States. Individuals addicted to drugs, such as METH, may have impaired inhibition. This study examines the neural network associated with inhibitory control to a prepotent response in METH users and controls with a Go-No-Go (GNG) paradigm using an event-related functional magnetic imaging (fMRI).
Methods: 64 subjects with acceptable motion during the scans are included in this study: 20 currently (< 1 month) METH-dependent users (ages: 33.1±9.5 yrs; 11 females & 9 males), 21 abstinent METH users (ages: 38.10±8.72 yrs; 9 females & 12 males, last METH used 229±151 days), and 23 non-drug user controls (ages: 35.0±11.5 yrs; 10 females & 13 males). The three groups were matched by education and nicotine-smoking status. Each subject had fMRI scans during three GNG trials (KX, KYX, KYWX) in a 3T Siemens scanner. The subjects pressed a button whenever they saw the letters, except when X was present.
Results: Female METH abstinent users showed less activation than female controls in dorsal parietal (BA 7) and visual areas (BA 17 and BA 19) across the three conditions (p-corrected < 0.01). Furthermore, in the KX condition, female METH abstinent users showed less activation than female controls in the inferior parietal (BA 40), temporal (BA 39), and limbic (BA 24) areas (all p-values (corrected) <0.01). Lastly, there were no consistent significant differences between male controls and male abstinent or dependent METH users for any condition.
Conclusions: The diminished brain activation during this inhibitory control task in these abstinent METH users involved primarily the attention network and emotional network, which might be related to depressive symptoms that they experience during abstinence. This decreased brain function appears to affect the female but not the male METH users. Further analyses with cognitive tasks and mood assessments will be performed.
Financial Support: NIH grants (U54-NS56883; 2K02DA020569; 2K24-DA16170; 2G12-RR003061)

214

CONCURRENT USE OF METHAMPHETAMINE AND MARIJUANA IN ADOLESCENTS SHOW MILD ALTERATIONS IN BRAIN MICROSTRUCTURE.

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Aims: Methamphetamine (METH) and marijuana (MJ) are two widely abused drugs among adolescents. In METH abuse, it has been reported that MJ may have a neuroprotective effect and increased expression of cannabinoid receptors (CB1r) in some brain regions. To our knowledge, no research has evaluated brain microstructure in concurrent adolescent METH+MJ users. We hypothesize adolescent METH+MJ users will not show microstructural alterations in brain regions rich in CB1 receptors, such as the prefrontal cortex, striatum, amygdala, and hippocampus.
Methods: We evaluated 23 concurrent METH+MJ users (16 females & 7 males; mean age: 18.0+0.5y; last use: 159+68d, lifetime use: 1537+734g) and 17 controls (10 females & 7 males; mean age: 17.8+0.6y) with diffusion tensor imaging (DTI) on a 3 T MR scanner. DtiStudio was used to calculate fractional anisotropy (FA) and trace diffusion. Automated region analyses using Large Deformation Diffeomorphic Metric Mapping were performed in 9 bilateral regions. DTI data were analyzed by mixed-model ANOVA (between-subjects factors: drug use & gender, within-subject factor: hemisphere). Significant main effects were analyzed further using a Bonferroni correction.
Results: Compared to controls, METH+MJ users had trends for lower FA in amygdala (p=0.02) and higher FA in caudate nuclei (p=0.03). Also, METH+MJ users had trends for higher trace than controls in amygdala (p=0.02), hippocampi (p=0.03), lateral fronto-orbital white matter (p=0.03), and superior frontal white matter (p=0.04). However, none of these effects remained significant after correction for multiple comparisons.
Conclusions: In summary, adolescent METH+MJ users showed relatively minor microstructural alterations in selected brain regions. The small effect observed may be due to neuroprotective effects of MJ, despite potential METH-induced neurotoxicity. However, additional "pure" METH and pure MJ groups, as well as a larger sample size, are needed to further confirm our DTI findings.
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215

MONITORING DEATHS BY TOBACCO USE: A BRAZILIAN GENDER PERSPECTIVE FOR DIRECT GENDER-SENSITIVE PREVENTION POLICIES.

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Aims: To compare differences in deaths by mental and behavioral disorders due to tobacco use in the states of Brazil, from 1996 to 2008, and to analyze trends of deaths across time by gender.
Methods: Secondary data analysis of the Mortality Information System of the Ministry of Health and the 2008 Brazilian National Household Sample Survey. Mortality data were generated through the register of underlying causes of death certificates, coded according to ICD-10, as the basic cause of death. The death coefficient was calculated by gender, age, years of schooling, marital status and per capita income (corresponds to the average number of minimum wages received by person, stratified according to categories defined by the Brazilian Institute of Geography and Statistics).
Results: There were 76,007 deaths, 11.4% female (8,676), yielding an average of 4.9 deaths per 100,000 inhabitants. On average, 6.0% (4,594) of psychoactive substance use deaths were related to tobacco use, 27.9% (1,282) of these were female deaths. This prevalence is higher than Americas and Europe, around 17% and 22% respectively. Brazilian greater index is found on Northeast region (0.231), where 14.8% of the population receives up to 0.74 times (US$ 745.00)the minimum Brazilian wage, by month.
Conclusions: Although regional differences may be associated with better data collection in some regions, our results point to increasing trends across time in using tobacco (r2=0.78). Consistent analyzes of differences between men and women harmful health effects of smoking are necessary to enforce policy-making for implementing gender-specific tobacco control strategies.
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216

REVISITING THE REINFORCING EFFECTS OF HALLUCINOGENS IN THE LABORATORY.

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Aims: The classic hallucinogens are characterized by chemical structure as either a simple tryptamine (psilocybin), an ergoline (LSD), or a phenethylamine (mescaline). Newer "designer" hallucinogens (substituted tryptamines) have been flagged by the Drug Enforcement Agency for abuse liability evaluation and we report on two of these compounds: 5-methoxy-N-isopropyl-N-methyltryptamine hydrochloride (5-MeO-MIPT) and 4-hydroxy-N,N-diisopropyltryptamine hydrochloride (4-OH-DIPT). The reinforcing effects of LSD (0.00032-0.032 mg/kg), MDMA (0.1-3.2 mg/kg), 5-MeO-MIPT (0.0032-1.3 mg/kg), 4-OH-DIPT (0.32-3.2 mg/kg), and vehicle were evaluated using IV self-administration procedures and a pool of 7 adult male baboons (Papio hamadryas anubis, olive baboons).
Methods: Demonstration of reinforcement was defined as occurring when the mean number of self-injections per session of a dose condition exceeded the mean+2SD of the mean of the drug vehicle condition (analogous to a one-tailed test considered significant at p<0.05). Food pellets were available 24 hours/day under an FR schedule of reinforcement and behavioral observations following self-injections were also conducted.
Results: Rates of self-administration were significantly above vehicle levels in 3 of 4 subjects (5-MeO-MIPT), 2 out of 3 subjects (4-OH-DIPT), 3 out of 4 subjects (LSD), and 3 out of 3 subjects (MDMA). The number of food pellets earned by individual baboons was generally suppressed when 5-MeO-MIPT, 4-OH-DIPT, and MDMA (but not LSD) were self-administered. Limb tremors, bruxism, ataxia, tardive dyskinesia, body jerks, and locomotor changes were observed in individual subjects following self-injection of the higher doses of these compounds.
Conclusions: While the notable exception to good correspondence between laboratory self-administration studies and human drug taking behavior has historically been the classic hallucinogens, our data suggest the reinforcing effects of hallucinogens can be detected in baboons and should be investigated further.
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217

CHILDHOOD MALTREATMENT AND THE PERSISTENCE OF ADULT NICOTINE, ALCOHOL AND DRUG DEPENDENCE.

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Aims: The persistence of nicotine, alcohol and drug disorders in the general population is emerging as an important and challenging public health problem. Much has been done to understand risk factors for onset of these disorders, but little is known about predictors of the persistence of these disorders once they have begun. The risk for nicotine, alcohol and drug use disorders is increased by a history of childhood maltreatment, but whether this predicts the persistence of these disorders is unknown.
Methods: Data were drawn from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a national survey of 34,653 U.S. adults interviewed with the AUDADIS in 2001-2002 and reinterviewed 3 years later. Childhood maltreatments included physical, sexual and emotional abuse, and physical neglect. Persistent nicotine, alcohol and illicit drug dependence was defined as present at baseline and fully symptomatic through the 3 years of follow-up. The associations between childhood maltreatment and persistent nicotine, alcohol and illicit drug dependence were determined separately with logistic regression, adjusted for demographics, other adverse childhood events, Axis I psychiatric and substance use disorders, and key personality disorders.
Results: Childhood maltreatment predicted persistent nicotine and alcohol dependence, but was unrelated to drug dependence. Exposure to two or more childhood maltreatment types was significantly and robustly associated with increased odds of persistence of nicotine (OR=1.48) and alcohol dependence (OR=2.03), even after adjusting for the covariates.
Conclusions: Exposure to multiple childhood maltreatments is a robust predictor of persistence of nicotine and alcohol dependence, suggesting that trauma may have a significant impact on the intractability of alcohol and nicotine dependence into adulthood. Information on history of childhood maltreatment may be important information for treatment programs—both for nicotine and alcohol—as such a history that is not addressed in treatment may complicate successful cessation/treatment.
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218

IMMUNE GENETIC PREDICTORS OF NEONATAL ABSTINENCE SYNDROME IN METHADONE-EXPOSED INFANTS.

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Aims: Genetic make-up of both the mother and infant may contribute to inter-individual variability in response to opioids which the mother consumed during pregnancy. Subsequently this may impact on the need to medicate infants to control Neonatal Abstinence Syndrome (NAS) and the infants' response to medication. This project therefore aimed to investigate the use of genetic inflammatory markers (particularly interleukin-1beta (IL-1B), linked with creating a proinflammatory environment that results in neuronal excitability to heighten opioid reward and dependence) to predict the occurrence of NAS, in an attempt to successfully manage NAS in methadone exposed infants.
Methods: This pilot study collected cheek cells for genetic analysis from seven methadone maintained mothers during pregnancy and their subsequent newborns following delivery.
Results: Five of seven infants required treatment with morphine to manage NAS. Non-parametric analysis of genetic material currently shows trends towards infants whose mothers carried the genetic variants (V) for IL-1B -31 and IL-1B -511 requiring higher maximum doses and more total morphine over a four week post natal follow up period to manage NAS, compared with infants whose mothers carried only wild-type (WT) alleles (-31 and -511: median maximum dose morphine: WT= 0.2; V= 0.24 mg; median total morphine: WT= 22.7; V= 29.1 mg).
Conclusions: By finding an association between immune genetic variability and NAS occurrence and severity, genetic markers could be used as a predictive tool to pre-determine the occurrence and severity of NAS, leading to better management of the infant by potentially minimising the amount of morphine administered to control NAS and reducing infant hospital stays. Data collection and analysis for this project continues.
Financial Support: Division of Health Sciences, University of South Australia Research Development Grant

219

TREATING PREGNANT FRENCH POLYDRUG-ABUSING WOMEN WHO FAIL TO COMPLY WITH SUBSTITUTION TREATMENTS: IS IT COST/EFFICIENT?

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Aims: To discuss criteria for success in treating the focused group.
To describe what can be expected for pregnancy, delivery and newborn child.
To explain and compare what happens to children in the first weeks after discharge from the mother&child healthcare unit.
Methods: Retrospective biographical records of 5 cases between 1996 and 2011 are analysed. Women were all included in substitution programs during pregnancy, either sublingual buprenorphine or oral methadone. They all lived in the same area in Northern Paris. None of them showed more than one negative urinalysis during the whole duration of their pregnancies. All of them showed one or more patterns of severity at inclusion: chronic psychosis, poor housing, no legal income, no contact with their own family or separation from the future child's father. A comparison is made with a former study in a similar population during the period just before the one when substitution treatments were made available in France.
Results: Social context seemed rather poor. Polydrug abuse appeared as the most frequent way of drug consumption for 8 mothers of 10. They showed a frequent abuse of opiate, cocaine, alcohol and/or benzodiazepines. Only 3 of them were mainly injectors Precise follow-up data is available
for the first 6 months for all infants. No deaths, HIV or HCV infection in children were recorded. In a group of babies who were legally fostered, 2 lived with both parents and 8 with only one of them. Focusing on scholar status, the eldest of the group (aged 18 in 2011) finished school with a low level degree. The youngest was not old enough (aged 6 months); 2 were not documented and 6 of 10 were pupils in regular schools (only one was 2 years late). Considering health status of mothers, the results seem very poor: one abruptly died when her child was 13, only 3 of 10 needed no medical care combined with substitution and 6 needed psychiatry and/or infectious diseases medicine backing.
Conclusions: It seems that, contrary to our initial belief, treating these poorly complying women as soon as possible during a confirmed pregnancy could benefit not so much mothers in their harmful way of living, but more likely their babies and finally the whole community and society.
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220

WITHDRAWN.

221

SUBSTANCE USE PATTERNS AS AN ASSOCIATED RISK FACTOR FOR HIGH RISK SEXUAL BEHAVIOR IN ADOLESCENTS.

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Aims: Engaging in various high risk behaviors during adolescence has been demonstrated consistently (Biglan et al., 1988). Two prominent behaviors that have been linked to one another include substance use and high risk sexual behavior (Cavasoz-Rheg et al., 2010; Poulin et al., 2001).
For the current study, we examined the relationship between adolescent substance use patterns as related to adolescent reported sexual activity.
Methods: The study utilized the data obtained by the Center for Disease Control (CDC) 2009 Youth Risk Behavior Surveillance System (YRBSS), sampling 196 schools, 9th-12th grades (N = 16,410).
Results: Regression analyses revealed, as hypothesized, that ever having utilized the following substances: cigarettes (B = 1.321,), alcohol (B = 1.097) marijuana (B = 1.537), cocaine (B = 2.108), glue (B = 1.023), heroin (B = 2.570), methamphetamines (B = 2.182), ecstasy (B = 2.120), steroids (B = 1.597), and intravenous drugs (B = 2.493) significantly predicted ($p < .001$) number of lifetime partners, respectively.
Further analyses revealed that use of drugs before engaging in sexual intercourse and lower contraceptive use was significantly predicted ($p < .001$) by use of cigarettes (B = 2.342, OR = 10.399; B =1.322, OR = 3.752), alcohol (B = 2.650, OR = 14.155; B = 1.495, 4.459), marijuana (B = 2.290, OR = 9.876; B = 1.395, OR = 4.034), cocaine (B = 2.076, OR = 7.971; B = 1.300, OR = 3.670), glue (B = 1.420, OR = 4.138; B = 1.001, OR = 2.720), heroin (B = 2.661, OR = 14.320; B = 1.797, OR = 6.033), methamphetamines (B = 2.202, OR = 9.042; B = 1.395, 4.036), ecstasy (B = 2.207, OR = 9.088; B = 1.418, OR = 4.129), steroids (B = 1.966, OR = 7.141; B = 1.370, OR = 4.129), and intravenous drugs (B= 2.650, OR = 14.155; B = 1.998, OR = 7.374), respectively.
Conclusions: These findings suggests that adolescents who are engaging in substance use are at increased odds of engaging in high risk sexual behavior. Future research efforts targeting the prevention and cessation of substance use, may also seek to address risky sexual behavior in adolescents.
Financial Support: No Financial Support

222

PERSONALITY AND ADDICTIVE BEHAVIORS: AN INTEGRATIVE REVIEW OF THE LITERATURE.

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Aims: 1) This review applies a neuropsychological framework to integrating nearly five decades of research on personality and addiction including:
a) The structure of an addictive personality
b) The causal function of traits (e.g. impulsivity, novelty-seeking, etc).
2) This review:
a) Integrates theories and empirical outcomes across diverse perspectives and instruments to draw overall conclusions useful to informing the design and direction of future research.
b) Elucidates how normal personality informs addiction-specific risk(s).
c) Demonstrates the importance of exploring addictive behaviors in concert with normal personality in order to identify the protective factors necessary to designing strengths-based prevention and treatment approaches.
Methods: Our transdisciplinary approach incorporates biological, behavioral and social science literature to organize theoretical, qualitative, and empirical insights on personality and addiction via:
1) The actions of addictive substances and processes on cholinergic, dopaminergic, adrenergic, and/or serotonergic receptors.
2) The relationship between acetylcholine, dopamine, epinephrine, and serotonin and four basic states: affective pleasure, physical pleasure, affective pain, and physical pain.
3) The function of those four states as common processes threading personality type and trait articulations across the theories of normal personality from which hypothesized personality-addiction synergies are drawn.
Conclusions: Historically personality-addiction research has focused primarily on differences between substance abusers and non-abusers however, as the field broadens to include non-substance related addictive processes, such as shopping and Internet use, it is becoming clear that those at risk of developing an addiction may represent the majority rather than the minority. Thus, explorations of the extent to which specific types of addiction risk may be endemic to certain normal healthy personalities across the range of individual difference is needed to inform broader prevention efforts and treatment approaches that are more precise.
Financial Support: N/A

223

RISK FACTORS OF COMORBID SUBSTANCE USE AND GAMBLING AMONG A COLLEGE SAMPLE.

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Aims: Studies have indicated high rates of alcohol and other drug use on college campuses (Johnson et al., 2008), as well as explored the prevalence of gambling among college students (LaBrie et al., 2003). However, less is known about comorbidity between disordered gambling and AOD disorders, and the unique factors related to comorbidity among college students. The purpose of this study was to examine rates of co-morbid disordered gambling (at-risk or probable pathological gambling) and AOD disorders (probable abuse or dependence) among a sample of college students who completed an online screening survey for a larger study of gambling and substance co-morbidity. The current study explored how factors of gender, Greek membership, and GPA related to comorbidity in students who screened into the study compared to those who did not screen in.
Methods: Screening criteria included receiving a score of 11 or higher for alcohol or a score of 4 or higher on any other drug (threshold for probable abuse) as measured by the ASSIST, as well as a score of 3 or more on the South Oaks Gambling Screen (at-risk gambling criterion) and 1 or more current symptoms endorsed on the Gambling Problem Index (N=1930; 57.5% female; mean age 19.7 years).
Results: 5.9% of the sample screened in based on the criteria. Results suggested fraternity members were significantly more likely to screen into the study (24.6% of students screened in as fraternity members compared to 7.5% of students who did not screen in). Similarly, men were more likely to screen in (61.4% of students who met inclusion criteria were male compared to 37.8% of those who did not meet criteria). Interestingly, GPA was not associated with screening into the study.
Conclusions: This is consistent with previous research suggesting males and fraternity members more often exhibit these behaviors, and extends this research by verifying similar rates when these behaviors are comorbid. These results indicate the importance of addressing co-morbidity among risk behaviors, and are useful for intervention efforts targeting college students at high risk.
Financial Support: Project Chance R01 DA025051

224

PERSISTENT ATTENUATION OF COCAINE-REINFORCED BEHAVIOR: EFFECTS ON NON-DRUG REWARD AND SEPARATING CHOLINESTERASE INHIBITION AND DRUG SELF-ADMINISTRATION.

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Aims: We recently observed that pretreatment with certain cholinesterase inhibitors can produce large and long-lasting reductions in drug-motivated behavior in some rats, described as persistent attenuation (PA). This study determined whether cholinesterase inhibition needed to be concurrent with access to cocaine in order to produce PA. In addition, we evaluated reacquisition of food reinforcement in rats that exhibited PA.
Methods: Rats trained to self-administer intravenous cocaine under FR-5 (reward after 5 lever-presses), and were then pretreated with either vehicle or 10 mg/kg-day of tacrine, as they remained in home cages over a four-day period. Reacquisition of cocaine-reinforced behavior was then evaluated. In additional animals pretreated with tacrine under conditions that produced PA, food-reinforced responding was reacquired as response requirement was gradually increased to FR-15.
Results: There was a trend for decreased self-administration in tacrine-treated rats over the initial two days of re-exposure to cocaine self-administration. Nonetheless, neither individual nor group data resembled the large and persistent decreases in cocaine self-administration seen when tacrine was administered immediately prior to self-administration sessions. As their schedule for food reinforcement was advanced, rats exhibiting PA received fewer food pellets during exposure to FR-5, but did not differ under most conditions.
Conclusions: These studies show that cholinesterase inhibition must occur as rats are self-administering cocaine to produce PA. It is possible that augmenting acetylcholine transmission increases the aversive properties of cocaine. A conditioned aversion occurring in some rats could explain the long-lasting effects of PA. In addition, PA of cocaine-reinforced behavior had small but limited effects on behavior motivated by a non-drug reinforcer. Unlike effects of PA on cocaine reward, changes on food-reinforced responding do not persist over time.
Financial Support: Supported by a grant to KG from the Department of Veterans Affairs.

225

THE WOMEN'S RECOVERY GROUP STUDY: PARTICIPANT CHARACTERISTICS AND SAMPLE GENERALIZABILITY.

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Aims: The Women's Recovery Group Study is a two-site, randomized controlled trial comparing single-gender (WRG; Women's Recovery Group) to mixed-gender group therapy (GDC; Group Drug Counseling). To provide a heterogeneous and clinically relevant sample, the study was conducted in two outpatient clinics: an academic teaching hospital and a community treatment program. The inclusion/exclusion criteria were designed to maximize generalizability. These analyses describe the study sample in relation to substance abuse treatment-seeking populations.
Methods: Participants 18 years or older were included if they were substance dependent and had used substances at least once within the past 60 days. 158 participants (100 women, 58 men) were enrolled. Women were randomized to WRG (n = 52) or GDC (n = 48), and 58 men participated in GDC.
Results: Participants were predominately white (94%) and non-Hispanic (99%), with a mean age of 47 years. Our sample was highly educated, with 75% reporting some college or more. At enrollment, the majority of participants (89%) were alcohol dependent, and the most common drug diagnoses were cocaine (18%) and opioid (17%) dependence. Overall, 73% of participants had a current Axis I diagnosis and 15% met criteria for an Axis II disorder. Co-occurring major depressive disorder (56%), GAD (20%), and PTSD (18%) were the most common Axis I disorders. Site differences were noted. Participants recruited to the teaching hospital had more years of education ($\chi 2$ =40.8, df=5, p<.001) and were more likely to be employed ($\chi 2$ =26.7, df=7, p<.001), and alcohol dependent ($\chi 2$ =5.0, df=1, p<.05).
Conclusions: The high co-occurrence of psychiatric disorders and prevalence of specific substance use diagnoses in this sample is consistent with treatment-seeking populations in the community, but these results indicate that site differences may contribute to variability in clinical trials populations.
Financial Support: Supported by 2R01DA15434 (NIDA)

226

MU- AND KAPPA-RECEPTOR SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) ARE ASSOCIATED WITH OPIOID USE PHENOTYPES IN HEROIN-DEPENDENT VOLUNTEERS.

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Aims: In addition to the role of mu receptors in opioid dependence, kappa receptors may also influence dependence behaviors. This study sought to determine whether SNPs in genes that encode these receptors (OPRM1 and OPRK1) are related to opioid-use phenotypes.
Methods: Daily heroin users (N=126) were genotyped (Illumina Golden Gate) and interviewed about past-month heroin-acquisitive behaviors. Micro-phenotypes (e.g. time, amount, frequency of heroin purchases) were input to principal component analysis to extract macro-phenotypes (factor scores reflecting behavior patterns) that were saved for regression analyses. Some of these volunteers underwent urine testing during outpatient buprenorphine (BUP) induction to measure opioid abstinence (N=50) and BUP dose taper with contingency management to measure opioid relapse (N=27).
Results: Stepwise multiple regressions – controlling race (blacks vs. whites), linkage disequilibrium (among SNPs that correlated with phenotypes), heroin use duration, and several functional non-opioid SNPs – found that OPRK1 rs3802280 and OPRM1 rs660756 and rs179971 (A118G functional SNP) significantly (p< .05) predicted factor 1 "income elasticity" scores (more income and daily use; r2= .131), whereas race (white) and BDNF rs6265 (66Met allele) predicted higher factor 2 "impulsive purchasing" scores (more weekly purchases, lower purchase times/amounts; r2= .166). OPRK1 rs6989250 predicted percent opioid free urines during BUP induction (r2= .165), whereas OPRM1 rs10485058 predicted days to relapse (r2= .209).
Conclusions: OPRK1 and OPRM1 explained substantial variance in several past-month and prospective opioid use phenotypes, whereas a BDNF functional SNP explained variance in impulsive purchasing. These findings provide a basis for understanding individual differences in baseline heroin use and potential treatment response.
Financial Support: NIH R01 DA015462 and Joe Young, Sr. Funds (State of Michigan) supported this research.

227

FINDINGS FROM A PILOT STUDY OF MEDICAL MARIJUANA USERS IN LOS ANGELES COUNTY.

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Aims: Medical marijuana (MM) dispensaries have proliferated in Los Angeles County, yet little information exists on individuals that use these dispensaries. The aim of this study was to obtain preliminary data on the characteristics of MM users.
Methods: Focus groups were conducted with 30 individuals who were recruited from MM dispensaries in Los Angeles County from February – May 2011. A majority of the sample (70%) was male; they were on average 38 years old; 60% were white, 30% African American, and 10% Hispanic. Most had some college education and 57% were employed. They obtained their recommendation for MM about 2½ years ago (avg = 29 mos).
Results: Most (83%) used MM primarily for a physical health problem; 17% used soley for a mental health problem. Most (70%) used MM daily, usually with others. The key themes derived from the focus groups are: (1) Nearly all had a long history of marijuana use, usually initiating use in adolescence. (2) Primary reasons for MM use were: sleep problems, anxiety, depression, or chronic pain. Many reported serious chronic health problems related to an accident or illness. (3) Participants preferred obtaining marijuana from legal dispensaries as compared to buying marijuana "on the streets," where they have no control over the quality of the product. (4) Dispensaries provide a respite from the social stigma associated with marijuana users. (5) Dispensaries are highly variable in their atmosphere. Consumers appreciated the many strains and forms of MM available, as well as the social aspects of the dispensaries. (6) Some participants articulated concerns about adolescents having access to MM, whereas others saw no problems related to its greater availability and use.
Conclusions: MM users in Los Angeles have diverse reasons for and patterns of use. Participants valued the dispensaries, although some acknowledged potential problems related to youth access. A future epidemiological survey of MM users in Los Angeles County is planned.
Financial Support: Supported by Los Angeles County Department of Public Health, Substance Abuse Prevention and Control Program (Contract PH-000179)

228

ESCALATING EXPOSURE TO METHAMPHETAMINE PRODUCES PERSISTENT ALTERATIONS IN DOPAMINERGIC BIOMARKERS AND INHIBITORY CONTROL IN MONKEYS.

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Aims: Alterations to the dopamine system are a neurochemical consequence of drug abuse, and it has been argued that inhibitory control deficits present in stimulant-dependent individuals are a biobehavioral manifestation of disruptions to this system. Few studies have combined neurochemical and behavioral measures to test this hypothesis directly. The current study was conducted to examine the effects of an escalating dose regimen of methamphetamine (MA) on dopaminergic markers using positron emission tomography (PET) and to relate these with measures of inhibitory control before and after MA exposure.
Methods: Fourteen male vervet monkeys were trained to acquire and reverse 3-choice visual discriminations. Subjects received PET scans to assess D2-like receptor and dopamine transporter (DAT) availability. They then were exposed to MA (or saline) on a dosing regimen in which treatments escalated in both dose and frequency. After cessation of MA exposure, two additional PET scans were conducted and task performance measured. Sensitivity of individuals to positive and negative feedback was calculated on a trial-by-trial basis.
Results: MA exposure significantly reduced D2-like receptor and DAT availability and produced behavioral deficits that were specific to the reversal of a stimulus-outcome association. Further, individual changes in D2-like receptor availability were correlated with the change in positive, and not negative, feedback sensitivity.
Conclusions: These data provide evidence that escalating-dose exposure to MA results in dopaminergic alterations similar to those reported in human MA users. Further, disruption of the D2-like receptor system specifically altered positive feedback sensitivity, suggesting that alterations to positive-feedback sensitivity that arise via dysfunction of the D2-like receptor system may be the mechanism by which inhibitory control deficits emerge in stimulant-dependent populations.
Financial Support: P20-DA022539, T32-DA024635 and F31-DA028812

229

PATIENT PREFERENCES FOR SHORTER TREATMENT DURATION DO NOT PREDICT EARLY DROPOUT FROM BUPRENORPHINE TREATMENT.

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Aims: To examine whether preferences for shorter treatment duration are related to early dropout in buprenorphine patients.
Methods: This study used data collected as part of a clinical trial of counseling level with 300 African Americans entering buprenorphine treatment in Baltimore, MD (USA). Preferences for treatment duration were assessed at baseline by asking participants whether they want to be in buprenorphine treatment 6 months from now and how long they intend to stay in buprenorphine treatment. Treatment retention at 6 months was determined through program records (original program) or self-report (buprenorphine treatment at a different provider). Predictors of treatment dropout were examined using logistic regression, and included gender, age, program site, baseline cocaine use, assigned counseling condition, and patient preference for short treatment duration with buprenorphine.
Results: Within 6 months, 36% of participants had discontinued buprenorphine treatment. Participants' preferences for short treatment duration were not significantly associated with dropout (OR=1.3; p=.38). Of the predictors examined, baseline cocaine use was the only variable significantly associated with dropout, such that patients who provided a cocaine-positive urine sample at baseline were more likely to have discontinued treatment by 6 months (OR=2.1, p<.01).
Conclusions: Participants' stated preferences for short treatment duration did not adversely affect their ability to remain in buprenorphine treatment through the first 6 months. Opioid-dependent individuals who also use cocaine may be at higher risk for premature discontinuation of buprenorphine treatment.
Financial Support: NIDA 1RC1 DA 028407

230

IMPACT OF PARTICIPATION IN DUAL-FOCUS 12-STEP GROUPS FOR PEOPLE WITH CO-OCCURRING DISORDERS.

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Aims: To identify experiences shared by participants who attend 12-step groups for persons with co-occurring disorders.
Methods: Participants at psychiatric/dual diagnosis clinics in New York City and Michigan who were attending a dual-focus 12-step support group for persons with co-occurring mental illness and substance abuse (Double Trouble in Recovery; DTR) participated in 2 focus groups (N=25) to discuss how DTR differed from single-focus groups such as AA/NA and the impact of DTR participation on their lives. All DTR groups were facilitated by a person in recovery. In NYC DTR was offered to patients attending a mental health clinic and in MI it was offered as aftercare.
Results: Themes shared by focus group participants included: affiliation (sense of community); support for sustaining "clean time;" knowledge and insight about the relationship between mental illness and substance use problems; appreciation that psychiatric medications/symptoms could be discussed and that medication adherence was supported. Spirituality and skill building for relapse prevention were cited by the NYC participants; MI participants cited reduced hospitalizations and access to needed support in the absence of insurance.
Conclusions: Emergence of psychiatric themes, especially medication adherence is noteworthy, because it underscores the importance of having the opportunity to talk about symptoms and medication, topics that are not typically discussed in single-focus groups. Differences between the NYC and MI DTR groups may reflect the different characteristics of the membership and availability of medical insurance.
Financial Support: NIDA Grant 5R01DA023119-04

231

DIFFERENTIAL EFFECTS OF OXAZEPAM AND ALPRAZALAM ON METHAMPHETAMINE CONDITIONED PLACE PREFERENCE IN RATS.

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Aims: Polydrug abuse has been on the rise in recent years. Specifically, benzodiazepines are often combined with psychostimulants, such as methamphetamine (METH), to achieve a greater high. Research has shown that benzodiazepines have different abuse potentials. Alprazolam (ALP) is one of the most widely abused benzodiazepines and is highly preferred by drug abusers. Oxazepam (OX) has a far lower abuse potential. In this experiment we studied the reward potential of these two benzodiazepines alone and in combination with METH to simulate polydrug abuse.
Methods: On the Friday prior to conditioning, adult male Wistar rats were placed into the conditioned place preference (CPP) apparatus for 30 min to establish their baseline preferences. For conditioning, the rats were randomly assigned to one of 12 groups of 8 rats each: vehicle (VEH) 1 ml/kg; METH 0.5 or 1.0 mg/kg; ALP 1 mg/kg; OX 10 or 20 mg/kg; METH 0.5 & ALP 1; METH 1.0 & ALP 1; METH 0.5 & OX 10; METH 1.0 & OX 10; METH 0.5 & OX 20; or METH 1.0 & OX 20. The rats were randomly assigned to a drug-paired compartment side. Conditioning began the following Monday and continued for 4 days. During this time, rats were injected with either VEH or drug, ip, on alternate days 30 min prior to being placed in the chamber. One compartment was paired with VEH and the other with drug for 30 min on alternate days. On the Friday following conditioning, the rats were placed into the middle of the apparatus and allowed free access to both compartments for 30 min. The time spent on each side was recorded.
Results: METH showed a dose dependent CPP (16% and 45% increase) as expected. ALP alone increased by 23%, while ALP with low dose METH increased 24% and ALP with high dose METH increased 23%. In contrast, low dose OX decreased by 10% while high dose OX increased by only 9%. Also in contrast, OX in combination with METH either showed no change or decreased by 3, 10 or 15%.
Conclusions: METH and ALP were rewarding by themselves and in combination with each other. OX attenuated the increase in METH CPP.
Financial Support: LSUHSC-S

232

LISDEXAMFETAMINE AND D-AMFETAMINE: IMPORTANT DIFFERENCES FOR THE RELATIONSHIPS BETWEEN EXTRACELLULAR STRIATAL DOPAMINE, LOCOMOTOR ACTIVITY AND PLASMA DRUG CONCENTRATIONS IN FREELY MOVING RATS REVEALED BY HYSTERESIS ANALYSIS.

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Aims: Lisdexamfetamine dimesylate (LDX; Vyvanse®) is a prodrug of d-amfetamine (d-AMF) that is approved for the treatment of ADHD.
Methods: The Culex Bambino automatically collects intracerebral microdialysates, intravenous blood samples and simultaneously measures locomotor behaviour in freely moving rats. The effects of immediate release (IR) d-AMF SO4 (d-AMF base = 1.5mg/kg ip) and LDX (d-AMF base = 1.5 and 5.0mg/kg ip) on extracellular dopamine levels ([DA]) in the striatum, locomotor activity and plasma d-AMF concentrations ([d-AMF]) were compared over 8hr.
Results: LDX dose-dependently increased striatal [DA] ≤300min. The effect of LDX (1.5mg/kg) on [DA] was gradual and sustained with maximum increase of 854% @ 75min. IR-AMF (1.5mg/kg) evoked a more rapid and substantial increase of [DA] (1291% @ 30min). LDX (1.5mg/kg) produced a small increase in locomotor activity, maximal between 90-120min returning to pre-drug levels by 195min. IR-AMF (1.5mg/kg) evoked much more locomotor activity with an earlier peak (30min) and shorter duration of effect. Three hysteresis analyses were performed. The most interesting and important difference came from the relationship between the changes in [DA] over time versus locomotor activity. The hysteresis was anticlockwise for LDX, but clockwise for IR-AMF (P<0.05). Thus, with LDX the rats were less prone to activation as extracellular [DA] was rising, but reduced activation was maintained for longer when [DA] declined; the opposite was found for IR-AMF.
Conclusions: The findings are clinically important because subcortical DA is implicated in efficacy and side-effects of ADHD drugs. The sustained increase in [DA] and reduced locomotor activation predict that LDX will have an enlarged "therapeutic window" compared with IR-AMF. Moreover, the maintenance of LDX's pharmacodynamic effect when CNS [DA] was declining indicates the unusual PK of LDX optimises the utilisation of its active metabolite, d-AMF
Financial Support: Shire Pharmaceuticals Ltd

233

IMPACT OF PHONE COUNSELING ON DRUG USE AND READINESS TO CHANGE IN ORGAN TRANSPLANT PATIENTS.

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Aims: Six months of abstinence is required before transplantation. Many patients are too ill to attend drug treatment and die before meeting this criterion. TAP assessed the efficacy of a phone-based MI/CBT intervention to interrupt substance use and enhance motivation to change drug use.
Methods: Thirty-six patients were randomized to TAP (12 weeks of MI/CBT phone counseling) or TAU (usual care); assessments were conducted at BL and during wks 12 & 24.
Results: Patients were 47 yrs old and 84% male. Half (49%) were Caucasian, 32% Hispanic, 18% African American and 15% Asian (remainder mixed). On CIDI, 49% had ETOH dependence, 65% drug dependence, 24% MAD, 22% each GAD and specific phobia,16% each panic disorder and 16% social phobia, 11% OCD and 3% agoraphobia (psychosis excluded). Signficant time effects were found for the Face Valid Alcohol ($p=.01$) and Face Valid Drug Scales ($p<.01$)of SASSI,indicating decreased substance use and problems over time. On URICA, an interaction was found for Pre-contemplation ($p<.01$); TAP patients became more aware of their addiction problems and more receptive to treatment, but TAU patients showed increased denial and treatment resistance. Time effects were found for Action ($p=.02$)and Maintenance ($p<.001$)suggest "compliance" for TAU patients in the absence of problem acceptance. Time effects also were found on the ASI ETOH ($p=.05$) and ASI Drug Scales($p<.01$). HABIT Drug scores decreased over time ($p=.04$), but no decreases were found for Tobacco, ETOH or Rx drugs. Both time ($p=.05$). An interaction ($p=.06$) was found for Stress/Coping; while TAU patients reported severe stress throughout the trial, TAP patients' scores decreased from severe to moderate (Week 12), before rebounding to severe (Week 24).
Conclusions: Advancing illness and surgery turn-down likely resulted in decreased substance use for both groups. Only TAP patients evidenced increased problem awareness and readiness to change. They also showed decreased stress and improved coping but this effect deteriorated somewhat from wk 12-24, suggesting the need for ongoing support during the 6 months pre-operative waiting period.
Financial Support: NIDA R01 DA015772

234

HOMELESS WOMEN VETERANS, SUBSTANCE ABUSE, TRAUMA, AND PSYCHOSOCIAL SERVICES.

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Aims: Women veterans are up to four times more likely to be homeless than non-veteran women. This population faces numerous challenges that are magnified by their unique experiences as women veterans. This paper provides person-centered perspectives on the impact of substance abuse and trauma histories on utilization of psychosocial services.
Methods: Three focus groups were held in Los Angeles, CA, with a total of 29 homeless women veterans. Data was analyzed using the constant comparison method.
Results: Participants represented a diversity of current age (mean age, 48 years) and age at post-military entry into homelessness (mean, 36 years). One quarter of participants reported using alcohol 2 or more times per week in the past year, but no women reported having alcohol or drug problems in the past 30 days. Most women had a history of at least one type of trauma, pre-, during, and/or post-military service. Women described three primary barriers to psychosocial services: lack of information about services, limited access to services, and lack of coordination across services. A sense of isolation and abandonment permeated women's descriptions of barriers to services. Homeless women veterans' access to services was often limited by restrictive entry criteria, e.g., a substance abuse history, or by lack of gender-appropriate care, e.g., male-dominated treatment programs.
Conclusions: Although homeless women veterans face many similar circumstances and barriers as non-veteran homeless women, women veterans potentially face additional challenges of trauma exposure during military service, post-military readjustment issues, and few services specific to women veterans. A minority of women in this study had current substance abuse; women found that they often could not access services without current substance use. Understanding homeless women veterans' service needs and experiences is critical to the development of relevant and appropriate services.
Financial Support: DHHS Office on Women's Health & Department of Veterans Affairs, Women Veterans Health Strategic Healthcare Group

235

ASSOCIATIONS OF WHITE MATTER TRACT INTEGRITY WITH IMPULSIVITY AND BEHAVIORAL ACTIVATION SYSTEM DIMENSIONS IN PRENATALLY COCAINE-EXPOSED ADOLESCENTS.

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Aims: Adolescents prenatally exposed to cocaine (PCE) have greater risks of abusing substances than adolescents who were not (NCE). Differential associations of impulsivity and behavioral activation system (BAS) and behavioral inhibition system (BIS) sensitivity with white matter (WM) microstructure may underlie this risk. This research was conducted to determine whether WM differences exist in PCE and NCE adolescents, and whether WM integrity differentially associates with impulsivity and BIS and BAS sensitivity in these groups.
Methods: Participants were 43 PCE and 20 NCE male and female adolescents who were followed from birth. We acquired Diffusion Tensor Imaging (DTI) data with a 3.0T Siemens Trio scanner and self-reported data on impulsivity and BIS and BAS sensitivity with the Barratt Impulsiveness Scale, version 11 (BIS-11) and BIS/BAS scales.
Results: PCE and NCE groups did not differ significantly on any of the constructs or DTI parameters. There was a significant difference in correlations between scores on the BAS Drive subscale and $\lambda 1$ in a cluster at the corona radiata (CR) and in bilateral clusters at the superior longitudinal fasciculus (SLF), with the correlations occurring in the NCE group only. When PCE and NCE participants were combined together as one group, significant positive correlations were observed between scores on the BIS-11 Nonplanning subscale and $\lambda\perp$ in clusters across the body of the corpus callosum (CC) and mean diffusivity in a cluster involving the left cerebellum.
Conclusions: PCE may disrupt typical associations of BAS Drive with WM integrity in the CR and SLF in adolescents. The extent to which this may contribute to substance abuse risk should be examined.
Financial Support: NIH grants P50 DA016556, UL1-DE19586, RL1 AA017539, R01 DA006025, R01 DA017863 and K05 DA020091, the Office of Research on Women's Health, and the NIH Roadmap for Medical Research/Common Fund.

236

GENDER COMPARISONS OF DRUG ABUSE TREATMENT OUTCOMES AMONG AAPI.

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Aims: Extant literature has demonstrated gender differences in patterns of drug use and treatment outcomes. However, few studies have focused on Asian Americans and Pacific Islanders (AAPI), despite indications of increased AAPI treatment admissions in recent years. This prospective longitudinal study aims to examine gender differences in substance abuse treatment outcomes among AAPI patients. We hypothesized that both AAPI women and men would respond to treatment with reduced drug use and related problems. As reflected in prior literature, we expected that AAPI men would have more criminal involvement, and AAPI women would have greater mental health problems.
Methods: The study included 567 (177 women, 390 men) AAPI patients drawn from CALTOP (32 community-based programs in 13 California counties) and the TSI project (36 treatment sites in 5 California counties). Baseline assessments utilized the Addiction Severity Index (ASI). Subsets of patients were assessed at 3, 9 (CALTOP), and 12 months (TSI).
Results: Significant gender differences were observed at baseline: Less women than men were employed (23% vs 47%), unmarried (28% vs 53%), living independently (68 % vs 74%), while more likely to live with alcohol users (13% vs 5%) and drug addicts (17% vs 7%). Methamphetamine was the primary drug for both women and men (52% vs 47%), followed by alcohol (9% vs 19%) and heroin (18% vs 11%). AAPI women reported less severe legal problems at intake. After controlling for intake differences, improvements at follow-up were observed for both genders in all ASI scales, except in psychiatric severity for women. Nevertheless, AAPI women reported greater satisfaction with treatment counselors at the 3 month follow-up survey. At the follow-up, the only gender difference was in drug use. Compared to AAPI men, AAPI women demonstrated a significantly greater improvement in drug problem ($\Delta ASI=0.07$, $p<0.05$).
Conclusions: Gender differences revealed in this study suggest placing greater treatment focus on psychiatric problems among AAPI women and drug use problems among AAPI men.
Financial Support: NIDA P30DA016383, & K05DA017648 (PI: Hser)

237

CHRONIC NALTREXONE MODULATES MARIJUANA'S REINFORCING, SUBJECTIVE AND CARDIOVASCULAR EFFECTS.

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Aims: Acute administration of the opioid antagonist, naltrexone (NTX: 12.5-100 mg), increases the intoxicating effects of marijuana in daily marijuana smokers (Cooper and Haney, 2010). Given that chronic and acute medication administration may produce opposite effects on drug intoxication, this placebo-controlled study assessed the effects of active and inactive marijuana before, during and after chronic NTX administration.
Methods: Non-treatment-seeking, marijuana smokers were randomized to receive NTX (50 mg) or placebo (0 mg) for 16 consecutive days. Each participant completed 10 laboratory sessions over 3-4 weeks: before NTX administration, after a single administration, after 1 and 2 weeks of daily NTX administration, and 1 week after termination of NTX administration. At each timepoint, the reinforcing, subjective, psychomotor, and cardiovascular effects of active (5.5% THC) and inactive (0.0%) marijuana were assessed.
Results: Data collection is ongoing. Forty-three non-treatment seeking, daily marijuana smokers have completed the study to date (n=22 placebo; n=21 NTX). NTX alone produced few effects. Marijuana (5.5% THC) alone significantly increased heart rate, subjective ratings of intoxication and self-administration compared to inactive marijuana (0.0%). Relative to the placebo group: MJ self-administration was reduced after 1 week ($p < 0.05$) and 2 weeks of NTX administration ($p < 0.09$). NTX also tended to decrease some of MJ's subjective effects (e.g., ratings of Good Effect) after 1 week ($p < 0.06$) and 2 weeks ($p < 0.003$) of administration, and this effect persisted after termination of NTX administration ($p < 0.006$). Ratings of marijuana high and craving were not significantly affected by NTX.
Conclusions: These preliminary findings show that daily administration of naltrexone decreased marijuana self-administration and certain ratings of intoxication, suggesting that chronic opioid antagonism may be a potentially useful strategy for the treatment of marijuana dependence.
Financial Support: Supported by DA19239 and DA09236.

238

CORTICAL EXCITABILITY IN CURRENT COCAINE USERS: A TRANSCRANIAL MAGNETIC STIMULATION STUDY INVESTIGATING GLUTAMATERGIC AND GABAERGIC PROCESSES.

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Aims: While the majority of the research on the effects of chronic cocaine on the brain has targeted subcortical areas, emerging evidence suggests that there are fundamental alterations in cortical excitability in cocaine users. Prior imaging and electrophysiological studies have demonstrated that current cocaine users have elevated cortical activity and a loss of typical cortical laterality when doing a basic motor task. It is unclear however if the elevated cortical activity observed in cocaine users is due to an increase in excitability or a decrease in inhibition.
Methods: In the present study, transcranial magnetic stimulation was used to assess multiple aspects of cortical tone in current cocaine users, abstainers, and matched controls. Users reported time of last use between 12-72 hours prior to the study which was verified with urinanalysis. Cortical tone was investivated with a suite of TMS measures: motor threshold, motor recruitment curve, paired pulse inhibition, facilitation, and cortical silent period.
Results: Consistent with prior stidies the abstainers had higher motor thresholds than the healthy controls. This was also true for active users. Additionally, this study reveals that current cocaine users have selective impairment in measures of cortical inhibition - specifically, shorter cortical silent periods (sensative to GABAb) and less paired pulse inhibition (sensative to GABAa). There was no significant effect of hemisphere on any of these measures, suggesting that this finding generalizes to multiple cortical brain areas.
Conclusions: Considered together these data suggest that the elevated functional activity observed in the left and right motor cortex of cocaine users is associated predominantly with GABAergic processes rather than glutamatergic dysregulation. Although this is a preliminary study, these data may provide insight into the relative value of GABAergic and glutamatergic agents as a treatment for these individuals.
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239

THE RELATIONSHIP BETWEEN EMOTIONAL AND FINANCIAL SUPPORT AND SUBSTANCE USE: EXAMINING IMMEDIATE AND LONG-TERM EFFECTS.

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Aims: Research has shown that social support can play a protective role in helping individuals abstain from illicit substance use (ISU). However, few studies have examined whether the positive effects of support persist over time or are only significant in the present. This study examines both emotional and financial support and their effects on current ISU, as well as ISU at six month follow-up.
Methods: Data from 446 African American females were collected during Waves 1, 2, and 3 of the Black Women in the Study of Epidemics protocol. Women were recruited from prison, probation offices, and the community. Logistic regression was used to examine the relationship between support and any past six month ISU at Wave 2. Then, Wave 2 measures of support were used to predict any ISU at Wave 3. Wave 1 substance use and criminal justice status were included as control variables in both models.
Results: Women with more emotional support were less likely at the $p<.05$ level to report any ISU at Wave 2 (O.R.=.80), however this relationship was not significant at Wave 3. Women who reported receiving financial support from a significant other (O.R.=1.86) or friend (O.R.=2.62) were significantly more likely to report any ISU at Wave 2 ($p<.05$). However, at Wave 3, only financial support from a friend remained significant (O.R.=2.25). The control variables, substance user and criminal justice status, were significant at both waves ($p<.01$).
Conclusions: Findings demonstrate that emotional support is significantly related to abstaining from substance use in the present, but this protective effect deteriorates over time. Additionally, the finding that receiving financial support from a friend or significant other is associated with a greater likelihood of ISU indicates that the effects of support are not necessarily positive. These findings emphasize the complex nature of support; It not only has different dimensions (emotional and financial), but can also have negative and positive effects depending on the nature and source of the support being offered.
Financial Support: Research supported by the National Institute on Drug Abuse (R01-DA22967; PI: Carrie Oser).

240

COGNITIVE PERFORMANCE PREDICTED BY LATENT CLASSES OF DRUG USE.

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Aims: The relationship between substance use and cognitive deficits is complex and requires innovative methods to enhance understanding. Although latent class analysis (LCA) has been used in increasing frequency, the present study is the first of which we are aware to use LCA to examine associations of drug use patterns with cognitive performance. More extreme drug use patterns (e.g., injection drug use) are expected to be associated with poorer executive functioning.
Methods: Cocaine/heroin users (N=552) completed urinalysis samples, questionnaires, and cognitive measures, including verbal IQ, as measured by the Shipley Institute of Living Scale, and executive functioning, as measured by the Wisconsin Card Sorting Task (WCST) and the Stroop. LCA was used to identify classes based on past-month drug use and adjust for probabilities of group membership when examining cognitive performance. Eight latent indicators were used: alcohol (ALC), cigarettes (CIG), marijuana (MJ), crack smoking (CS), nasal heroin (NH), injection cocaine (IC), injection heroin (IH), and injection speedball (IS).
Results: BLRT supported a 5-class model. Prevalent indicators (having an estimated probability of over 50%) for each class are as follows: "Nasal Heroin/Crack Smokers" (NH/CS, n=227.2): ALC, CIG, NH, CS; "Polysubstance" (P, n=105.2): ALC, CIG, MJ, CS, IH, IC, IS; "Multi-Injectors" (MI, n=88.0): CIG, IH, IC, IS; "Heroin Injectors" (HI, n=87.4): CIG, IH; and "Heroin Injectors/Marijuana" (HI/M, n=44.1): CIG, ALC, MJ, IH.
NH/CS had the lowest number of perseverative errors on the WCST; significantly lower than P, HI, and HI/M. NH/SC also had the best performance on the Stroop task; significantly better than HI/M. This is despite NH/CS having the 4th lowest verbal IQ; the only class significantly lower than HI/M.
Conclusions: A latent class of non-injection heroin and cocaine users performed best on two tests of executive functioning, despite having a significantly lower verbal IQ. This supports and extends research suggesting that executive functioning deficits are an important and specific component of substance abuse.
Financial Support: NIDA-R01-DA1449 and NIDA-T32-DA007292

241

PSYCHIATRIC FOLLOW-UP FOR DUALLY DIAGNOSED PATIENTS DISCHARGED FROM LEVEL-III DETOXIFICATION IN CENTRAL MASSACHUSETTS.

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Aims: The appropriate treatment and follow-up of dual-diagnosed patients is of great clinical importance due to potential for improvement of not only psychiatric and substance use outcomes but also in application of health care services in a more efficient and cost-effective manner. There are limited studies looking at the effectiveness of adding a psychiatric intervention in situations in which a dual-diagnosis patient is identified in a substance use treatment setting. The Enhanced Acute Treatment Service (EATS) at Community Healthlink (CHL) addresses the psychiatric needs of patients undergoing a level-3 detoxification. The aim of this project is to describe what is currently known about follow-up within the CHL system of a cohort of patients evaluated by EATS during detoxification and propose potential areas for future research and intervention.
Methods: A review of administrative data during the month of March 2011 was conducted to evaluate the disposition and likelihood of follow-up at CHL. Billing data identified 60 separate patients who were evaluated at the EATS level of care. Subsequent documented visits were categorized based on where they received care within the CHL system.
Results: Ten patients (14.5%) were admitted to residential treatment within CHL; fourteen patients (20.3%) were readmitted to the detoxification unit at CHL during this time period without any interim visit at CHL. Two (2.9%) were readmitted to detoxification following an interim outpatient visit, and finally 3 (4.3%) were seen only subsequently in the outpatient clinic without readmission. Notably, 39 (56.5%) patients had no subsequent follow-up within the CHL system, suggesting that either they relapsed or they moved to another location in Massachusetts to continue treatment for recovery.
Conclusions: Most patients had no subsequent follow-up within the CHL system. Further research is needed to determine the actual disposition of these patients to assess whether they relapsed and abandoned treatment or they continued further treatment, focusing on what kinds of treatments they engage.
Financial Support: None

242

EFFECTS OF VARIOUS TAMPERING METHODS ON EXPOSURE TO OXYCODONE IN HEALTHY SUBJECTS.

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Aims: Reformulated OxyContin® (oxycodone HCl controlled-release) tablets (ORF) use a polyethylene oxide controlled-release formulation that imparts resistance to physical and chemical manipulations. Original OxyContin® tablets (OC) provided no tamper resistance. Intact and tampered ORF and OC pharmacokinetics were evaluated vs immediate-release solution (OxyIR).
Methods: Study treatments contained 40mg oxycodone. Study Part A compared OC and ORF PK following various tampering methods (chewing, mortar & pestle grinding, pre-softening in water) vs OxyIR. In Part B subjects chewed OC & ORF vigorously, while subjects in Part C chewed normally, simulating accidental or inadvertent chewing. Oxycodone exposure assessments included AUC, Cmax, Tmax, and abuse quotient (AQ = Cmax/Tmax).
Results: Mortar and pestle grinding of ORF did not affect control of oxycodone release. Under both normal and vigorous chewing conditions, control of oxycodone release from OC was lost, while ORF retained some control of oxycodone release. Mean Cmax following chewing was lower for ORF than OC, 13.5% lower (90% CI 8.5-18.3%) following vigorous chewing and 23.6% lower (90% CI 19.1-27.8%) following normal chewing. Following vigorous chewing, median Tmax was higher for ORF (1.5 h) than OC (1.0 h). Following normal chewing, median Tmax was higher for ORF (2.4 h) than OC (1.1 h). Pre-softening ORF did not increase susceptibility to vigorous chewing. AQ was highest for OxyIR and chewed OC (84.5 and 80.8 ng/mL/h, respectively). In contrast to OC, chewed ORF AQ values were 21-33% lower than OxyIR. Following vigorous and normal chewing, ORF AQ values were statistically significantly lower ($p \leq 0.03$) than the chewed OC AQs.
Conclusions: Compared to OC, ORF demonstrated improved resistance to physico-chemical manipulations intended to disrupt the control of oxycodone release. Reduced Cmax and increased Tmax for ORF vs OC indicate that average oxycodone absorption rate is lower for ORF following both grinding and chewing manipulations.
Financial Support: Purdue Pharma LP

243

SUBJECTIVE, BEHAVIORAL AND COGNITIVE EFFECTS OF ORAL VS. INHALED ALPRAZOLAM.

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Aims: Increasing the speed of onset of some psychoactive drugs may have therapeutic advantages, however the subjective, behavioral and cognitive effects of the drug may be altered. The purpose of this study was to characterize inhaled alprazolam delivered via Alexza Pharmaceutical's Staccatto® device compared to oral alprazolam.
Methods: Fourteen participants with a history of sedative abuse received each of the following conditions in a randomized, double-blind manner: placebo, 1, 2 and 4 mg of oral and 0.5, 1.0 and 2.0 mg of inhaled alprazolam. Subjective, behavioral and cognitive measures were assessed repeatedly after drug administration.
Results: Orderly, dose dependent effects were observed for both oral and inhaled alprazolam. Subject and staff ratings of drug strength, psychomotor performance decrements, and cognitive impairment generally showed dose-related effects with higher doses associated with greater effects. The time to onset of significant drug effects relative to placebo (planned comparisons) was substantially lower after inhaled versus oral alprazolam and generally decreased with increasing doses. For example, time to onset of subject rated drug strength after oral alprazolam was 150, 45, and 30 min at 1, 2, and 4 mg, respectively. In contrast, time to onset of subject rated drug strength after inhaled alprazolam was 30, 2, and 2 min at 0.5, 1, and 2 mg, respectively. At the same absolute doses (e.g. 1 mg vs. 1 mg; 2 mg vs. 2 mg), the magnitude of peak effects did not differ between oral and inhaled alprazolam on these same measures. Additional analyses will be conducted in order to more fully elaborate on the effects of inhaled versus oral alprazolam.
Conclusions: Delivery of alprazolam via Staccato® differed in both onset and duration of action.
Financial Support: Alexza Pharmaceuticals, Inc. supported conduct of this study.

244

ADAPTIVE PROGRAMMING IN DRUG COURT: 24-MONTH RECIDIVISM OUTCOMES.

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Aims: We report on rates of criminal recidivism among a group of individuals who participated in a study that examined the effects of adapting judicial supervision to offenders risk level in a misdemeanor drug court (Marlowe, 2007). In the original study, 268 drug court participants were classified as either high risk or low risk. High risk participants met criteria for Antisocial Personality Disorder or had prior substance abuse treatment. They were randomly assigned to either a matched or an unmatched condition. Participants in the unmatched condition were scheduled to hearings every 4-6 weeks. Participants in the matched condition and low risk were scheduled to hearings only if needed, while those who were high risk attended bi-weekly hearings. Findings revealed that high risk participants who were matched had higher rates of graduation and lower rates of drug use than their unmatched counterparts. The current study examines between-group criminal recidivism rates at 24 months post-intake.
Methods: At two-years post-intake, we completed criminal record checks on all participants who were still enrolled in the study (N = 265). Data were then analyzed by group on arrests for any offense and a number of specific charges.
Results: Results are quite encouraging although they did not reach statistical significance. Consistent with our prior findings, the greatest differences in overall recidivism were found between matched and unmatched high-risk offenders (26% vs. 38%). Rates of overall recidivism between matched and unmatched low-risk offenders were virtually identical (26% vs. 25%).
Conclusions: The results mirrored those reported for the primary outcomes in the initial publications and suggest that adjusting the level of judicial supervision in response to identified risk factors may have lasting effects for reducing recidivism. These findings are important as they suggest communities and courts could reap long-term benefits and increase public safety by distinguishing between high and low risk offenders and allocating resources appropriately.
Financial Support: NIDA grant #R01-DA-13096, Matching Services to Client Needs in Drug Court.

245

TEACHING JUVENILE AND FAMILY COURT JUDGES ABOUT THE NEUROSCIENCE OF ADDICTION: IMPLICATIONS FOR INFLUENCING DISPOSITIONAL DECISIONS IN JUVENILE COURT.

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Aims: Of the more than 2.1 million young people involved in the juvenile justice system in 2008, almost 80% tested positive for drugs; committed alcohol/drug-related offenses; were under the influence of drugs and/or alcohol while committing their crime; and/or admitted to having a substance abuse problem (Young et al., 2007; Puzzanchera, 2009). The link between substance use disorders (SUDs) and juvenile delinquency is well-documented. However, resources to assist juvenile and family court judges (Judges) identify and treat juvenile offenders with SUDs are limited (Sickmund, 2004). The purpose of this study was to examine the extent of training Judges receive on adolescent-specific SUDs, and their attitudes about how that training could inform dispositional decisions.
Methods: A web-based survey was used to assess Judges' SUD-specific training and attitudes. The target population was the National Council of Juvenile and Family Court Judges listserv. An initial recruitment message and three reminder emails were sent to each name on the list at one week intervals. A total of 188 individuals participated, resulting in a 36% response rate.
Results: Roughly two-thirds (67%) of Judges estimated that 60-90% of adolescents appearing in their court have substance abuse-related problems. However, 85% reported feeling 'Not Very Confident' in dealing with substance abusing juvenile offenders. In addition, most indicated they had received less than two hours of training on topics such as adolescent brain development (61%) and neuroscience of addiction (71%).
Conclusions: Data from this study suggest that, given the number of juvenile offenders who have substance abuse-related problems, it is important that Judges receive training that increases their knowledge regarding the relationship between adolescent brain development, neuroscience of addiction, and recidivism.
Financial Support: Funded by the Center for the Application of Substance Abuse Technologies (CASAT), University of Nevada, Reno

246

SLEEP QUALITY AND STRESS REACTIVITY AMONG INDIVIDUALS WITH PRESCRIPTION OPIOID DEPENDENCE.

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Aims: It is well documented that opioid use disturbs sleep architecture and functioning (Dimsdale et al., 2007, Oyefeso et al., 1997, Sharkey et al., 2011). However, no study to our knowledge has investigated sleep disturbances or the effect of sleep on stress reactivity among individuals with prescription opioid (PO) dependence. Given the significant rise of prescription opioid non-medical use over the past decade, this is an important area with direct clinical implications.
Methods: Participants were non-treatment seeking prescription opioid dependent individuals (n=26) and healthy controls (n=34) who completed one overnight stay at an academic hospital. An Actigraphy watch was used to measure nocturnal activity, including movement and sleep efficiency. All participants wore the watch from 2300 on the night of hospital admission until 0700 the next morning and completed a sleep diary self-report measure. Testing the next day included a psychosocial stressor (Trier Social Stress Task) and exposure to a drug cue paradigm.
Results: PO dependent individuals, as compared to controls, showed more severe sleep impairment as evidenced by lower levels of sleep efficiency (74.4 vs. 80.8; p=.05), sleep onset latency (51.9 vs. 27.9 minutes; p=.05), total time awake (47.2 vs. 31.3 minutes; p=.02), total time mobile (41.3 vs. 27.2 minutes; p=.02) and sleep quantity (356.8 vs. 394.3 minutes; p=.006). PO dependent individuals also reported a greater number of sleep interruptions (3.5 vs. 2.2; p=.04). Time awake (p=.02) and time mobile (p=.005) were negatively associated with subjective craving in response to the Trier. Additionally, time awake (p=.05) and time mobile (p=.009) were positively associated with the amount of money a participants were willing to spend on POs after exposure to the cue.
Conclusions: The findings from this study, although preliminary, add to the current knowledge of sleep impairment and prescription opioid dependence. Data collection is ongoing and the full sample will be included in final analyses.
Financial Support: NIDA grant K23 DA021228 (SEB)

247

GENDER DIFFERENCES IN BOLD FMRI RESPONSE TO CUE-ELICITED CRAVING AND RESISTING DURING NRT FOLLOWED BY AD-LIB DENICOTINIZED CIGARETTE USE.

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Aims: Areas of regional brain activation during fMRI cue-induced craving and resisting the urge to smoke were examined at baseline, after 3 days of confirmed abstinence on nicotine patch, and after 3 days of smoking only denicotinized cigarettes.
Methods: Thirty (female=14) nicotine-dependent smokers underwent a BOLD fMRI scan with presentation of visual smoking cues, neutral cues, and rest periods in a block design under 2 conditions: craving and resisting craving. Data were analyzed with FMRIB Software Library 4.1.7, mixed effects FLAME1+2 focused on smoking vs. neutral contrast, clusters threshold p=0.05 (corrected) at the group level.
Results: No significant gender differences were seen in age, level of dependence or craving ratings. More women (5) than men (1) dropped following the baseline scan. During the crave condition, on the nicotine patch, men demonstrated greater activation than women in visual processing centers including bilateral occipital, L supramarginal, and L superior parietal cortices. Using denicotinized cigarettes greater activation was seen in the R superior, middle, and planum temporale gyri in women than men. During the resist condition using denicotinized cigarettes, women displayed greater activation than men in the bilateral insula and R pallidum, areas associated with decision making and planning. During craving, women who dropped out compared to women scanned a 2nd time displayed increased activation in the bilateral anterior cingulate cortex, prefrontal cortex, precuneus and right thalamus using a lower statistical threshold, p=0.05 (uncorrected). In contrast, during the resist condition, the women dropouts demonstrated increased activation in the bilateral prefrontal and occipital cortex.
Conclusions: These preliminary finding confirms that women are less responsive to NRT. Women with greater cue-elicited activation were more likely to smoke and drop out. This unconscious response may have contributed to the women's reduced success.
Financial Support: 5 K12 HD055885-02, NICHD 5R21DA026085-02 & UL1 RR029882

248

NEGATIVE EMOTIONAL REACTIVITY AND SUBSTANCE USE IN ADOLESCENTS DIAGNOSED WITH ADHD.

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Aims: To examine the impact of negative emotional reactivity (NER) on substance use and its association with Oppositional Defiant Disorder (ODD) in a sample of individuals shown to be at risk for poor substance use outcomes.
Methods: This study consisted of a sample of 142 youth diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) in childhood and 100 demographically similar comparison youth without ADHD recruited from the surrounding community (Mean age15.2; 94% male; 87% Caucasian). NER, characterized by elevated ratings of distress, irritability, frustration, and anger to everyday events, was assessed by mother report on the Buss and Plomin temperament measure (α=.87, 9 items). Parent reported ODD items were summed. Report of 30 day cigarette use and 6 month frequency of cigarette use, heavy drinking, drunkenness, and marijuana use were youth reported. Linear regressions were used to determine the contributions of group status, NER and ODD (alone and combined) to substance use.
Results: NER and ODD were independently associated with 30 day (β=.04, p< .001; β =.28, p<.001) and 6 month (β=.42, p=.001; β=.23, p=.001) cigarette use and only NER was significantly associated with frequency of drunkenness (β=.04, p=.04; β=.13, p=.29). Analyzed simultaneously, both NER (β=.02, p=.05) and ODD (β=.21, p=.01) were significantly associated with 30 day cigarette use only. ADHD diagnosis was not significantly associated with cigarette use and drunkenness when NER/ODD was added to the models.
Conclusions: NER and ODD symptoms appear to have unique and overlapping associations with cigarette and alcohol use. NER may reflect a stable negative reactive response style that, in interaction with social context, produces opposition to authority and increases substance use risk.
Financial Support: This study was principally supported by grants AA00202, AA011873, and DA12414.

249

A NOVEL THERAPEUTIC USE OF CANNABINOIDS IN TRANSPLANT THERAPY.

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Aims: Marijuana has been used for centuries and continues to be one of the most widely used illicit substances. It is established that cannabinoids modulate immune responses. Two cannabinoid receptors have been identified, CB1 and CB2. CB2 is primarily expressed on cells of the immune system. We have previously reported that a CB2- selective agonist, O-1966, inhibits the Mixed Lymphocyte Reaction (MLR), an in vitro correlate of graft rejection, through the CB2 receptor. This inhibition was found to occur via a direct effect on T-cells and not accessory cells. The present study sought to determine mechanisms for the immunosuppressive action of O-1966 and to test its efficacy in blocking acute skin graft rejection in mice.
Methods: A gene array analysis of mouse T-cells treated with O-1966 in the MLR showed a significant reduction in expression of mRNA for CD40 ligand and CyclinD3, and an increase in mRNA for IL-10. Treatment with O-1966 also increased the percentage of the inhibitory T-cell subclass, T-regs, as assessed by flow cytometry. The ability of O-1966 treatment to block rejection of skin grafts in vivo was also tested.
Results: Mice received skin grafts from a histoincompatible donor, and the time to graft rejection was analyzed. Mice that received O-1966 treatment had significantly prolonged graft survival, as compared to mice that received the vehicle.
Conclusions: The results show that a CB2 selective cannabinoid can suppress the MLR by increasing levels of an anti-inflammatory cytokine and of suppressor T-cells, as well as by dampening molecules involved in T-cell activation. The suppressive effect of O-1966 in vitro translated to retardation of graft rejection in vivo. These data support the potential of this class of compounds as useful therapies to prolong graft survival in transplant patients.
Financial Support: This work was supported by NIDA grants Temple University Seed Grant, DA13429, DA06650, and T32-DA07237.

250

COMMUNITY TREATMENT PERCEPTIONS OF CONTINGENCY MANAGEMENT: A MIXED-METHOD APPROACH TO EXAMINING FEASIBILITY, EFFECTIVENESS, AND TRANSPORTABILITY OF INCENTIVES.

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Aims: Aims: The efficacy of contingency management (CM), a behavior therapy utilizing operant conditioning principles to reinforce treatment adherence, is recognized yet dissemination is limited by reluctance in the treatment community to adopt monetary incentives. This reluctance may be better understood by eliciting treatment community views of the feasibility, effectiveness, and transportability of monetary and non-monetary incentives. This study employed a mixed-method approach to examine views among community treatment directors, supervisors and clinical staff.
Methods: Methods: Site visits to 16 treatment programs were conducted involving individual interviews with the director, a supervisor, and two clinical staff (N=64). Interviewees provided Likert ratings, augmented by qualitative elaboration. Interviews were audio-recorded, and later transcribed with content codes noting salient themes. ANOVA compared ratings for monetary vs. non-monetary incentives, with personnel tier of interviewees and CTN-affiliation status of programs included as covariates.
Results: Results: ANOVA revealed much greater perceived feasibility for non-monetary incentives, though this discrepancy was attenuated among CTN-affiliate programs. Common qualitative themes were cost, staff time for delivery, and logistics as impracticalities of monetary incentives. ANOVA revealed both greater perceived effectiveness and transportability for non-monetary incentives. Common qualitative themes focused on generalizable and long-term therapeutic impacts of non-monetary incentives, and their procedural simplicity and philosophical congruence for staff, respectively.
Conclusions: Conclusions: Findings are consistent with prior survey-based studies of incentive preferences, but provide greater depth for treatment community perspectives. Training and promotional efforts for CM may be more effective if such perspectives are recognized and incorporated into presentations of how operant conditioning principles may be therapeutically applied.
Financial Support: K23 DA025678-01A2 (Hartzler, PI)

251

HEALTHCALL: A RANDOMIZED TRIAL OF TECHNOLOGICALLY ENHANCED BRIEF INTERVENTION FOR HEAVY DRINKING IN 255 HIV PRIMARY CARE PATIENTS.

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Aims: Heavy drinking In HIV-infected patients predicts mortality and risk behaviors. In overburdened HIV primary care, alcohol interventions must be effective, yet demand little time or resources. To enhance one session of brief (25 min) Motivational Interviewing (MI), we developed "HealthCall" using automated telephone Interactive Voice Response (IVR) technology. With HealthCall, patients call an IVR daily (1-3 min) to report alcohol and health behaviors, and meet with their MI counselor at 30 and 60 days to discuss personalized feedback graphs generated from their call data.
Methods: Participants were urban HIV primary care clinic patients who drank ≥4 drinks at least once in the prior 30 days. We included patients with and without alcohol dependence to determine if their outcomes differed. Patients were randomized to parallel arms: attentional control (n=88); MI-only (n=82); or MI+HealthCall (n=85). At 30 and 60 days, patients were assessed and briefly discussed drinking with a counselor; in MI+HealthCall, this included their graph. Primary 30- and 60-day outcomes were mean number of drinks per drinking day (NumDD) and % days abstinent (PDA), analyzed with generalized linear mixed effects models (SAS PROC GLIMMIX).
Results: All groups reduced drinking over time. Among alcohol dependent patients, mean NumDD declined significantly more over time in the MI+HealthCall arm than among those in MI-only (t=2.17 df =93, p=0.03) or control (t=3.53, df=93, p=0.0007), while change in mean NumDD did not differ between MI-only and control. Patients without alcohol dependence did not differ across arms on NumDD; PDA did not differ by arm.
Conclusions: Alcohol dependent patients in MI+HealthCall reduced drinking significantly more than others, while requiring little additional staff time. Among alcohol dependent patients in resource-limited HIV primary care settings, HealthCall may offer the extra enhancement needed to make brief alcohol intervention effective.
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252

TRAINING COUNSELORS ON AN HIV RISK-REDUCTION INTERVENTION: HOW MUCH PRACTICE IS ENOUGH?

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Aims: In the 'Real Men Are Safe-Culturally Adapted' (REMAS-CA) study we 1) developed an adherence scale for REMAS-CA; 2) measured improvement in counselors' intervention delivery skills over time; and 3) identified which modules were hardest to deliver.
Methods: REMAS-CA, a 5-session HIV risk reduction intervention, was piloted at 4 addiction treatment programs. Two counselors per site ran 3 or 4 rounds of REMAS-CA groups over ~9 months. Group recordings were reviewed by a team of 4 (lead- and co-investigator + 2 undergrads) for 1) manual adherence; 2) avoidance of proscribed behaviors; and 3) global empathy and co-therapy. Inter-rater reliability was calculated via intraclass correlation coefficient (ICC). ICC was calculated for all raters, 2 sets of 3, and 2 pairs of raters. Adherence and skill scores were compared for counselors' first and last cohorts using paired t-tests.
Results: ICCs were 0.845 (4 raters; 105 items), 0.618 and 0.696 (3 raters; 210 items), and 0.734 (2 raters; 1006 items). Counselors did not improve delivery of REMAS-CA over time, except in global empathy which showed significant improvement from first cohort (M = 4.44, SD = 0.77) to last (M = 4.76, SD = 0.53), t = 2.28, p = 0.04. Discussions of current and past relationships, and role plays of communication skills with partners, were most difficult for counselors.
Conclusions: A highly reliable system for rating counselor skill and adherence to REMAS-CA was developed. Counselors' lack of significant improvement in skill, co-therapy, global empathy, and avoidance of proscribed behaviors may have been because they scored relatively high even in their first round of REMAS-CA. Results suggest that the 2-day training and subsequent certification process, manual structure, and early supervision may have solidified counselors' skills, leaving little "room for improvement."
Financial Support: Supported by NIDA grant 1RC1DA028245-01 (D. Calsyn, PI).

253

PREDICTORS OF NONFATAL OVERDOSE IN A LONGITUDINAL COHORT OF RURAL PRESCRIPTION DRUG USERS.

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Aims: Rates of overdose among rural prescription drug users now eclipse that of heroin and cocaine users, yet little is known about risk factors for overdose in rural areas. The purpose of this study was to determine the predictors of overdose in a longitudinal cohort of rural Appalachian prescription drug users.
Methods: Data on overdose, drug use and social networks were collected at baseline, 6-, and 12-months post-baseline among 503 prescription drug users. To determine incident overdose, participants were asked if they had overdosed at any time between visits. Discrete-time survival analysis was used to determine the predictors of overdose, allowing drug use and network variables to vary over time.
Results: Twenty-three overdoses were observed between the baseline and 6-month and 6- and 12-month follow-up periods, corresponding to a rate of 4.69 overdoses per 100 person-years. Drugs most commonly used on the day of the overdose included: benzodiazepines (68.2%), methadone (36.4%), and OxyContin® (45.4%). More than half (56.5%) were injecting on the day of their last overdose. The following emerged as multivariate predictors of nonfatal overdose over time: previous overdose (AOR: 6.32, 95% CI: 2.47, 16.2), having more drug network members (AOR: 1.09, 95% CI: 1.00, 1.18), heroin use in the 30 days prior to the overdose (AOR: 7.20, 95% CI: 1.66, 31.0) and meeting the DSM-IV criteria for PTSD (AOR: 2.56, 95% CI: 1.03, 6.36).
Conclusions: While heroin use was relatively rare, it was nonetheless a strong predictor of nonfatal overdose among rural drug users who are predominantly using prescription opiates and benzodiazepines to get high. These findings point to the need for comprehensive overdose education and training around the use of naloxone in order to prevent fatal overdose in this population of rural drug users.
Financial Support: We gratefully acknowledge funding from the National Institute on Drug Abuse (R01DA024598).

254

THE INFLUENCE OF METROPOLITAN LOCATION AND HOMELESSNESS ON TREATMENT COMPLETION.

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Aims: To examine the influence of metropolitan location and homelessness on the likelihood of completing substance abuse treatment.
Methods: Data were extracted from the SAMHSA 2008 TEDS-D datatset to examine the influence of geographic location and homelessness on treatment completion in the 10 largest cities (MSAs) in the US. Logistic regression analyses were employed to predict treatment completion. Independent variables included demographic characteristics, primary substance of abuse at admission, treatment modality, metropolitan statistical area, and homelessness.
Results: Results indicate that the likelihood of treatment completion increases for veterans (OR =1.17), older individuals(OR=1.58), and those whose primary substance was alcohol (OR=1.67) or cocaine (OR=1.16). Treatment completion was less likely for women (OR=0.90), non-whites(OR=0.85), those with less than 12th grade education(OR=0.83), and the unemployed (OR=0.56). Heroin users were less likely to complete treatment (OR=0.52). The likelihood of treatment completion for residential service settings was 2.5 times greater (OR=2.49) than for outpatient treatment. Controlling for demographic characteristics, treatment setting, and primary drug of choice, there was considerable variation in completion across metropolitan locations. Compared to New York, the probability of completing treatment in Miami, Dallas, and Houston was several times greater (OR=5.41; OR=2.71; OR=3.32, respectively). Finally, after accounting for these other factors, homeless individuals were somewhat less likely to complete treatment than domiciled clients (OR=0.93).
Conclusions: The results show that major cities vary considerably in their treatment completion rates. In addition, various demographic characteristics as well as homeless status were associated with differences in treatment completion. Further research should examine what factors account for these variations. Treatment effectiveness may be improved by recognizing the various factors that are associated with program completion or non-completion.
Financial Support: None

255

PROFILES OF LISDEXAMFETAMINE AND METHYLPHENIDATE IN RATS TRAINED TO DISCRIMINATE D-AMFETAMINE FROM SALINE.

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Aims: Lisdexamfetamine (LDX; Vyvanse®) is a prodrug that is metabolised to d-amfetamine (d-AMF) exclusively in red blood cells (Pennick 2010, Neuropsychiat Dis Treat 6:317), while methylphenidate (MPH) is a pharmacologically active stimulant. In the USA, both are Schedule 2 Controlled Drugs used to treat ADHD. Studies in drug experienced human volunteers suggest that the unusual pharmacokinetics of LDX may reduce aspects of its liability for abuse (Jasinski & Krishnan 2009, J Psychopharmacol 23:410, 419).
Methods: We have compared the subjective effects of LDX and immediate release MPH (IR-MPH) in groups of 6-9 female rats trained to discriminate d AMF (0.5mg/kg ip) from saline. LDX and IR-MPH were tested by the oral (po) and intraperitoneal (ip) routes.
Results: 15min post-dosing, LDX (0.5-1.5mg/kg [d-AMF base]) generalised to saline. At 60min, LDX (0.5-1.5mg/kg po) generalised partially to d-AMF (26-75%) at 0.5-1.0mg/kg and fully (≥76%) at 1.5mg/kg. At 120min, these doses of LDX generalised either to saline or partially to d-AMF. 15min after po dosing, IR-MPH (3.0-10mg/kg) dose-dependently generalised to d-AMF. Switching to the ip route reduced the interval required for LDX (0.5-1.5mg/kg) to be recognised as d-AMF-like, but it did not alter the potency of the prodrug. After ip administration, IR-MPH dose-dependently generalised to d-AMF, but the dose required for full generalisation decreased from 10mg/kg po to 3.0mg/kg ip.
Conclusions: The results show LDX generalised to d-AMF in rats trained to recognise this discriminative cue. However, LDX's amfetamine-like subjective effects were delayed in onset after po dosing and of relatively short duration. Furthermore, its potency was not increased by switching to the ip route. In contrast, generalisation to d-AMF occurred rapidly after po or ip administration of IR-MPH and the potency of the drug was increased 3-fold when dosing was switched to ip. These data are consistent with Jasinski's human findings. They also support the view that the stimulant potential of LDX is lower than IR-MPH.
Financial Support: Shire Pharmaceuticals Ltd

256

COMPUTER-BASED DELIVERY OF THERAPY FOR ADDICTION: A PATIENT SURVEY OF ACCESS TO ELECTRONIC DEVICES.

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Aims: Studies indicate that computer-based therapy can be effective as a supplement to established treatment. While these efforts can aid in engaging and maintaining patients in treatment, little is known about the patients' access to resources needed to participate in such services outside of a clinic. As patients in substance abuse treatment often have limited resources, access to electronic devices with internet capability may be inadequate and restrict benefit.
Methods: This study surveyed access to electronic devices for individuals in treatment for substance dependence at an outpatient opioid treatment clinic. The survey assessed access to computers, internet services, and cellular data networks. 44 patients participated (39% female, average age of 47.4 years [range 22-64]).
Results: 22 (50%) of subjects were found to have access to working computers where they lived; 18 (41%) were connected to the internet. Only 8 patients were employed; 3 of these accessed the internet at work for personal use. 20 of 26 without internet on their home computer could access the internet at the homes of family/friends, or at the public library. Overall 42 subjects (93%) could access a computer. 35 patients were interested in computer-based substance abuse counseling, 28 of which expected it to be at least "moderately helpful." 18 patients (41%) noted they would chose to continue exclusive face-to-face therapy. 41 of 44 patients had cell phones, 13 of which could access the internet via their handheld device. 34 patients stated they would be interested in trying substance abuse treatment via their phone.
Conclusions: These findings suggest patients in outpatient substance abuse treatment have resources ready for accessing computer-based therapy, although access was not always readily available. Across a range of ages, many patients were open to trying this form of therapy and would expect to find it helpful as a supplement to face-to-face interactions.
Financial Support: Support: DA023186

257

COMPARATIVE EFFECTIVENESS OF METHADONE AND BUPRENORPHINE FOR THE TREATMENT OF OPIOID DEPENDENCE DURING PREGNANCY: A RETROSPECTIVE COHORT STUDY.

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Aims: The aim of the present study was to compare maternal and infant outcomes among a cohort of opioid-dependent pregnant women treated with methadone in an opioid treatment program (OTP) versus buprenorphine in office-based opioid treatment (OBOT).
Methods: 490 pregnant, opioid-dependent women were treated in an OTP (n=261) or OBOT (n=229) between 2000-2010 at a single institution. Treatment modality was determined by availability, acuity, transportation needs, prior drug use history, failure of prior therapy, and patient choice. The OTP included methadone maintenance, mandatory counseling, psychiatric evaluation, and case management. OBOT consisted of buprenorphine maintenance treatment by community-based providers (some by the obstetric provider), with counseling recommended.
Results: A number of significant differences between treatment modalities were observed. Gestational age was longer in OBOT vs. OTP mothers (39.6 vs. 38.9 weeks), although there was no difference in preterm delivery rate (14%). Infants born to OBOT vs. OTP mothers were heavier (3114 vs. 2877 grams) and had a larger head circumference (33.4 vs. 32.9 cm), differences at least partially accounted for by increased gestational age. Infants born to OBOT vs. OTP mothers required treatment for neonatal abstinence less often (20 vs. 43%) and for a shorter period of time (88 vs. 137 days).
Conclusions: Compared to women treated with methadone in an OTP, women treated with buprenorphine in OBOT delivered newborns with better physical birth parameters and less severe neonatal abstinence. These data suggest pregnancy outcomes following OBOT with buprenorphine are as good and often better than outcomes with OTP methadone. These results are consistent with efficacy data from randomized clinical trials (e.g., Jones et al., 2010) and support the use of buprenorphine in OBOT for the treatment of opioid dependence during pregnancy.
Financial Support: None

258

PILOT RANDOMIZED TRIAL OF BUPROPION FOR METHAMPHETAMINE ABUSE/DEPENDENCE IN ADOLESCENTS.

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Aims: To perform a pilot clinical trial of bupropion versus placebo for the treatment of methamphetamine (MA) abuse/dependence among adolescents.
Methods: Nineteen youth aged 15-19 with MA abuse or dependence were randomized to receive bupropion (N=12) or placebo (N=7) with standard drug counseling for 8 weeks. Urine drug screen results, retention, and adverse events were compared for bupropion versus placebo.
Results: Youth receiving placebo provided significantly more MA-negative urine drug screens during treatment (mean = 8.9 MA-negative drug screens, S.D. = 4.5) and were retained longer (mean = 49.5 days, S.D. = 9.8) than youth receiving bupropion (mean = 5.0 MA-negative drug screens, S.D. = 3.2, $p = 0.04$ and mean = 33.3 days, S.D. = 21.2, $p = 0.04$). Youth receiving bupropion reported 13 adverse events compared to 3 adverse events in youth receiving placebo. There was one serious adverse event, suicidal ideation requiring hospitalization, in a youth receiving bupropion.
Conclusions: This is a pilot study limited by the small sample size. Still, results do not support use of bupropion for the treatment of MA abuse/dependence in adolescents.
Financial Support: The study was funded by NIDA grant 1 R21 DA 026513 (Heinzerling).

259

EFFECT OF ZONISAMIDE ON COCAINE CRAVING AND REINFORCEMENT: AN INTERIM ANALYSIS.

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Aims: Medications that act to antagonize the glutamate system and/or increase the GABA system may reduce the craving for and the reinforcing properties of cocaine. In an ongoing human laboratory clinical pharmacology trial, zonisamide (ZNS), an antiepileptic agent, glutamate antagonist (GLT-1 activator), and GABA modulator, is being evaluated for therapeutic potential in treatment of cocaine dependence.
Methods: In a double-blind, within-subject study, five healthy, adult cocaine dependent volunteers enrolled on our residential unit for 44 days were evaluated on changes in (1) their subjective response to cocaine and (2) their cocaine self-administration under three ZNS dose conditions (week 1: 0mg; weeks 2-3: 300mg; weeks 4-5: 600mg). Cocaine challenge sessions were conducted on weeks 1, 3, and 5. During cocaine dose-response sessions, volunteers received three injections of cocaine (1, 20, and 40mg/70kg, i.v.) in ascending order (45-min apart) and rated their drug experience on 100-point visual analog scales (VAS). During choice sessions, volunteers had seven opportunities to choose between a dose of cocaine (sampled in the morning) and varying amounts of money (starting at $19 and decreasing by $3 with each trial).
Results: Comparison of area-under-the-curve subjective responses showed that cocaine produced significant dose-dependent increases in ratings of "drug effect," "rush," "drug liking," and "desire for cocaine" on the VAS. Treatment with ZNS significantly decreased ratings for "desire for cocaine," and decreased (but not significantly) ratings of "drug effect," "rush," and "drug liking." The average number of cocaine choices during choice sessions increased significantly as a function of cocaine dose. ZNS treatment produced orderly decreases in drug choices, however the effect was not significant.
Conclusions: Interim analysis suggests there may be some effect of ZNS treatment on subjective effects of cocaine and cocaine reinforcement. These initial data are encouraging but limited by a lack of power (small n) and of between-group comparison with the placebo zonisamide condition.
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260

CHARACTERIZING NICOTINE WITHDRAWAL IN PREGNANT SMOKERS.

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Aims: Little is known about nicotine withdrawal in pregnant smokers. Our 2006 report found that pregnant smokers had mild increases in withdrawal scale scores following cessation. These relatively modest increases in withdrawal scores after cessation could have been a result of high scores prior to cessation, but lack of comparison conditions limited the conclusions that could be drawn.
Methods: The present study examined nicotine withdrawal during 14 days of biochemically-verified abstinence in pregnant smokers (n=63) and matched non-pregnant female smokers (n=20), as well as in pregnant non-smokers (n=33). The Minnesota Nicotine Withdrawal Scale was administered once prior to smoking cessation (baseline) and at 8 points during the 14-day abstinence period.
Results: Pregnant smokers had significantly higher mean overall withdrawal scores at baseline compared to both comparison conditions (1.40 vs. 0.88 and 0.96, respectively, $p<.05$). During the first five days of abstinence, withdrawal scores of pregnant and non-pregnant smokers were significantly higher than those of pregnant non-smokers ($p<.05$). However, contrary to our prior report, withdrawal did not vary over time among pregnant smokers; that is, pregnant smokers did not report further increases in withdrawal following cessation. To investigate this inconsistency, the number of cigarettes smoked per day (CPD) at baseline was examined as a potential moderator of nicotine withdrawal among pregnant smokers. Baseline levels of withdrawal were not different in those smoking < vs. ≥ 10 CPD (n's=49 & 14), but pregnant women smoking ≥10 CPD had significantly higher scores during the first two days of abstinence compared to those smoking <10 CPD ($p<.05$).
Conclusions: These results suggest that pregnant smokers have elevated levels of withdrawal at baseline, perhaps related to spontaneous reductions in smoking upon learning of pregnancy, and that pregnant women smoking ≥10 CPD have higher levels of withdrawal following cessation, which may contribute to the poorer cessation outcomes often observed among this subset of pregnant smokers.
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261

EFFECTS OF ALCOHOL USE ON PATIENT OUTCOMES IN VETERANS WITH MILD TBI AND/OR MENTAL DISORDERS.

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Aims: The primary aim was to describe self-reported alcohol use in Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans with mild traumatic brain injury and/or mental disorders such as PTSD. The secondary aim was to determine prevalence of functional and cognitive impairments, sleep disturbances, anxiety, and depression, according to self-reported alcohol use.
Methods: This was a prospective study at Hines VA of a pilot sample (N=66) that was abstracted from a larger study of OEF/OIF veterans. Individuals were classified as: confirmed mTBI (n=5), mental disorder(MD) (n=19), mTBI+MD (n=14) and healthy controls (HC; n=14). Main Outcome Measures: Structured neuropsychological interview, Clinically Administered PTSD Scale, Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), Alcohol Use Disorders Identification Test (Audit-C), World Health Organization Disability Assessment Schedule (WHODAS-II) and Wisconsin Card Sorting Task-64 (WCST).
Results: 42.4% of the sample tested AUDIT-C positive. BAI and BDI scores were higher in the BH (BAI=12±7, BDI=14±7) and mTBI+MD groups (BAI=14±9, BDI=18±8) compared to HC (BAI=2±2, BDI=5±4) and mTBI participants (BAI=3±3, BDI=6±4; ANOVA with post hoc Tukey, P<0.05). Higher WHODAS total scores, for the MD (28±19) and mTBI+MD groups (33±23), indicated greater functional difficulty compared to controls (9±10, ANOVA with post-hoc Tukey, P<0.05). MD individuals with alcohol use disorder tended to have more difficulty with an executive function cognitive task (WCST mean = 52±5) compared to BH Audit-C negative subjects (47±6, t-test, p=0.06).
Conclusions: Alcohol use disorder is prevalent amongst veterans returning from the current conflicts. While this pilot analysis is not powered to detect significant between-group differences, results suggest that abstracting a larger sample to examine effect of alcohol use disorder on behavioral and congitive outcomes is warranted.
Financial Support: Edward Hines Jr VA Health Services Research & Development (HSR&D) Locally Initiated Project LIP# 42-130
VA HSR&D SDR-409

262

COMMUNICABLE DISEASE AMONG VETERANS RECEIVING CARE IN THE PUBLIC-SECTOR SUBSTANCE ABUSE TREATMENT SYSTEM IN LOS ANGELES COUNTY.

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Aims: Hepatitis C, tuberculosis (TB), and sexually transmitted infections (STIs) are common in substance abuse (SA), and a substantial burden among veterans of the armed forces. The Veterans Health Administration (VHA) is the single largest provider of HIV/AIDS care in the US, and one-third of all VHA patients with HIV are also infected with hepatitis C. Previous work has not examined the prevalence of communicable disease among Veterans in care for SA outside of the VHA system. This study compares the prevalence of hepatitis C, TB, and STIs among veterans and non-veterans receiving care in the public sector SA treatment system in LA County, California in 2009.
Methods: Program intake data were collected from 2,247 veterans and 61,282 non-veterans (n=63,529) and analyzed using descriptive and multivariate statistics.
Results: A higher percentage of veterans than non-veterans reported hepatitis C (15.2% and 9.4%, respectively; p<.001) and TB (4.0% and 2.6%, respectively; p<.001). There were no differences between veterans and non-veterans in STIs (3.6% and 3.1%, p<.20) In multivariable models controlling for age, gender, race/ethnicity, education, severity of drug use, treatment modality, and histories of homelessness and mental illness, veterans had greater odds of reporting hepatitis (OR=1.42, 95% CI=1.19, 1.69; p=.001) than did non-veterans. Restricting the analysis to veterans, higher odds of hepatitis were found for those who were older, White, had a history of mental illness, and were attending opioid replacement treatment.
Conclusions: Veterans in SA treatment in the LA County public system have a relatively high prevalence of hepatitis C. Research to improve the care of veterans with these diseases is a high priority in the VHA. The care of veterans with SA problems outside of the VHA could be informed by evaluation findings from the VHA's national Quality Enhancement Research Initiative, which includes targeted work on hepatitis C and HIV.
Financial Support: VHA Emergency Management Evaluation Center

263

COMPARISON OF CONTINGENCY MANAGEMENT REINFORCEMENT SCHEDULES PROVIDED WITH BUPRENORPHINE FOR THE TREATMENT OF OPIOID DEPENDENCE.

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Aims: Contingency Management (CM) procedures have been successful in initiating periods of abstinence and in producing relatively long periods of abstinence. Research has addressed the contingency value, but no study has compared schedules of reinforcement provided in tandem with buprenorphine for opioid dependence.
Methods: This study utilizes data from a study investigating behavioral treatment added to pharmacotherapy with buprenorphine to examine whether a relatively large dollar amount (CM-L) is associated with better treatment outcome compared to a smaller dollar amount (CM-S). Using the "fishbowl" method of providing reinforcement, 98 participants randomly assigned to either CM alone or in combination with counseling (CM+CBT) were given CM-L or CM-S incentives for opioid-negative urine samples collected at each of 2 weekly clinic visits over the 16-week treatment period. The fishbowl included 100 chips each corresponding to one of four dollar amounts. Procedural differences between the CM schedules included the dollar value of the chips, the number of chips marked with each value, replacement of the chips with each draw, and the maximum number of chips that could be drawn.
Results: No differences were found in baseline demographic or drug use characteristics between the CM-L (n = 41) and CM-S (n = 57) groups. For the total sample, the mean age is 39.2 years, and includes 29% females. As expected, the groups differed in mean number of draws with 268.2 (sd = 230.2) for CM-L, and 81.6 (sd = 91.7) for CM-S (p < 0.0001). Mean earnings also differed by group with $1,379 (sd = $1,302) for the CM-L group, and $159 (sd = $175) for the CL-S group (p < 0.0001). Despite these differences, no differences were found in session attendance, treatment retention, or opioid use.
Conclusions: Providing a larger monetary incentive was not more effective in reducing opioid use or increasing retention.
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264

GENDER DIFFERENCES IN RESPONSE TO BUPROPION IN METHAMPHETAMINE USERS.

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Aims: To investigate gender differences in subjective and physiological responses to methamphetamine post-bupropion treatment in non-treatment seeking methamphetamine dependent individuals.
Methods: Participants met diagnostic criteria for methamphetamine abuse or dependence. Twenty participants completed a clinical trial using a double-blind, placebo-controlled study design. Participants were given intravenous methamphetamine (0, 15, and 30 mg) pre- and post-bupropion/placebo randomization (150 mg BID for 6 days). At baseline and post- methamphetamine administration, participants completed VAS questionnaires assessing ratings of positive and negative subjective effects. VAS objectives included; 'Any Drug Effect', 'High', and 'Good Effect' with the scores ranging from 0 (not at all) to 100 (strongest ever). Participants' blood pressure and heart rate were measured at baseline and post-methamphetamine administration intervals.
Results: Females exhibited higher systolic and diastolic blood pressure response to methamphetamine compared to males (F=6.7, p= .025 and F=6.0, p= .032, respectively). We found no significant differences for systolic and diastolic blood pressure within groups at baseline or post-bupropion administration (F=0.2, p=.962 and F=1.8, p=.115). Following methamphetamine administration, there were no statistically significant differences in heart rate between males and females (F=1.2, p=.339). In addition, females reported higher ratings for 'High' and 'Any drug effect' compared to males for most time points.
Conclusions: Males and females differ in physiological and subjective effect responses to bupropion treatment and these findings merit further investigation to enable development of gender-appropriate treatment options for methamphetamine addiction.
Financial Support: Research was funded by contracts from NIDA: DAo8804, DA014593, and RR00865.

265

ATTC NETWORK'S ITRAINING SERIES DEMONSTRATES VALUE OF WEBINAR-BASED INFORMATION DISSEMINATION.

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Aims: Health professionals are looking for innovative professional development opportunities that provide evidenced-based information and fit into their schedules. In response, the Addiction Technology Transfer Center (ATTC) Network began a monthly webinar series, ATTC Network's Third Thursday iTrainings, in October 2010. Aim: The project aimed to determine the perceived usefulness of webinar-based trainings in the addiction treatment field, and ascertain if this initiative could be used to extend the reach of the ATTC Network.
Methods: The webinar series focused on four topical learning clusters: Preparing the Field for Healthcare Reform; Shining the Spotlight on Evidence-Based Practices; Meeting the Needs of Special Populations; and Building the Skills of Clinical Supervisors. In the first year, 1,794 individuals participated in the series, with a range per webinar of 86-243 attendees. Quantitative and qualitative data were collected on attendees' experiences.
Results: Findings include: 94% of respondents indicated they were very satisfied/satisfied with their overall experience; 97% of respondents indicated they found the information presented very useful/useful; 88% of respondents indicated they intended to share the information with colleagues; and 90% of respondents indicated they planned to participate in future ATTC Network iTrainings. In addition to live web events, recordings of past webinars have been viewed 640 times and the iTrainings webpage, where visitors can download the slides and resources from past webinars, has been visited 7,753 times.
Conclusions: Conclusion: It appears that 1) professionals in the addiction treatment field were receptive to this mode of information dissemination and found it a valuable use of their time, and 2) the iTraining series was an effective vehicle to share information on the work of the ATTC Network, thereby extending its reach. As a result, the ATTC Network plans to continue this monthly webinar series in the future.
Financial Support: Supported by: The ATTC National Office is funded by the Substance Abuse and Mental Health Services Administration (SAMHSA), award 5UD1TI013592-10.

266

ADOLESCENT CONDUCT AND SUBSTANCE USE DISORDERS DIAGNOSES PREDICT PREMATURE DEATH IN EARLY ADULTHOOD.

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Aims: Very little is known about the overall mortality of clinical samples of conduct and substance use disordered adolescents, who are often involved in delinquency, which, in turn, increases their mortality risk.
Methods: A clinical sample of adolescents with substance use disorders (SUD) and conduct disorder (CD) (n= 1529), their siblings (n= 252), and their community counterparts (n= 431) were interviewed between 1993 and 2008. Deaths were determined by the National Death Index, or by Accurint-confirmed family report up to 2009. We tested the hypothesis that both SUD and CD diagnoses predict premature death, using Cox regression modeling.
Results: Among the 2212 participants, 44 deaths occurred (2%): 39 among clinical sample adolescents (2.6%), 3 among the siblings sample (1.5%), and 2 among the community sample adolescents (0.5%). Causes of death were identified in 41 events: 12 homicides, 10 suicides, 1 legal intervention, 9 motor vehicle accidents, 7 overdoses, 2 non-specified accidents. Survival time was predicted by being arrested before study enrollment (OR (95% CI) = 0.71 (0.60-0.84), p<.0001, CD diagnosis (5.63 (3.01 – 10.52), p=0.0057), and count of SUD diagnoses (1.21 (1.10 - 1.45), p=0.0426). The mortality rate of adolescents in the clinical sample was greater than 35 times the mortality rate of Denver metropolitan area adolescents in the same age range.
Conclusions: Premature death in this study seemed to be associated with risk behaviors and delinquency often seen among adolescents with SUD and CD. A protective factor, arrest before study enrollment, was identified. We speculate that adolescents, who have been supervised for longer, through drug monitoring, parole, probation or incarceration after that first arrest, seem to have a better chance at survival.
Financial Support: Dr. Hoffenberg is supported by T32 MH015442
This study was funded by NIDA: DA-011015, DA-021913, DA-012845, DA-021905

267

SOCIAL EXCLUSION AND INCREASED RISKY PROPENSITY AMONG FEMALE CRACK COCAINE USERS.

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Aims: Crack cocaine users are vulnerable to HIV infection due to elevated rates of risk behavior. Women in this group have been identified as particularly vulnerable for HIV infection due to higher rates of risky sexual behavior which suggests the need to understand the factors that may increase their vulnerability for such risky behaviors. Among these factors, social rejection has been proposed to play an important role. Recent evidence shows its relationship with engagement in sexual behavior with multiple partners among female crack-cocaine users. In an effort to better understand this relationship, the current study examined the link between social rejection and risk taking propensity among crack cocaine users and the moderating role of gender. We hypothesize that the experience of social rejection will predict higher risk taking propensity in female, but not male, crack cocaine users.
Methods: 269 drug users in treatment who reported using crack-cocaine at least twice a month in the past year participated in a Cyberball computer game designed to induce the experience of social rejection followed by a self-report questionnaire assessing the level of rejection experienced. They subsequently completed the Balloon Analogue Risk Task (BART), a computer game designed to assess differential levels of risk taking propensity by engaging participants in a balloon popping task for monetary reward.
Results: Experienced social rejection was related to risk taking propensity for women only. Among women, experience of social rejection was positively associated with higher scores on the BART. Among men, experiencing social rejection during the computer game was not significantly related to BART scores.
Conclusions: The results of this study indicate that increased sensitivity to rejection may be related to women crack cocaine users' vulnerability for engagement in risk taking in general. This may have important assessment and treatment implications regarding the role of social rejection in the risky sexual behavior of female crack/cocaine users.
Financial Support: R01 DA19405

268

SELF-ADMINISTRATION OF IV COCAINE DURING EXTENDED ACCESS IN ADOLESCENT AND ADULT RATS SELECTIVELY BRED FOR HIGH AND LOW SACCHARIN INTAKE.

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Aims: Adolescent rats and rats selectively bred for high (HiS) saccharin intake display drug-prone behavioral profiles compared to adult rats and those bred for low saccharin intake (LoS). The aim of this study was to examine the interaction these vulnerability factors, age and sweet preference, using an animal model of cocaine bingeing.
Methods: Adolescent and adult HiS and LoS female rats were given daily sessions of 2-hr access to iv cocaine (0.4 mg/kg) self administration under an FR 1 schedule of reinforcement for two days. Following this short-access phase (ShA), rats entered a long-access phase (LgA) in which session length was increased to 6-hr for 16 days. Session length was then decreased to 2-hr for a second ShA phase when groups were compared under an FR 1 and progressive-ratio (PR) schedule.
Results: Adolescent LoS rats increased cocaine intake when comparing the first 4 days of LgA with the last. Furthermore, adolescent LoS rats self-administered more cocaine than adult LoS rats over the entire LgA phase. During the ShA phases. Both LoS and HiS adolescent rats self administered more cocaine than their adult counterparts.
Conclusions: These results indicate that the genetically-mediated, addiction-protected profile of the LoS rats may not be expressed until adulthood, and the findings further illustrate that adolescence is period of particularly elevated vulnerability to substance abuse.
Financial Support: This research was supported by NIDA/NIH grants R01 DA019942 and K05 DA015267 (MEC).

269

THE EFFECTS OF BRIEF STRATEGIC FAMILY THERAPY ON PARENT SUBSTANCE USE AND ITS IMPACT ON ADOLESCENT SUBSTANCE USE.

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Aims: Parent substance use has significant effects on adolescent substance use. Dysfunctional family structure and inadequate parenting practices, resulting from parent substance use, are strongly associated with adolescent substance use.
The aims sought to determine the effects of Brief Strategic Family Therapy (BSFT) on parent substance use; to determine the impact of parent substance use on adolescent substance use; and to examine the mediating effects of family functioning on the relationship between parent substance use and adolescent substance use.
Methods: ASI lite was used to assess parent alcohol and drug use at baseline and at 12 months post randomization. Timeline Follow Back was used to assess adolescents' substance use at baseline and monthly for 12 months post randomization. Family Environmental Scale and Parenting Practices Questionnaire were used to assess family functioning at baseline, 4, 8 and 12 months post randomization.
Results: Generalized estimated equations revealed that parents in BSFT significantly decreased their alcohol score from baseline to 12 months at a rate of 0.74 (RR=0.74, 95% CI [0.59, 0.93]). Wilcoxon analyses revealed that children of parents who reported substance use at baseline had twice as many days of reported drug use at baseline compared with children of parents who did not use or only used alcohol ($\chi 2(2)=7.58$, $p=0.02$). Mixed model longitudinal analyses showed that adolescents in BSFT had a significantly lower trajectory of substance use than those in TAU ($\beta=-7.82$, $p<0.001$) if their parents used substances at baseline. Mediation analyses indicated a statistically significant effect ($\beta=-0.01$, 95% CI [-0.0002, -0.0003]), evidence that change in family functioning significantly predicts parent alcohol use.
Conclusions: Results indicate that BSFT is effective in reducing alcohol use in parents, and in reducing adolescent's substance use if their parents were also using at baseline.
Financial Support: This work supported by NIDA Grant (U10 DA 13720), José Szapocznik, Principal Investigator.

270

NEUROPSYCHOLOGICAL IMPAIRMENT IN DRUG ABUSERS: IMPLICATIONS FOR ADDICTIONS TREATMENT.

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Aims: Aim: While neuropsychological impairment from the neurotoxic effects of selected drugs of abuse is well accepted, it is less well accepted which abused drugs of abuse cause neuropsychological impairment. The relationship of neuropsychological impairment in different types of drug abusers has important implications for addictions treatment. This poster discusses data on the Trail Making test (TMT), a neuropsychological test, with respect to neuropsychological impairment in different types of drug addicts and implications for addictions treatment.
Methods: Method: Data from a national federally funded study of drug abuse treatment on a sample of over 10,000 subjects all of whom were administered the TMT will be presented. TMT scores for different types of drug abusers (Cocaine, Heroin, etc.) will be contrasted and compared to commonly accepted criteria for neuropsychological impairment. Different degrees of neuropsychological impairment on the TMT for different drugs of abuse will be used as a basis for drawing implications for addictions treatment.
Conclusions: Conclusions: Different drugs of abuse have varying levels of neuropsychological impairment. Implications for addictions treatment are that the level of neuropsychological impairment should be considered when planning addictions treatment for different types of drug abusers.
Financial Support: Supported by private funding (data used are now available to the public)

271

THE STATE OF CLINICAL SUPERVISION IN COMMUNITY-BASED SUBSTANCE ABUSE TREATMENT PROGRAMS: A SURVEY OF OUTPATIENT TREATMENT PROVIDERS IN THE MID-ATLANTIC AND MOUNTAIN WEST ATTC REGIONS.

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Aims: Researchers and practitioners agree that clinical supervision is essential for providing quality substance abuse treatment services. However, what is less clear is what constitutes clinical supervision practices in community settings and the best methods for training clinical supervisors in rural/frontier areas. The purpose of this study was to determine the type, amount, and frequency of clinical supervision being conducted in community-based substance abuse treatment programs in 10 rural and frontier states.
Methods: Using SAMHSA's Substance Abuse Treatment Facility Locator, 638 adult outpatient treatment providers were identified in Colorado, Idaho, Kentucky, Montana, Nevada, Tennessee, Utah, Virginia, West Virginia, and Wyoming. A brief web-based survey was conducted to examine clinical supervision practices using a randomly selected sample of providers.
Results: Findings show that clinical supervision facilitates clinical skills development, encourages self-awareness, and prevents burnout. However, it is primarily problem-oriented and conducted on an as needed basis, and with counselors who have less than one year experience.
Conclusions: Clinical supervision is considered a critical element in providing quality care and has been shown to be positively associated with staff retention. However, many community-based treatment providers report a disconnect between the agency and staff to establish the reason for supervision, specifically related to: 1) individual skills & ability development versus providing a tool for the agency in the development of their personnel evaluation procedures; and 2) the agency is required to have someone conduct supervision for funding, but agency and/or staff members have little investment in supervision outcomes.
Financial Support: Funded by SAMHSA/CSAT: Mid-Atlantic ATTC and Mountain West ATTC

272

THE ROLE OF DRUG MARKET FACTORS IN SHAPING INJECTING INITIATION AND CURRENT PATTERNS OF DRUG USE: FINDINGS FROM THE MELBOURNE INJECTING DRUG USER COHORT STUDY.

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Aims: Drug markets have been identified as a key driver of drug-related harm within the broader risk environment of people who inject drugs (PWID). Few studies however have examined how changes within drug markets affect drug use patterns and associated harms. We examined the impact of changes in heroin availability on injecting initiation and patterns of drug use among a cohort of PWID in Melbourne, Australia.
Methods: Socio-demographic and drug use information was collected from 688 PWID. Participants were grouped by the year in which they initiated injecting (pre-2001, 2001-2005, post-2005) and patterns of drug use at initiation, and currently, were compared using chi-square tests.
Results: The greatest proportion of participants initiated injecting during a time of high heroin availability (pre-2001, 62%). These PWID were significantly younger at injecting initiation compared with newer injectors (median age 16y vs. 21y among post-2005 initiates; $p<0.01$). Patterns of drug use at initiation reflected drug market characteristics; 53% of PWID initiated with heroin during the period 2001-2005, a period associated with a dramatic decrease in heroin availability, compared with 67% in the pre-2001 group ($p<0.01$). There were no significant differences between newer and long-term injectors in drug types currently used or frequency of injecting in the month preceding interview, although a greater proportion of long-term injectors were on OST ($p<0.01$).
Conclusions: Drug market factors appear to play a role in influencing both patterns of injecting initiation, and current drug use, independent of duration of injecting. These findings point to the need to consider both drug market and drug user characteristics when developing and implementing public health programs.
Financial Support: Colonial Foundation Trust; Australian National Health & Medical Research Council.

273

GROWTH MIXTURE MODELS PREDICTING EARLY ADULT SUBSTANCE USE FROM TRAJECTORIES OF INATTENTION, IMPULSIVITY-HYPERACTIVITY, DELINQUENCY, AND IMPAIRMENT.

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Aims: Identify distinct trajectories of change in ADHD symptoms, delinquency, and impairment that describe differential substance use outcome in young adulthood.
Methods: Children with DSM-IV ADHD Combined Subtype (n=579), who participated in the multi-site Multimodal Treatment of ADHD study, completed follow-up interviews 12 years post baseline (ages 17 to 25). Up to 4 assessments during childhood treatment and up to 4 assessments during adolescence measured symptoms of inattention, impulsivity-hyperactivity, delinquency, and impairment. Binge drinking and marijuana use were assessed in early adulthood. Growth mixture models identified latent classes (subgroups) showing distinct symptom and behavior trajectories preceding early adult binge drinking and marijuana use.
Results: Models identified trajectory classes distinguishing high substance use (binge drinking about once per month; marijuana use > once per week) from low substance use (binge drinking 1-7 times per year; marijuana use 0-3 times per year). Trajectories associated with high substance use showed worsening post-treatment and adolescent symptoms and behavior. Trajectories associated with low substance use showed stable or improving post-treatment and adolescent symptoms and behavior.
Conclusions: Findings show that patterns of persistent and worsening ADHD symptoms, delinquent behavior, and functional impairment imply greater risk for elevated substance use in early adulthood. Symptom and behavior stability or gradual improvement, irrespective of severity, implied low risk. Results suggest the importance of developing interventions to address ADHD symptoms and impairment in adolescence; childhood treatment success by itself does not insure against adult substance use because adolescent sequelae are varied.
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274

INVESTIGATION OF BASELINE FACTORS PREDICTING LONGITUDINAL METHAMPHETAMINE USE IN TWO CONTINGENCY MANAGEMENT CLINICAL TRIALS.

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Aims: This investigation evaluated the ability of multiple baseline factors (e.g., baseline methamphetamine use, education, income, etc.) to predict longitudinal methamphetamine (M-AMP) use while receiving contingency management (CM) and psychosocial treatment in 2 different clinical trials to treat patients with a M-AMP dependence diagnosis. Our primary hypothesis was that baseline M-AMP use would be positively predictive of M-AMP use while in treatment.
Methods: Data from 2 concurrent CM clinical trials (N=237) were used for this investigation. These two trials were identical except for the type of CM intervention. One trial manipulated the duration of CM (standard treatment, 1 month of CM, 2 months of CM, or 4 months of CM) while the other manipulated the schedule of CM reinforcement (standard treatment, continuous CM, intermittent-predictable CM, or intermittent-unpredictable CM). Each intervention period was 4 months in length. Robust generalized estimation equation procedures were the analytic approach used to evaluate M-AMP positive urine (UA+) over time.
Results: Baseline M-AMP UA+ significantly predicted an increase in M-AMP use over time (OR= 13.15, CI: 8.24-21.00). In addition, lower education (OR= 3.68, CI: 2.21-6.13), lower income (OR= 2.29, CI: 01.41-3.73), the addiction severity index drug composite (OR= 33.46, CI: 3.07-364.61) and legal composite (OR= 2.97, CI: 1.03-8.54) were also associated with increased M-AMP use over time. Lastly, a higher psychiatric composite score was associated with a decrease in M-AMP use (OR= 0.62, CI: 0.10-0.37) over time.
Conclusions: Consistent with our hypothesis, baseline M-AMP use was predictive of M-AMP during treatment. Taken with the additional baseline factors that were predictive of M-AMP use during treatment, these results suggest that key baseline factors may help inform future interventions designed to effectively target and treat M-AMP dependent individuals.
Financial Support: Department of Justice, Life Science Discovery Fund, and grants R01DA017407 and R01DA017084 from the National Institute of Drug Abuse (NIDA; Roll, PI).

275

MATERNAL SUBSTANCE ABUSE AND CHILD BEHAVIOR: A 10-YEAR PROSPECTIVE STUDY.

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Aims: Abuse of alcohol and illicit drugs can cause serious psychological and physical health problems for mothers and their children. This study examined children of substance-abusing mothers approximately 10 years after mothers' admission to drug abuse treatment, with the aim of identifying maternal characteristics that may be risk factors for child behavior problems on the Child Behavior Checklist (CBCL).
Methods: Data were obtained from 396 mothers who were included in a sample consecutively admitted to 44 treatment programs in 13 California counties during 2000-2002. Addiction Severity Index was administered at both intake and follow-up. Each mother completed the CBCL for one child 6-17 years of age.
Results: About 22% of the children of substance-abusing mothers demonstrated borderline or clinical range problem behaviors. Child behavior problems were related significantly to the mothers' ethnicity (lower among Hispanics relative to white), and problem severity in family/social relationship and mental health, marginally related to her prior medical/health problem, and not related to severity in alcohol, drug, legal and employment.
Conclusions: Assisting mothers to address their family/social relationship and psychological problems may have an added value to prevent or reduce their children's behavioral problems.
Financial Support: This study is funded by the National Institute on Drug Abuse Grant No. R01DA021183 & P30DA016383 (PI: Hser). Dr. Hser is also supported by K05DA017648.

276

SYNTHESIS AND MONOAMINE TRANSPORTER BINDING AFFINITY OF ENANTIOMERIC HYDROXYLATED 1-[2-[BIS(4-FLUOROPHENYL)METHOXY]ETHYL]-4-[3-(FLUOROPHENYL)PROPYL]PIPERAZINES.

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Aims: To develop novel positron-emission tomography (PET) imaging agents for dopamine transporter (DAT), potent and selective DAT inhibitors with appropriate pharmacokinetic properties, such as lipophilicity, are sought. In this report, a series of enantiomeric fluoro-substituted hydroxyl-containing derivatives of 1-[2-[bis(4-fluorophenyl)methoxy]ethyl)-4-(3-phenylpropyl)piperazine (GBR12909) was synthesized. The binding affinities of these hydrophilic GBR12909 derivatives for DAT, serotonin transporter (SERT), and norepinephrine transporter (NET) were determined.
Methods: The optically pure target compounds 1-12 were prepared from chiral synthons, which were obtained by asymmetric synthesis. The logP values of compounds 1-12 were determined by reverse-phase HPLC and are in the range of 3.44-3.83.
Results: In the series, (S)-enantiomer of p-fluorophenylpropan-3-ol derivative 7 exhibited the highest DAT binding affinity (Ki = 1.70 nM) and possessed 90- and 22-fold selectivity for DAT over SERT and NET, respectively. Compound 8, the corresponding (R)-enantiomer of 7, also showed high DAT binding affinity (Ki = 3.00 nM) and demonstrated 52- and 21-fold selectivity for DAT over SERT and NET, respectively.
Conclusions: Based on the preliminary data, compounds 7 and 8 are potential leads for the development of PET tracers for DAT.
Financial Support: NSC, ROC (NSC 100-2325-B-002-008) and Intramural Research Program, NIDA, NIH, DHHS.

277

DEVELOPMENT OF OBESITY AND RISK BEHAVIORS IN ADOLESCENCE.

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Aims: This study examines pathways of obesity among U.S. children from age 6 to 18 and associations of such pathways with substance use, delinquency and psychosocial health in adolescence.
Methods: Using group-based trajectory modeling on obesity status (BMI percentile≥95%) from age 6 to 18, the study examines trajectories of obesity among 5,156 adolescents from the child sample of the 1979 National Longitudinal Survey of Youth (NLSY79).
Results: Four distinctive obesity trajectories were identified and labeled as "High," "Decreased," "Increased," and "Low". About 8.5% of adolescents remained at a high level of risk of obesity from ages 6 to 18 (High), indicating individuals as chronically obese. Another 5.7% (Decreased) and 5.1% (Increased) respectively exhibited a decelerated and an accelerated trajectory. Individuals in the former group were obese at early ages but had normal weight at later ages; conversely, individuals in the latter group had normal weight at early ages but become obese at later ages. Majority of adolescents (80.7%) remained with normal weight across ages and showed a consistently low obesity trajectory (Low). Males were overrepresented in the High and Increased groups; females were more likely to belong to the Decreased group. Blacks were overrepresented in the in the High, Increased, and decreased groups. Adolescents in the Increased group were more likely than other trajectories to experience poorer psychosocial health. Though obesity trajectories were not predictive of alcohol or marijuana use, adolescents in the High group had the highest increase of smoking over time compared the Low and Decreased groups. Those in the Increased group were most likely to smoke across all trajectories. Those in the High group also had the lowest levels of delinquency across adolescence.
Conclusions: Adolescents having a transition into obesity status in adolescence are the most vulnerable group and need additonal assistance.
Financial Support: This study is supported by R03HD064619 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

278

PREFRONTAL ACTIVATION DURING FACIAL EMOTION-PROCESSING DIFFERENTIATES YOUTH AT HIGH VS. LOW RISK FOR THE DEVELOPMENT OF SUBSTANCE USE DISORDERS.

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Aims: Several recent longitudinal studies have demonstrated that addiction risk may be influenced by a cognitive, affective and behavioral phenotype that emerges during childhood. We aim to characterize neural activation on a facial emotion-processing task in a sample of children deemed high- (HR) or low-risk (LR) for the eventual development of a substance use disorder (SUD).
Methods: The HR group was composed of 10-14 year old children with 1) a paternal history of SUDs, 2) another relative with a SUD, and 3) ADHD and disruptive behavior. The LR participants had no such history. Exclusion criteria were current non-stimulant psychotropic use, >5 instances of substance use, or other mental illness. We acquired functional MRI scans during a facial emotion-matching task.
Results: 22 children (59% males; mean age 12.09 years) were recruited according to HR (n=12) and LR status (n=10). Groups were demographically matched. On the facial emotion matching task, high rates of accuracy when matching shapes (HR: 93% LR: 93%) and faces (HR: 77% LR: 72%) were seen, suggesting adequate attention to the task. There were no accuracy differences between the groups. Whole brain voxel-wise analyses revealed that the LR group had significantly greater BOLD signal activation (faces – shapes) in the superior frontal cortex (BA10; p<.01; Talairach cluster peak coordinates: [-25 35 36], K=91 voxels).
Conclusions: Consistent with existing knowledge on the prefrontal cortex's (PFC) role in emotion processing and regulation, these data suggest that compared to the HR group, LR youth demonstrate greater activation within the PFC on a facial emotion-processing task. They support our hypothesis that HR youth demonstrate neural activation impairments that predate substance use. Interventions that modulate PFC circuitry may hold promise in preventing the onset and escalation of problem drug use.
Financial Support: Funding from NIDA/AACAP (K12DA000357) supports this research.

279

DEVELOPING QUALITY INDICATORS FOR ADOLESCENT SUBSTANCE USE TREATMENT PROGRAMS: DOES URINE DRUG SCREENING MATTER?

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Aims: Little information exists about adolescent treatment program features that predict good client outcomes. Moreover, little is known about the post-treatment effectiveness of urine drug screening (UDS) provision within adolescent treatment settings.
Methods: In order to determine whether a program characteristic, such as UDS, may identify programs associated with better client outcomes, we examined data from 67 community based treatment providers that were awarded Center for Substance Abuse Treatment funding to provide outpatient adolescent treatment services. Through an administrative survey conducted with program administrators, we categorized programs that provided UDS (n = 55) from those that did not (n = 12). Using propensity weighting to balance the two client groups on 22 pretreatment characteristics, we tested the hypothesis that programs using UDS would be more effective than non-UDS programs by comparing client outcomes at 6- and 12-months post intake in terms of substance frequency, substance problems, recovery and institutionalization using responses from the Global Appraisal of Individual Needs.
Results: In contrast to our hypothesis, preliminary findings indicate that youth enrolled in the non-UDS programs experienced either better outcomes or outcomes that were no different from similar youth enrolled in the UDS programs. However, these findings must be placed in context since they do not control for the specific types of treatment services received by youth in the programs. Additional analyses are being conducted to rule out possible confounding variables such as (e.g., criminal justice involvement) and to provide more information on how programs that do and do not UDS differ beyond pretreatment characteristics.
Conclusions: These results suggest that UDS provision in the context of adolescent treatment may not result in better outcomes as evidenced at 12 months post-treatment.
Financial Support: R01 DA017507-05 (Morral, PI)

280

AGE-DEPENDENT DIFFERENCES IN MORPHINE-INDUCED TASTE AVERSIONS.

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Aims: Adolescence is a developmental period of particular importance given the host of neurobiological changes that occur during this stage of development which may leave adolescents more susceptible to the use of addictive substances. Given that drug use and abuse is said to be a function of the balance of its rewarding and aversive effects (with the aversive effects acting to limit overall drug intake), any age-dependent differences in morphine's aversive effects could differentially impact subsequent drug intake. The present experiments examined the ability of morphine sulfate to induce taste aversions in adolescent and adult rats.
Methods: Adolescent and adult rats were given every other day a novel saccharin solution to drink and were subsequently injected with morphine (0, 3.2, 10, 18 mg/kg). On intervening days, they were given water access with no drug injection; a procedure repeated for four cycles.
Results: During conditioning, adults exhibited aversions by Session 2, whereas the adolescents did not exhibit aversions until Session 3. Further, aversions were significantly stronger in adults. On a subsequent two-bottle aversion test, all morphine-treated subjects drank significantly less saccharin relative to vehicle-treated controls; however, adults exhibited significantly stronger taste aversions at 10 and 18 mg/kg than adolescents with Age predicting the degree of morphine-induced aversion expressed.
Conclusions: Adolescents displayed a reduced sensitivity to the aversive properties of morphine as evidenced by weaker taste aversions which took longer to be acquired relative to adults. These differences in morphine-induced CTAs extend the findings with other drugs of abuse for which adolescents exhibit weaker aversions, suggesting that they differ in their sensitivity to the aversive effects of drugs. This differential sensitivity may shift the balance of reward and aversion evident with such drugs, increasing the general vulnerability to use and abuse in the adolescent population.
Financial Support: Supported by a grant from the Mellon Foundation to ALR and to ZEH and APM.

281

EFFICACY OF FIVE WEEKS OF ESCALATING AND FIXED CONTINGENCY MANAGEMENT REINFORCEMENT ON ILLICIT DRUG USE IN OPIOID-DEPENDENT PREGNANT PATIENTS.

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Aims: Contingency management (CM), reinforcing target behaviors with vouchers, improves treatment adherence and decrease substance use in pregnant women. The Drug Abuse Incentive Systems (DAISY) study compared the relative efficacy of 13 weeks of escalating vs. fixed CM voucher schedules for reducing opioid and cocaine use in methadone-maintained opioid-dependent pregnant women. No significant difference in efficacy by CM schedule was observed. Explanations for these results included temporal delays in receiving reinforcers after providing urine samples and resetting escalating vouchers after positive but not missed samples. This secondary data analysis aims to determine CM efficacy after 5 weeks and to examine how failure to reset the escalating group after missed urines impacts efficacy.
Methods: This is a secondary data analysis of 90 women (escalating CM, n=52; fixed CM, n=38) who completed the DAISY study. Drug abstinence variables and missing urines from the escalating vs. fixed groups were analyzed at 5 weeks using t-tests. Missing urines were assumed positive.
Results: No statistically significant difference in abstinence variables was found between escalating and fixed conditions after 5 weeks: mean(SD) number of drug negative urines were 8.1(4.5) and 7.4(4.3), for escalating and fixed groups, respectively (p=0.46). Assessment of missed urines showed no difference between escalating and fixed groups. No difference was found between number of missed urines at 5 vs. 13 weeks.
Conclusions: Study results do not support the hypothesis that lack of findings in 13 weeks was attributable to not resetting the escalating group to baseline earnings after missed urines. The results extend the hypothesis that time-to-reinforcement is critical to CM efficacy and underscore the behavioral principle regarding the importance of immediately delivering the reinforcer after the target behavior is emitted.
Financial Support: NIDA: DA 14203

282

EXPOSURE TO ETHANOL DURING ADOLESCENCE OR ADULTHOOD ALTERS COCAINE SELF-ADMINISTRATION IN ADULT RATS.

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Aims: Although alcohol is one of the most commonly used drugs during adolescence, little work has examined the long-term effects of adolescent alcohol exposure on the response to other drugs in adulthood. The present study examined the effects of adolescent alcohol exposure on cocaine self-administration in adult rats. To determine if effects were due to the adolescent developmental period, the same procedure was replicated in adults.
Methods: Male rats were exposed to ethanol (2 g/kg) or vehicle for 10 days (PND 30-39 or 70-79). On PND65 or 105, operant training began with fixed-ratio 1 (FR1) responding for food. This was continued until each animal had 3 consecutive days of 100 or more responses. Following the FR1 sessions, animals were given 2 days of progressive-ratio (PR) responding for food. Subjects were then implanted with an indwelling jugular catheter. After recovering, animals underwent 10 days of FR1 responding for either 0.25 or 0.75 mg/kg/infusion cocaine, followed by 2 days PR responding for cocaine.
Results: Animals exposed to ethanol during adolescence showed decreased PR responding for food relative to vehicle-treated controls. During cocaine acquisition, animals preexposed to ethanol and conditioned with 0.25 mg/kg/infusion cocaine administered significantly less drug across the session than any other group. No differences were seen with PR responding for cocaine. Animals exposed to ethanol as adults did not show any preexposure differences in food responding, but displayed a similar decrease in responding for the 0.25 mg/kg/infusion dose of cocaine following ethanol preexposure. No preexposure effects were seen during cocaine PR responding.
Conclusions: Exposure to alcohol during adolescence or adulthood alters cocaine self-administration later in life. Early life ethanol exposure reduced PR responding for a natural reinforcer, and responding for a low dose of cocaine was altered in both age groups. These changes may indicate a change in sensitivity to the rewarding effects of cocaine following ethanol preexposure.
Financial Support: This work was supported by a grant from the Mellon Foundation to ALR.

283

SUBSTANCE USE HISTORIES OF ADULTS SEEKING A MEDICAL MARIJUANA CARD.

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Aims: Despite the fact that numerous states have legalized the use of marijuana for medical purposes, very little is known about medical marijuana users. The present study intended to describe the substance use of adults seeking medical marijuana in the state of Michigan.
Methods: Research staff recruited 347 patients from the waiting area of a clinic in Michigan that writes prescriptions for medical marijuana. Research staff approached all patients in the waiting room; 94% of those approached consented to participate.
Results: Most participants (95.1%) reported some lifetime marijuana use; however, within the 3 months prior to visiting the medical marijuana clinic, 23.6% of the sample reported that they had not used marijuana or only used it occasionally. Extramedical use of opioid pain medications was common; 73% of participants reporting that they had used prescription opioids differently than prescribed (i.e., more than prescribed, used medications belonging to someone else, or used medications for reasons other than pain relief) in the past 3 months. Approximately, 44% of participants indicated that they were trying to cut down their use of prescription opioid pain medication. The percentage of participants reporting lifetime use of specific substances was as follows: cocaine- 32.9%, amphetamine- 22.2%, sedatives without a prescription- 23.3%, hallucinogens- 33.3%, and heroin/street opioids- 8.3%. However, past 3-month use of these substances was relatively rare.
Conclusions: In addition to marijuana, adults seeking medical marijuana cards report extensive prior substance use. In terms of current substance use, extramedical use of opioids was common, with many participants reporting that they hoped to decrease use of opioids once they gain access to a medical marijuana card.
Financial Support: This project was supported with pilot funds from the Department of Psychiatry at the University of Michigan.

284

COMPARING ALCOHOL AND OTHER DRUG PROBLEMS AMONG JUVENILE DETAINEES IN AUSTRALIA AND THE UNITED STATES.

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Aims: Similar to what is found in the United States, problematic drug and alcohol use among juvenile detainees in Australia is more prevalent than in the general community. This study will compare characteristics of drug and alcohol abuse among juvenile detainees in Australia and the United States.
Methods: Analysis of the 2009 New South Wales Young People in Custody Health Survey which recruited 361 juvenile detainees and had an 80% response rate. The survey included a physical health exam, a dental check, a health questionnaire, psychometric testing for IQ and mental health and a criminal history. Comparisons will be made with published research (Teplin et al, 2002) on American juvenile detainees.
Results: The Australian sample was 88% male, 48% of Aboriginal origin and with an average age of 17 years. The American sample was similarly over-represented by African-Americans (55%) but had a higher proportion of young women (36%) and a younger average age of 15 years. Australian participants had poor social determinants of health including 27% being placed in care, 45% who had parents' previous incarcerated, and 60% with a history of child abuse or trauma. Nearly two-thirds (64%) of Australian juvenile detainees met diagnostic criteria for an alcohol or substance use disorder, compared to approximately 50% of juvenile detainees in the United States. Further, Australian juvenile detainees had nearly twice the prevalence of alcohol use disorder (49% males, 54% females) compared to American juvenile detainees (26% males, 27% females).
Conclusions: In both the United States and Australia, young people in juvenile detention have extremely high rates of alcohol and drug problems and come from more disadvantaged backgrounds compared to the general community of Australia. More resources and programs are needed to intervene with these high risk young people in contact with the criminal justice system.
Financial Support: This Australian study was funded by Juvenile Justice NSW, Justice Health NSW, and the NSW Department of Health Centre for Aboriginal Health.

285

TO EXERCISE OR NOT TO EXERCISE?: POSING THE QUESTION TO WOMEN WITH SUBSTANCE USE DISORDERS.

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Aims: Substance use disorder (SUD) treatments often yield modest effects. Strategies to improve outcomes & prevent relapse are important, especially for women. A promising therapeutic adjunct may be exercise, which is associated with decreased craving and increased abstinence rates in cigarette smokers. However, few published studies have examined effects of exercise on recovery from other SUDs. The purpose of this ongoing study is to identify facilitators and barriers to regular exercise in women with SUDs.
Methods: Participants completed anonymous surveys about demographic, substance use, mood, stress and personality traits, and exercise-related variables. Recruitment occurred at a CTN-affiliated residential women's treatment program. To-date, N=40 (final projected sample: N=100) women have completed the survey. Descriptive statistics were used to summarize preliminary findings.
Results: Participants were predominantly single (78%) and African-American (75%) with average age of 40 years. Heroin (48.7%) and crack/cocaine (28.2%) were the most frequent drugs of choice and two-thirds of sample scored in the moderate to severe range for depression. Nearly half (48%) expressed strong interest in regular exercise during SUD treatment and over two-thirds believed healthy diet was important to recovery. Over half (52%) of women reported serious medical problems, however, and depressed women were more likely to report that health issues limited their activity levels.
Conclusions: There is significant interest among SUD women in treatment about exercise as a supplement to their recovery program. Interventions that focus on overall health in this at-risk population may provide a unique opportunity to reduce relapse risks. More research is needed to better understand how best to integrate exercise with SUD treatment and promote compliance.
Financial Support: This research is supported by NIH R36 DA30619,2U10 DA013034, and Institute for Women's Health (VCU).

286

INCREASED HISTONE ACETYLATION STRENGTHENS THE EXPRESSION OF COCAINE-ASSOCIATED CONTEXTUAL MEMORY.

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Aims: Epigenetic regulation of chromatin structure is an essential molecular mechanism that contributes to the formation of synaptic plasticity and long-term memory (LTM). An important regulatory process of chromatin structure is acetylation and deacetylation of histone proteins. Inhibition of histone deacetylase (HDAC) increases acetylation of histone proteins and facilitate learning and memory. The present study investigated the effect of the HDAC inhibitor sodium butyrate (NaB) on induction and extinction of cocaine-induced conditioned place preference (CPP).
Methods: In experiment 1, adult male C57BL/6 mice received a single injection of NaB (1.2g/kg) prior to conditioning by cocaine (15mg/kg x 4 days). In experiment 2 mice were conditioned by ascending doses of cocaine and NaB was given a) immediately following memory retrieval and during extinction trials or b) during extinction trials only.
Results: A single injection of NaB (1.2g/kg) increased total H4 histone acetylation in the hippocampus (160%) and amygdala (190%). In experiment 1, pre-conditioning administration of a single injection of NaB had no effect on the magnitude of CPP but it prolonged the expression of CPP (resistance to extinction) compared to control. In experiment 2, administration of NaB immediately following memory retrieval, beginning on the first CPP test, augmented the expression of CPP in subsequent tests compared to controls. Administration of NaB following the second CPP test, and during the extinction trials, did not accelerate extinction learning. However, reconditioning by saline (confinement) extinguished CPP in the NaB and control groups. Reinstatement tests showed no further differences between the two groups. Reinstatement of CPP was achieved by a) footshock stress and b) cocaine priming.
Conclusions: Results suggest that an increase in H4 histone acetylation has long-term effects on strengthening the expression of cocaine-associated contextual memory. However, NaB neither accelerated extinction nor prevented reinstatement of CPP.
Financial Support: Supported by R01DA026878 and R21DA029404

287

THE REWARDING EFFECTS OF NICOTINE ARE ENHANCED IN DIABETIC RATS.

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Aims: Diabetic patients are more prone to the harmful effects of tobacco abuse; however, it is unclear whether they experience enhanced rewarding effects of nicotine. Much research has shown that the rewarding effects of nicotine are mediated by dopamine transmission in the nucleus accumbens (NAcc). The goal of the present study was to examine the role of dopamine in modulating the rewarding effects of nicotine in diabetic versus healthy control rats. Nicotine self-administration (SA) and changes in NAcc dopamine levels in response to nicotine were compared in diabetic and control rats. Dopamine transporter (DAT) expression in the NAcc was also compared in diabetic and control rats that self-administered nicotine.
Methods: Rats were given vehicle or streptozotocin (45 mg/kg), a drug that produces toxicity to insulin-producing pancreatic cells. Following diabetes induction, rats were given 23-hour access to saline or nicotine (0.03 mg/kg/0.1 ml inf). Following 10 days of SA, DAT levels were compared via Western blot procedures. In a subsequent study, dopamine levels in the NAcc were assessed following nicotine administration using in vivo microdialysis procedures.
Results: Diabetic rats displayed enhanced nicotine intake in a graded manner, such that rats with the highest levels of nicotine SA also displayed high blood glucose levels. Diabetic and control rats displayed similar levels of DAT following nicotine SA. Similarly, diabetic rats displayed an increase in NAcc dopamine that was similar to control rats following nicotine administration.
Conclusions: Our results suggest that dopamine systems in the NAcc may not mediate enhanced vulnerability to nicotine in diabetic rats. Our finding that diabetic rats display enhanced rewarding effects of nicotine, suggests that strong rewarding effects of nicotine may contribute to enhanced tobacco abuse in patients with diabetes.
Financial Support: Financial support: 5G12 RR008124 and 2T34GM008048

288

COSTS AND SAVINGS OF OFFENDER DRUG DIVERSION: AN SEM ANALYSIS OF CALIFORNIA'S PROPOSITION 36.

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Aims: Proposition 36 was meant to divert low-level California offenders arrested for non-violent, drug-offenses into Substance Use Disorder (SUD) treatment in lieu of incarceration. Previous work revealed the beneficial cost-savings associated with the law's passage and their dependence on demographic and contextual factors. We extend prior findings by conducting a multi-level structural equation model (MLSEM) assessment of Proposition 36's cost savings to provide the most comprehensive assessment of its cost effect.
Methods: We utilized a time-lagged cohort approach comparing individuals convicted of Proposition 36 eligible offenses before, and immediately after, its passage. Individual-level, administrative data from a number of criminal justice, health, SUD treatment, and employment sources were combined with county-level data. A MLSEM model was fit assessing the direct, and mediating, role of Proposition 36 in producing cost-effects across eight cost domains: prison, jail, parole, probation, arrest, conviction, health, and SUD treatment.
Results: Supporting and extending previous findings, results revealed unique roles for Proposition 36 across the eight domains, with differential effects for gender and racial subgroups. Specifically, substantial savings on prison and jail costs, and increased SUD treatment costs, were revealed for male participants and for Black, rather than White or Hispanic participants. Post-conviction earnings, and past criminal history were also found to play differential roles for costs across racial groups.
Conclusions: Proposition 36 was found to produce substantial cost-savings for men with more severe criminal histories and those with minority status. The relative ineffectiveness of participation for women should be noted and examined further, especially within the domains of re-arrest and re-incarceration. To improve cost-effectiveness, additional services, increased supervision, and greater availability of residential treatment may be needed for particular sub-populations of Proposition 36 participants.
Financial Support: This work was supported by funding from the Anglin Research fund

289

UTILITY OF PEER RECOVERY COACHES IN ENGAGING SUBSTANCE-ABUSING PARENTS INTO TREATMENT.

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Aims: We examined the effectiveness of peer recovery coaches (PRCs) in facilitating engagement into substance abuse treatment for child welfare-involved parents with substance exposed newborns or parents who use methamphetamine. We hypothesized that clients with PRCs would engage at a higher rate and more rapidly, and would remain in treatment for a longer period of time, than clients without PRCs.
Methods: Administrative data were obtained for 7506 parents or caregivers referred to a specialized substance abuse outpatient treatment program over a three year period from the treatment agency and the state child welfare agency. The treatment condition consisted of 681 clients with PRCs. To minimize the likelihood of spurious relationships, propensity score matching on key variables was used to identify a matched control sample (n=681). Across both samples, average client age was 29 (SD=7) years, approximately 80% were female or Caucasian, 67% used methamphetamine, and about 71% had a substance-exposed newborn. Index children's median age was one day.
Results: According to statistical tests, PRCs were associated with more rapid successful outreaches (M=3.2 days quicker), engagement in an assessment (M=4.1 days quicker), and services initiation (M=3.8 days quicker). A higher rate of services initiation (7.1% increase), and a greater length of treatment (M=27.1 days longer) was observed among clients who received a PRC.
Conclusions: The research provides strong evidence that PRCs are effective in engaging and retaining child welfare-involved clients who are methamphetamine using parents or parents of substance exposed newborns. Specifically, the provision of a peer recovery coach reduced the duration of time from referral to successful outreach and clinical assessment, as well as improved service initiation. Peer recovery coaches significantly increased length of treatment.
Financial Support: Regional Partnership Grant awarded to the State of Arizona from SAMHSA.

290

RESTING STATE BRAIN NETWORKS DIFFER BETWEEN NICOTINE-DEPENDENT SMOKERS AND NON-SMOKERS.

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Aims: Brain dysfunction in regions such as the prefrontal cortex (PFC) and dorsal striatum (DS) contributes to habitual drug use. These regions are constituents of cortical and sub-cortical brain networks thought to be involved in drug addiction. To investigate whether these networks differ between nicotine dependent female smokers and age-matched non-smoking controls, we employed functional MRI (fMRI) at rest.
Methods: Data were processed with independent component analysis (ICA) to identify "resting state" networks (RSNs). In all subjects, we identified a subcortical limbic network and three discrete PFC networks: a medial prefrontal cortex (mPFC) network and right and left lateralized fronto-parietal networks (FPN). To identify potential alterations associated with habitual drug use, a dual regression approach was used to compare RSN coupling between smokers and non-smokers.
Results: In comparison to non-smokers, smokers had increased coupling between the left FPN and the mPFC network ($p < 0.01$). Smokers with the greatest FPN-mPFC network coupling had the highest dorsal striatal smoking cue reactivity ($r = 0.55$, $p < 0.03$). This may be significant because the dorsal striatum plays a critical role in maintaining drug-cue associations. Further, there was a correlation between the strength of network coupling and nicotine dependence, assessed using the Fagerstrom test for nicotine dependence ($r=0.46$, $p < 0.06$).
Conclusions: Striatal and prefrontal brain regions play critical roles in cued reward-prediction and behavioral response selection following conditioned learning. Our results support the idea that these brain regions may work as part of networks to facilitate conditioned drug-cue responding, which may contribute to continued drug use. Our findings also suggest that PFC network interactions can differentiate nicotine-dependent smokers from controls, and that resting-state PFC network interactions may be a useful biomarker for dependence severity and possibly for treatment efficacy.
Financial Support: Support provided by NIDA and GlaxoSmithKline.

291

ON THE RELATION BETWEEN DELAY DISCOUNTING AND DEMAND IN COCAINE ADDICTS.

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Aims: Bickel et al. (2011a) described addiction as pathological patterns of behavior resulting from persistent overvaluation of an addictive reinforcer and excessive preference for immediate reinforcers. These behavioral characteristics mirror the behavioral economic concepts of demand and delay discounting. Unfortunately, few studies have examined the relation between these concepts in addiction. The current study examined these relations.
Methods: The relation between delay discounting (i.e., discounting rate; ln[k]) and demand curve measures (i.e., breakpoint, p-max, and o-max) was examined in a sample of 37 treatment-seeking cocaine addicts. Delay discounting rates for: money now, money later (M-M); money now, cocaine later (M-C); cocaine now, cocaine later (C-C); cocaine now, money later (C-M); were collected using the procedures outlined in Bickel et al. (2011b). Demand measures were collected using a hypothetical cocaine purchase task modified from the procedures used by Jacobs and Bickel (1999).
Results: Breakpoint (i.e., the highest price at which drugs were hypothetically purchased) was positively correlated with discounting rate in each of the conditions that entailed immediate money (M-M, $r= 0.37$, $p<.05$; M-C, $r=0.33$, $p<.05$) and O-Max (i.e., the maximum spent on drug) was positively correlated with discounting rates in each of the conditions that included cocaine (C-C, $r=0.39$, $p<.05$; M-C, $r=0.38$, $p<.05$; C-M, $r=0.38$, $p<.05$). Moreover, robust and significant correlations were obtained between each of our discounting conditions (all $r = 0.52$ to 0.72, all $p<.001$
Conclusions: Delay discounting rates seem to be more closely related to o-max than p-max, although breakpoint is related to discounting during all conditions that include choices about money
Financial Support: This work was funded by NIDA Grants R01 DA012997 and R01 DA030241.

292

EFFECTS OF INTRA-ACCUMBAL SHRNA AGAINST CART PEPTIDES ON BODY WEIGHT, CART PEPTIDE LEVELS, AND COCAINE-INDUCED LOCOMOTOR ACTIVITY IN RATS.

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Aims: Cocaine- and-Amphetamine-Regulated-Transcript (CART) peptides are peptide neurotransmitters/ neurohormones (rlCART 55-102 and 62-102, Rogge et al Nature Rev Neurosci 9:747, 2008) and are well known regulators of: food intake, body weight, the actions of psychostimulants, other drugs, and other physiologic states (Douglass et al., 1995; Koylu et al., 1998; Lambert et al., 1998; Kristensen et al., 1998; Rogge et al., 2008). To examine the effect of CART peptide depletion in adult rats, CART shRNAs or scrambled control shRNA were administered bilaterally into the nucleus accumbens (NAc).
Methods: Four different shRNA sequences were used (as a cocktail) with a scrambled sequence as a control. Six Male Sprague–Dawley rats (365-425 g) were prepared for bilateral microinjection once into the NAc with either CART shRNAs ($n = 3$) or scrambled shRNA ($n = 3$). Rats were allowed to recover before the first locomotor activity (LMA) experiment. On experiment days (8, 14, 23 weeks after surgery), LMA due to no treatment (baseline), saline, and cocaine (10 mg/kg, ip) was measured. Thereafter, immunohistochemistry (IHC) was done to determine CART peptide levels in the NAc of these same rats.
Results: There was an increase in body weight of the shRNA injected rats compared to the rats injected with the scrambled shRNA (**$p<0.01$), even though this change required an unexpectedly long time - 23 weeks. At this time, there was also an increase in cocaine-mediated LMA in the shRNA injected rats compared to the control rats (*** $p<0.001$). IHC showed a decrease in the staining density of CART peptide in the NAc of the shRNA injected rats compared to the controls (*$p<0.05$).
Conclusions: These data show that shRNA can reduce CART peptides in the NAc and that endogenous CART peptides influence body weight and cocaine-induced locomotor activity. These novel findings are critical support for the hypothesis that endogenous CART peptides in the NAc inhibit and regulate the actions of cocaine and other psychostimulants.
Financial Support: We acknowledge NIH grant support; RR00165, DA15162, and DA015040.

293

TECHNOLOGY TRANSFER PROGRAM: DEVELOPMENT OF AUTOMATED PRIZE-BASED CONTINGENCY MANAGEMENT SOFTWARE FOR DISTRIBUTION TO COMMUNITY TREATMENT CLINICS.

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Aims: Hundreds of studies have shown contingency management (CM) to be one of the most effective known behavioral treatments for substance dependence. The main barriers to its implementation in community clinics are its cost and its technical complexity. The latter problem is addressed by Motivational Incentives Implementation Software (MIIS), which we developed as part of collaborative technology-transfer project between NIDA and SAMHSA. MIIS, which is available to clinics at no cost, is a user-friendly stand-alone program designed for settings where there may be only one computer, and where that computer may be outmoded. MIIS tracks and helps reinforce behaviors such as drug abstinence and counseling attendance. The reinforcement schedule, target behaviors, and prizes can be tailored to the specific needs of the clinic and its patients.
Methods: As part of the development process, we conducted a field test in 25 outpatient volunteers who were also enrolled in other treatment studies in our clinic. Our counseling staff used working versions of MIIS to reinforce participants' attendance at up to 12 counseling sessions for up to 14 weeks. Participants earned opportunities to draw for prizes for each on-time attendance to their regularly scheduled weekly counseling session.
Results: The MIIS software was well received by both staff and participants and improved participant counseling attendance. We used feedback on usability, functionality, and simplicity from staff and participants to modify the software iteratively until a final version was created.
Conclusions: We have evaluated MIIS for usability and robustness under conditions simulating those of a community treatment program with minimal technology support. Availability of MIIS may improve technology transfer of a proven effective treatment to the community.
Financial Support: Supported by the Intramural Research Program (IRP) of the National Institute on Drug Abuse (NIDA), National Institutes of Health.

294

DISCOUNTING OF DELAYED SEXUAL REWARDS IN COCAINE DEPENDENCE IS RELATED TO REAL WORLD SEXUAL RISK BEHAVIOR.

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Aims: Cocaine dependence is associated with high rates of sexual risk behavior and HIV infection. The purpose of this study was to investigate the association between sexual risk behavior and the discounting of future rewards among cocaine-dependent individuals. Discounting for delayed hypothetical sexual outcomes and real monetary outcomes was examined to determine if any relation between sexual risk and discounting was specific to delayed sexual outcomes or applied to delayed outcomes generally.
Methods: 62 Cocaine-dependent individuals completed: (1) the Sexual Discounting Task assessing decisions between immediate unprotected sex and delayed sex with a condom with four hypothetical partners (most and least likely to have a sexually transmitted infection (STI), and most and least sexually desirable); (2) a real rewards money delay-discounting task; and (3) the HIV Risk-Taking Behavior Scale (HRBS) sexual risk subscale to assess self-reported sexual risk behavior during the past month.
Results: Sexual Discounting Task results showed a strong effect of delay in decreasing condom use. Greater sexual risk on the HRBS was significantly associated with increased delay discounting in 3 of the 4 Sexual Discounting Task partner conditions (the "most want to have sex with" condition was not significant). No significant association was found between HRBS sexual risk and money delay discounting. Preference for immediate money in the money discounting task was weakly associated with preference for immediate unprotected sex in the Sexual Discounting Task, with only the correlation in the "most likely to have STI" condition reaching statistical significance.
Conclusions: Results indicate the delay discounting of sexual outcomes is associated with real world sexual risk behavior. The lack of association between sexual risk behavior and money delay discounting suggests domain specificity, consistent with previous research showing that empirical relations involving delay discounting may depend on the nature of the commodity being discounted.
Financial Support: NIDA R21DA026967 & T32DA07209

295

EVALUATION OF THE EFFECTIVENESS OF OVERDOSE RESPONSE TRAINING IN NEW YORK CITY.

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Aims: Drug overdose is a significant cause of mortality in New York City (NYC), with opioids being the most commonly noted drug class in overdose deaths. In an effort to reduce opioid overdose deaths, New York has implemented programs where laypersons are provided brief instruction in recognizing opioid overdoses, and how to provide first aid, including naloxone use. This ongoing study assessed overdose and naloxone administration knowledge among heroin users in NYC.
Methods: Fifty-five participants completed a brief questionnaire that included ratings of 16 putative overdose scenarios for: (i) whether an overdose was occurring and (ii) if naloxone administration was indicated. Thirty individuals completed the questionnaire following a NYS Department of Health overdose prevention training, while a control group (n= 25) received no training.
Results: The trained and un-trained groups, respectively, did not significantly differ in their: age (41.2, 43.6 yrs), education (11.4, 12.0 yrs), heroin use (5.6, 7.1 bags/day) or # of overdoses witnessed (3.5, 2.3). Those who completed training scored significantly higher on opioid overdose recognition ($p < .05$), though training did not increase participants' knowledge of when naloxone should be used. This investigation also revealed interesting data concerning the actions drug users initiated while witnessing an overdose. Approximately half of the participants (53.7%) reported calling 911, with a similar percentage attempting to reverse the overdose by shaking (45.2%) or inflicting pain (54.5%) upon the victim. A minority of individuals reported having attempted ineffectual techniques such as milk (11.9%)or salt water injections(18.6%).
Conclusions: The data indicate that brief opioid overdose training improves participants' ability to recognize opioid overdoses, and stresses the continued need to educate drug users on effective ways to intervene when an overdose is occurring.
Financial Support: Supported by NIDA grant P50DA09236.

296

MOTIVATIONAL-ENHANCED CASE MANAGEMENT UTILIZATION AND ATTENDANCE OF HCV CLINICAL EVALUATIONS.

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Aims: Drug users (DUs) have a high prevalence of hepatitis c (HCV) and many are not engaged in care. We conducted a clinical trial examining the impact of a motivational-enhanced case management (ME-CM) intervention on engagement of HCV positive DUs (recruited in Methadone Maintenance Treatment Programs (MMTPs)) in HCV care. We examined the intensity of ME-CM utilization among those HCV positive in ME-CM and its association with attending an HCV evaluation.
Methods: 144 HCV positive DUs in the enhanced arm were included. We examined the relationship between ME-CM utilization (number of sessions attended; average (avg) time in and total time of ME-CM) and attending an HCV evaluation.
Results: Of the 144, 69% attended an HCV evaluation within 6 months. Overall, the mean time in ME-CM was 179 minutes (min) (SD= 209 min; range 5-1591 min). Due to skewness in total time, the log of total time (logtime) was calculated. The avg time spent in any given session was 16 min (SD= 9 min; range 2-67.5 min). The avg number of sessions was 7 (SD= 5; range 1-46). In 3 logistic regression models (logtime, avg time per session, number of sessions were dependent variables, respectively) the avg ME-CM time per person was not a significant predictor however both logtime and number of ME-CM sessions were significantly positively related to attending HCV evaluations (AORs 1.6 (95% CI:1.02-2.54) and 1.1 (95% CI: 1.02-1.2).
Conclusions: Among HCV-infected DUs receiving ME-CM, greater utilization was associated with an increased likelihood of attending an HCV evaluation suggesting that more net ME-CM time and sessions contributed to intervention impact and possibly suggesting that greater use of ME-CM may further enhance intervention potency in engaging DUs in HCV evaluations.
Financial Support: National Institutes on Drug Abuse, RO1 DA020781, RO1 DA020841 P30 DA011041

297

ATOMOXETINE TREATMENT IN ADOLESCENT RATS WITH AN ADHD PHENOTYPE DOES NOT AUGMENT VULNERABILITY TO COCAINE ADDICTION.

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Aims: Cocaine addiction and ADHD are often co-morbid. We previously demonstrated that adolescent treatment with the stimulant methylphenidate (DAT/NET inhibitor) augmented acquisition and maintenance of cocaine self-administration during adulthood using the SHR model of ADHD (Harvey et al 2011). We hypothesize that adolescent treatment with the nonstimulant atomoxetine (NET inhibitor) will not augment acquisition and maintenance of cocaine self-administration behavior in SHR.
Methods: SHR, WKY and WIS rats (N=6-8/strain) received ip injections of either 0.3 mg/kg atomoxetine or vehicle from P28-P55. At P77, rats began acquisition of cocaine self-administration (0.3 mg/kg/infusion; 2hr sessions; FR1). Acquisition criterion was defined as earning ≥20 infusions for 2 consecutive days, and having an active to inactive lever response ratio of 2:1. Number of sessions to reach criterion, as well as number infusions earned at criterion, were recorded.
Results: Overall, SHR acquired cocaine self-administration more quickly than WIS ($p<0.01$) but not WKY. At criterion, SHR earned more cocaine infusions than WKY and WIS ($p<0.05$). Importantly, prior atomoxetine treatment did not augment acquisition of cocaine self-administration in SHR, but did so in WKY ($p<0.05$).
Conclusions: Co-morbidity between cocaine addiction vulnerability and ADHD was once again demonstrated in the SHR model of ADHD. Unlike adolescent treatment with methylphenidate, adolescent atomoxetine treatment did not augment the acquisition and maintenance of cocaine self-administration in SHR, possibly due the medications' differential effects on DAT and NET inhibition. These preclinical findings suggest that a nonstimulant medication may represent an important alternative for adolescents in whom addiction is a concern. Interestingly, atomoxetine enhanced acquisition of cocaine self-administration in the WKY comparator strain, a result that emphasizes the importance of proper diagnosis for ADHD.
Financial Support: DA011716 and SMA-0835976

298

SOMETHING FEELS DIFFERENT: ALTERED NEURAL PROCESSING OF AVERSIVE INTEROCEPTIVE STIMULI IN PROBLEM USERS VS. DESISTERS.

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Aims: Interoception is the central nervous system's representation of visceral feelings in the body and has been implicated in addictive processes. The inability to properly integrate visceral aversive stimuli at a neural level is likely a factor in initiating substance use and developing dependence. The insula receives and integrates interoceptive afferents and has been proposed to play an important role in drug addiction. We therefore investigated the involvement of the insula and other brain regions during the anticipation and experience of aversive stimuli in current and former stimulant users.
Methods: Individuals, who were previously identified as recreational users of stimulants were followed up 3 years later. Of these, 16 individuals progressed to problem users, and 12 subjects desisted using. These individuals and 17 healthy comparison subjects performed a simple continuous performance task during which they experienced 40 sec episodes of 40 cm H20/sec inspiratory breathing load. The screen background color indicated anticipatory periods, with a ¼ chance for of experiencing the load.
Results: All subjects had similar reaction times on the task, but problem users and desisters performed significantly more accurately than comparison subjects. Bilaterial insula and right cingulate cortex activation was attenuated in problem users and desisters during anticipation and restricted breathing conditions. During restriction, desisters exhibited significantly higher activation in left anterior cingulate cortex (ACC) than problem users. Several significant brain-behavior correlations were found.
Conclusions: Both problem users and desisters exhibit attenuated neural representation of interoceptive stimuli, suggesting that a higher magnitude of stimuli may be necessary to achieve a similar level of feeling. The differences in ACC activation between desisters and problem users supports the hypothesis that some brain processing may return to normal functioning once drug use ceases.
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299

KYNURENINE 3-MONOOXYGENASE INHIBITION BY RO 61-8048 BLOCKS THC SELF-ADMINISTRATION AND PREVENTS RELAPSE IN SQUIRREL MONKEYS.

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Aims: Kynurenic acid (KYNA) is an astrocyte-derived neuroinhibitory agent, which primarily blocks alpha7 nicotinic acetylcholine (α7nACh) receptors in vivo. These receptors are involved in modulating motivational effects of delta-9-tetrahydrocannabinol (THC), the main psychoactive ingredient of marijuana.
Methods: Here we studied effects of the kynurenine 3-monooxygenase (KMO) inhibitor Ro 61-8048, which indirectly raises brain KYNA levels, on the reinforcing and relapse-inducing effects of THC in squirrel monkeys using a fixed-ratio intravenous THC self-administration procedure.
Results: Pretreatment with Ro 61-8048 (20 mg/kg) markedly and significantly reduced THC self-administration behavior, which was demonstrated by a downward shift of the THC dose-response curve. When self-administration was extinguished by substituting vehicle for THC or removing all cues, a priming injection of THC or reintroduction of cues (respectively) dramatically reinstated the monkeys' drug-seeking behavior (animal model of relapse to human marijuana use). Pretreatment with Ro 61-8048 (20 mg/kg) blocked THC-induced as well as cue-induced reinstatement of extinguished drug-seeking behavior. Ro 61-8048 blockade of THC self-administration, as well as cue- and drug-induced reinstatement, were reversed by pretreatment with galantamine (1-3 mg/kg), an agonist at an allosteric potentiating site of α7nACh receptor where KYNA acts as an antagonist.
Conclusions: These findings suggest KMO inhibition can counteract motivational effects of THC, probably through elevations in KYNA levels acting on α7nACh receptors, and point to modulation of brain KYNA levels as a novel target for treatment of marijuana dependence and prevention of relapse.
Financial Support: Supported in part by the Intramural Research Program of NIDA, NIH, DHHS and in part by the Department of Psychiatry, University of Maryland School of Medicine.

300

ADOLESCENT EXPOSURE TO DELTA(9)-TETRAHYDROCANNABINOL (THC) INDUCES RAPID ESCALATION OF COCAINE INTAKE IN ADULT MALE RATS.

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Aims: Marijuana is the most frequently used illicit drug by teenagers, and its repeated use has been proposed to increase the vulnerability to neuropsychiatric and addiction disorders. The aim of this study was to evaluate the effects of adolescent THC exposure in male rats on cocaine self-administration and depressive-like behaviors in adulthood. We hypothesized that adolescent THC exposure would increase cocaine self-administration and induce depressive-like behaviors in adulthood.
Methods: Adolescent male rats were given (i.p.) vehicle, 5 or 10 mg/kg delta(9)-tetrahydrocannabinol once daily on post-natal days (P) 28-45 (N=8 per treatment group). On P90, rats were trained to nosepoke for cocaine (0.32 mg/kg/injection) or food under a fixed ratio (FR) schedule of reinforcement that gradually increased from FR1 to 5 over 16 d. Following acquisition, cocaine dose effect curves were evaluated within daily self-administration sessions for 15 d. On P90, other groups of rats were evaluated in a modified forced swim test. Data were analyzed by repeated measures ANOVA.
Results: Adolescent THC exposure did not alter acquisition of cocaine self-administration or food self-administration behavior in adult rats. Across daily cocaine dose effect curve evaluations, cocaine intake escalated more rapidly in rats treated with THC during adolescence as compared with vehicle-treated rats. Adolescent THC exposure did not induce depressive-like behaviors in male rats.
Conclusions: Overall, these data suggest that exposure to THC during adolescence may accelerate the transition to excessive cocaine use in adulthood.
Financial Support: This research was supported by a grant from the University of Michigan Substance Abuse Research Center.

301

GENDER DOES NOT INFLUENCE NEUROCOGNITIVE PERFORMANCE IN METHAMPHETAMINE- AND COCAINE-DEPENDENT PARTICIPANTS.

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Aims: The goal of this project is to evaluate the relationship between gender and neurocognitive performance in methamphetamine (meth)- and cocaine-dependent volunteers.
Methods: Participants completed a demographic/drug use questionnaire and completed the following neurocognitive assessments: Continuous Performance Task (a measure of attention), N-Back (a measure of working memory), Hopkins Verbal Learning Task (a measure of verbal memory), and the Weschler Adult Intelligence Scale (a measure of IQ). Males and females were matched on the following variables: age, education, years of stimulant use, and daily use of stimulant.
Results: Meth-dependent individuals (16 Males, 16 Females) and Cocaine-dependent individuals (15 Males, 15 Females) were statistically similar with regard to all demographic/drug use variables.
Meth-dependent participants were primarily Caucasian and ~30 years of age. Volunteers reported using meth for ~8 years, 20 days out of the last 30, and used ~1.2 grams of meth/day. Males and females were statistically similar ($p>0.05$) on all domains of neurocognitive functioning assessed; however, on the CPT, there were trends toward significance with females performing better than males on sensitivity ($p=0.07$), hit rate block change ($p=0.07$), and commissions ($p=0.06$).
Cocaine-dependent individuals were primarily African-American and ~42 years of age. Volunteers reported using cocaine for ~15 years, 15 days out of the last 30, and used ~1.7 grams of cocaine/day. Males and females were statistically similar ($p>0.05$) on all domains of neurocognitive functioning ($p>0.10$).
Conclusions: The results indicate that meth-dependent and cocaine-dependent males and females do not demonstrate significant gender differences in the domains of attention, working memory, verbal memory, and IQ.
Financial Support: This study is sponsored by NIH via support to RDLG (DA023964, DA027134, DA023624, DA023588, DA028387) and TFN (DA024756, DA018197).

302

WHICH COCAINE USE OUTCOME IS MOST ASSOCIATED WITH CLINICAL IMPROVEMENT IN COCAINE TREATMENT TRIALS?

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Aims: Currently there are a number of different ways commonly used to measure success in cocaine dependence treatment trials. Some investigators evaluate cocaine use based simply on the number of cocaine-negative urine drug screens submitted by patients. Others measure the number of weeks of urine drug screen verified cocaine abstinence. Success is often defined as achieving two or three weeks of continuous abstinence, either at the end of the trial, or at any point during the trial. Some investigators compare the longest duration of continuous abstinence. Little is known about which cocaine use outcome is most closely associated with overall clinical improvement in cocaine dependent patients.
Methods: Using data from ten cocaine pharmacotherapy trials conducted at our Center from 1996-2010, we evaluated the ability of several commonly used measures of cocaine use to predict overall clinical improvement in cocaine dependent patients. Cocaine use measures included the Treatment Effectiveness Score, the number of weeks of cocaine abstinence and various measures of continuus abstinence including three weeks of abstinence achieved at the end of the trial, 3 continuous weeks of abstinence achieved at any point in the trial, and longest duration of continuous abstinence attained during the trial. Overall clinical improvement was measured by instuments including the clinical global improvement scale, rated both by clinicians and patients, and by the Addiction Severity Index.
Results: Prelimary results suggested that three weeks of continuous cocaine abstinence at the end of the trial was less likely to correlate with lower ASI composite scores at the end of the trial compared to TES scores, total number of weeks of cocaine abstinence and three weeks of continous abstinence attained at any point during the trial. Complete data will be available at the meeting.
Conclusions: Attaining three weeks of continuous abstinence at the end of the trial might not be the best way to identify clinical improvement in cocaine dependence treatment trials.
Financial Support: Supported by NIDA grant P50 DA12756

303

DEVELOPMENT OF DRUG COUNSELING FOR CO-OCCURRING HEROIN AND ATS ABUSE.

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Aims: Amphetamine type stimulants (ATS) abuse and opioid dependence are highly prevalent,frequently co-occur,and are the major drivers of the HIV and other major public health problems in Malaysia and Asia. ATS abuse by methadone maintenance treatment (MMT) patients may also undermine the effectiveness of MMT. We are developing a drug counseling intervention to enhance the effectiveness of MMT for patients with co-occurring ATS and heroin dependence.
Methods: ATS abusing MMT patients (N=10) were enrolled in a therapy development pilot study in Kuala Lumpur, Malaysia. 2 M.D psychiatrists were trained to provide a 12 week behaviorally oriented, individual drug counseling,based on CBT principles.
Results: Study participants were 9/10 male,with the mean (SD) age of 42 (7.7) years. At baseline they reported the mean (SD) 23 (8) days per month of ATS (crystal meth) use. All participants recognized ATS use as a problem and expressed strong desire to stop ATS use. Negative consequences of ATS use reported by the participants included sleep disturbances,mild memory impairments,and financial burden. Behavioral interventions incorporated in our study included behavior changes/modifications aimed at activating and energizing patients,helping them to better recognize adverse consequences of ATS use and to develop pleasurable activities alternative to ATS use. Most study participants were able to achieve only short periods of ATS abstinence (up to 3 days)and/or moderate reductions in ATS use frequency or amounts,but were unable to achieve prolonged ATS abstinence. During treatment 80% of urine tests were positive for ATS while 23% were positive for opiates.
Conclusions: Consistent with other studies of psychotherapies for ATS abuse or dependence,we found that treatment of ATS abuse is difficult and psychosocial treatments on their own may have relatively limited efficacy,pointing to the critical need to develop and incorporate pharmacological approaches to treat ATS abuse.
Financial Support: Supported by Research University Grant Scheme,USM& CMHC/DMHAS/State of Connecticut

304

ALCOHOL AND DRUG PREVALENCE RESULTS FROM THE 2007 U.S. NATIONAL ROADSIDE SURVEY.

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Aims: To assess, among weekend drivers, whether drugged driving (defined as driving after consuming an illegal drug) is more prevalent than drinking and driving and, whether drugged driving is more prevalent at night time.
Methods: The survey involved randomly stopping drivers at 300 locations across the continental United States; sites were selected through a stratified random sampling procedure. Biological measures included breath alcohol measurements on 9,413 respondents, oral fluid from 7,719 respondents, and blood samples from 3,276 respondents. Samples were analyzed using enzyme-linked immunosorbent assay (ELISA) screening, followed by a confirmatory analysis by Liquid Chromatography-Tandem Mass Spectrometry (LC/MS-MS) or Gas Chromatography/Mass Spectrometry (GC/MS). Analyses of the oral fluid and blood samples were conducted to identify the presence of some 75 drugs and metabolites, including illegal, prescription, and over-the-counter drugs.
Results: Among night-time drivers, 12.4% were positive for some level of alcohol with 2.2% of these drivers being over the legal limit (0.08+ g/dL). Very few (1%) of daytime drivers were positive for alcohol and virtually none (0.01%) were over the legal limit. With respect to drug prevalence (based on oral fluid analysis), 11% of daytime drivers were drug-positive and 14.4% of night-time drivers. Comparison of drug categories by time of day revealed that almost 6% of daytime drivers tested positive for drugs in the "Illegal" category (primarily marijuana and cocaine), as opposed to over 10% of night-time drivers. Overall, examining both oral fluid and blood, 16.3% of night-time drivers were positive for at least one drug.
Conclusions: This study presents the first national prevalence estimates for drug-involved driving, from the 2007 National Roadside Survey (NRS). Results reveal that more drivers, particularly night-time drivers, are positive for drugs, including illegal drugs, than drivers with BACs in the illegal range.
Financial Support: National Highway Traffic Safety Administration, National Institute on Alcohol Abuse and Alcoholism, National Institute on Drug Abuse.

305

METHADONE WITH VS. WITHOUT COUNSELING: OUTCOMES BY PAROLE AND PROBATION STATUS.

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Aims: To conduct secondary analyses to examine the impact of parole/probation status on outcomes over 12 months of methadone treatment.
Methods: In the parent study, 230 newly-admitted methadone patients in Baltimore were randomly assigned to receive either standard methadone or methadone without counseling for 4 months followed by standard methadone. This study compared drug and criminal activity outcomes for participants on parole or probation at baseline (n=93) with outcomes for participants not on parole or probation (n=137). All participants were administered the Addiction Severity Index at baseline and 4- and 12 month follow-up and the Treatment Readiness Motivation Scale at baseline. Generalized Estimating Equations was used to analyze changes over 12 months in days of heroin and cocaine use and criminal activity by parole/probation status and parole/probation status by study condition. Analyses controlled for gender, race, age, age of onset of heroin use, treatment readiness, and whether participants had ever injected drugs or previously attended methadone treatment.
Results: In the total sample over 12 months, older age and greater treatment readiness (TR) were associated with reduced heroin use; male gender and having never injected drugs were associated with reduced cocaine use; and female gender, older age, later onset of heroin use, and greater TR were associated with reduced criminal activity (ps<.05). Participants did not significantly differ by parole/probation status or parole/probation status by study condition on any outcomes (ps>.05).
Conclusions: This study suggests that factors other than parole/probation status appear to be related to drug and criminal outcomes for participants. Findings from the parent study have shown that the total sample reduced their drug use and criminal activity over 12 months. Thus, parolees/probationers did as well as non-parolees/probationers in methadone treatment. Criminal justice agencies should make this treatment available to their clients.
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306

IMPULSIVITY AND D-AMPHETAMINE SELF-ADMINISTRATION.

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Aims: Impulsivity, a biologically based trait composed of independent behavioral processes of reinforcement-based activation and punishment-based inhibition, has been linked to drug abuse vulnerability. Impulsive individuals initiate drug use at earlier ages, escalate to heavy use and transition to abuse and dependence more quickly, and are less likely to remain abstinent following treatment than non-impulsive individuals. This ongoing study examined d-amphetamine self-administration as a function of activation (sensation-seeking status) and inhibition dimensions of impulsivity.
Methods: Fifteen of forty young healthy adults scoring in the upper and lower median of population norms on inhibition and sensation seeking items of the Zuckerman-Kuhlman Personality Questionnaire have participated in an 8-session study consisting of four 2-session test blocks. During the first session of each block, subjects received 8 identical capsules containing either 0, 1 or 2 mg of d-amphetamine. During the second session of each block, subjects could earn up to 8 capsules from the previously sampled d-amphetamine dose. The first capsule was earned by completing 50 responses, and the response requirement for each subsequent capsule is doubled, such that 12,750 responses are required to earn all 8 capsules. Verbal-report, performance and cardiovascular assessments were completed before and hourly for 3 hours after dose administration. Data were analyzed using ANOVA.
Results: A preliminary analysis indicated that the number of earned capsules increased as a function of dose (0: 5.1 ± 1.5; 1: 5.7 ± 1.8; 2: 6.0 ± 1.8), demonstrating that d-amphetamine functioned as a reinforcer. Dose-related increases in capsules were observed in high (0: 4.6 ± 1.3; 1: 5.73 ± 2.1; 2: 5.9 ± 2.2) but not low (0: 6.2 ± 0.3; 1: 6.5± 1.0; 2: 6.2 ± 1.0) sensation seekers, independent of inhibition. Drug effects on other measures did not vary as a function of impulsivity.
Conclusions: These preliminary results demonstrate that the reinforcing effects of d-amphetamine vary as a function of sensation-seeking but not inhibition dimensions of impulsivity.
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307

A COGNITIVE BEHAVIORAL THERAPY-BASED TEXT MESSAGING INTERVENTION FOR METHAMPHETAMINE DEPENDENCE.

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Aims: To develop a fully automated cognitive behavioral therapy (CBT)-based text messaging intervention to be used with CBT therapy for methamphetamine (MA) dependence. Messages will be sent in real-time, when craving and risk of use are high and patients are not in the clinic.
Methods: We convened an expert panel, held 3 focus groups with current and former MA users, and conducted individual semi-structured interviews with 11 MA users completing outpatient treatment. In order to derive new messages, focus group participants and interviewees were asked open-ended questions about what types of messages might help reduce their craving and/or use of MA. Additionally, focus group participants provided input on messages developed by the expert panel. Subjects were also asked whether and how to individualize some of the text messages, based on a screening interview.
Results: Subjects gave favorable reviews to text messages that were "positive," affirmative, succinct, and personalized. They also preferred messages that involved a request to help others, reminders to use concurrent CBT group therapy for support, or 12-step program aphorisms. They gave negative feedback on messages seen as too demanding or "guilt inducing." Several methods of individualizing messages were endorsed: interviewing subjects about consequences of using as well as their reasons for entering treatment; and tailoring individual messages to subjects with children, those who participate in 12-step programs, find exercise helpful, or view prayer as supportive. A differentiation was endorsed between messages that would be sent at random intervals throughout the day ("pushed") and those that would be requested when craving is high ("pulled").
Conclusions: Participants successfully assisted with development of a CBT-based text messaging intervention for MA dependence. Individual semi-structured interviews are ongoing and a Phase I trial is scheduled to start in January 2012.
Financial Support: NIH DA024714

308

TERORRISM, WAR, ONE-SIDED VIOLENCE AND GLOBAL BURDEN OF DRUG USE DISORDERS.

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Aims: Terrorism (including war and one-sided violence) have not received the attention of drug researchers as have other causes of drug use disorders and political scientists have been more interested in the economic and political causes of terrorism and related violence than on its impact on public health. This study was premised on the concept that terrorism and related violence adversely affects public health long after fighting and bombings are over. This study integrates epidemiology, political science and economic perspectives to examine the impact of terrorism and related violence in 1994-2000 on morbidity and mortality due to drug use disorders in 2002, as measured by disability-adjusted life years (DALYs).
Methods: Regression analyses were adjusted for economic/political variables at baseline in 1994 including the number of refugees, number affected by natural disasters, health expenditures, ethnic heterogeneity and life expectancy. Controlling for the prevalence of drug use also provided for a measure of vulnerability for drug use disorders at baseline.
Results: In 2002, illicit drug use disorders were responsible for 7.4 million DALYs worldwide. The prevalence of drug use was 4.0% (185 million people). Overall and among each of the 10 sex-age subgroups, deaths from terrorism and related violence were significantly related to drug use disorder DALYs, even after controlling for economic and political factors and pre-existing illicit drug use. For each 1.0% increase in deaths due to terrorism and related violence, there was a 0.12% increase in drug use disorder DALYs.
Conclusions: The impact of terrorism and related violence deaths on drug use disorder DALYs was pervasive across all sex-age subgroups, highlighting the devastating toll of death and disability that defines armed conflict and related violence. Unlike results using analyses at the individual level, the prevalence of drug use was strongly related to drug use disorder DALYs regardless of sex or age. The results of this study can inform post-conflict interventions and inform decisions to use force.
Financial Support: NIDA Fellowship

309

PROGESTERONE DECREASES COCAINE CHOICE IN INTACT FEMALE RATS.

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Aims: Sex differences in cocaine dependence have indicated that women relative to men exhibit a more severe addiction prolife. In animal experiments, female rats exhibit enhanced behavioral responsiveness to cocaine and will engage in higher operant responding for cocaine reinforcement relative to males. These sex differences are modulated by both estrous cycle and exogenous steroids. Recently, we have shown that female rats will choose cocaine reinforcement over food reinforcement more frequently than will males and that this effect is estrogen dependent. In the present study, we assess the impact of progesterone on the choice between cocaine and food reinforcement in intact female rats.
Methods: On alternating days, intact female Sprague-Dawley rats were trained on a FI:20s schedule to respond on distinct levers for food (2 x 45 mg pellets) or cocaine (1.0 mg/kg). After training, rats completed "choice tests" during which the rats could choose between the two reinforcers on 25 trials per daily sessions. Throughout training and testing groups of females received either daily progesterone (0.5 mg) or vehicle (0.1 ml of peanut oil).
Results: All rats acquired operant responding for both food and cocaine at approximately equivalent rates. During choice tests, females treated with vehicle exhibited a preference for cocaine over food (selecting cocaine on > 70% of choice trials). Conversely, females treated with progesterone exhibited a preference for food over cocaine.
Conclusions: These data replicate our previous finding of high cocaine choice in female rats and, further, indicate that progesterone can suppress cocaine intake in females under choice conditions. However, it remains unclear as to whether these effects are due to the genomic neurosteroid effects of progesterone and its metabolites.
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310

ILLICIT DRUG USE TRAJECTORIES AND HOSPITAL USE OVER 22 YEARS (THE CARDIA STUDY).

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Aims: While it is known that persons with drug use disorders experience excess hospitalizations, it is not known if this applies to general population adults whose use of drugs tends to be more modest, and to decline with age. We hypothesized that such drug-using adults would have excess hospitalizations overall, and for specific causes (trauma, addiction, mental health, infection).
Methods: Data on opiate, cocaine & amphetamine use (combined "non-marijuana") came from the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a cohort of adults balanced for race & gender (Black Men, Black Women, White Men, White Women) recruited 1985-6, ages 18-30. SAS PROC TRAJ was used to iterate drug trajectories based on repeated queries of last 30 days' drug use over 18 years (n=4300). We compared hospitalization incidence rates over 22 years, by cause, across drug trajectories, stratifying by race and sex.
Results: There were 4 drug groups: Non-Users (NON, n=3691), Early Occasional Users (EOU, n=340), Persistent Occasional Users (POU, n=160), Early Frequent/Later Occasional Users (EF/LOU n=110), with 2980 admissions (excluding pregnancy-related & elective stays) over 92,167 person- years of follow-up (median 21.9 p-y) (32 admissions/1,000 person-years). Last 30-day drug use was low (<5 days) even in the POU group. Where comparison to Nonusers for a gender/race group is significant that group is shown in parentheses (*p<.05; † p<.01). POU had excess hospitalizations for infection (WM†, WW†), mental illness (WM†, WW†), trauma (BM†, BW*), addiction (BM†, BW*), digestive problems (WW†) and overall (WM†,WW†, BM†). EF/LOU had excess hospitalizations for addiction (WM*, BM*), infection (BM*), mental (WW†) and overall (BW*).
Conclusions: During 22 years of follow-up among community adults in 4 cities, use of 3 non-marijuana drugs was associated with excess hospital use overall and for causes that varied by race and gender.
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311

IF YOU SCHEDULE IT, THEY WILL COME...OR WILL THEY? FACTORS ASSOCIATED WITH WORKSHOP SESSION ATTENDANCE AND EMPLOYMENT OUTCOMES IN DRUG-DEPENDENT MEN AND WOMEN.

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Aims: Unemployment is associated with negative outcomes during and after drug abuse treatment. The Job Seekers' Workshop (JSW) is a three session, manualized program designed to train patients in skills needed to find and secure a job. The present study examined the relationship between JSW session attendance and employment outcomes at 12 and 24 week follow-up.
Methods: Participants were recruited through the NIDA Clinical Trials Network from six psychosocial and five medication assisted treatment programs and assigned to standard care (n=329) or standard care plus JSW (n=299). Current analyses were restricted to the JSW group. The relationship between JSW attendance and new job acquisition at follow-up was examined with JSW attendance defined in 3 ways: 1) number of sessions attended (0-3); 2) any attendance (1-3 sessions) vs no attendance (0 sessions); and 3) full attendance (all 3 sessions) vs all else (0,1,or 2 sessions). Chi-square analyses were used to test these relationships, followed by secondary analyses of potential mediators and moderators (eg, certified disability, active drug use, treatment modality).
Results: At 12 week follow-up, a 4x2 chi-square of JSW sessions (0-3) by new job (y/n) was significant (p=.034), but the relationship was not linear. Rates of employment varied from 11.6% (0 sessions) to 22.0% (1 session) to 11.1% (2 sessions)and 26.2% (all 3 sessions). A similar pattern was seen at 24 week follow-up. Chi-square analyses for new job and any vs no JSW attendance and full JSW vs all other attendance were significant with higher rates of new job employment among those with higher attendance rates(p=.021).
Conclusions: JSW session attendance was related to employment outcomes. The relationship was non-linear, however, affirming the need to examine potential mediators and moderators of the relationship (eg, treatment modality, gender, active drug use).
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312

CONJOINT TRAJECTORIES OF DRUG USE AND TRAJECTORIES OF DEPRESSIVE SYMPTOMS IN ADULTS: A 2-DECADE PORTRAIT OF COMORBIDITY (THE CARDIA STUDY).

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Aims: AIM: In population-based adult cohort studies, drug use predicts depressive symptoms at end of follow-up. However, little is known about the concurrent relationship of depression and drug use when both are assessed repeatedly over time.
Methods: METHODS: Repeated measures of opiate, crack/cocaine and amphetamine use (combined as "non-marijuana") and depressive symptoms (CES-D) were obtained in the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a cohort of adults balanced for race and gender, recruited in 1985-6, aged 18-30. SAS PROC TRAJ was used to iterate 1) non-marijuana drug trajectories based on repeated queries of recent (last 30 days) drug use over 18 years and 2) depression trajectories using repeated assessments of CES-D Score ≥16 over 15 years. We tested whether any drug/depression trajectory pairs co-occurred more commonly than would be expected under conditions of independence, controlling for sample characteristics (ie age, race, sex, education, partnered status, economic difficulty, age of depression onset, and childhood environment).
Results: RESULTS: There were four non-marijuana groups: Non-Users (n=3691), Early Occasional Users (n=340), Persistent Occasional Users (n=160), Early Frequent/Later Occasional Users (n=110) and three depression trajectory groups: Low Depression (n=1567), Early Moderate Later Decreasing Depression (n=821) and Chronically High Depression (n=252). Excessive co-occurrence was observed for one trajectory pair (Persistent Occasional User and Chronically High Depression), crude OR for Persistent User to be a member of Chronically High Depression Trajectory 3.5[95% CI, 2.2-5.8]. This remained significant after controlling for covariates, AOR 1.9 [1.1-3.4].
Conclusions: CONCLUSIONS: During 15 years of observation, Persistent Occasional Users were more likely to exhibit Chronically High Depressive symptoms, even after adjusting for risk factors common to both groups.
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313

CONTINGENCY MANAGEMENT IMPROVES ADHERENCE TO PSYCHIATRIC CARE IN OPIOID-DEPENDENT OUTPATIENTS.

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Aims: The present study evaluates the efficacy of contingency management for improving psychiatric service adherence and utilization in opioid-dependent patients with any current psychiatric disorder at a community-based drug abuse treatment program.
Methods: Male and female opioid-dependent patients at Addiction Treatment Services with any current psychiatric disorder are randomly assigned to one of two psychiatric service conditions: 1) reinforced on-site integrated care (ROIC), with voucher incentives (worth $25.00) contingent on full adherence to each week of scheduled psychiatric services; or 2) standard on-site integrated care (SOIC) without vouchers. Participants in both conditions receive access to the same schedule and range of psychiatric services, including weekly individual and group counseling sessions, and biweekly psychiatrist appointments. Participants complete the Symptom Checklist (SCL-90-R) monthly throughout the 3-month study to evaluate changes in psychiatric distress (the Global Severity Index (GSI) was used for this study).
Results: Data from the first 80 participants to complete the entire study are presented (ROIC: n = 40; SOIC: n = 40). No differences in study retention were observed. ROIC participants have attended almost twice the percent of overall psychiatric services (75% vs. 40%; $p < .001$). ROIC participants have attended a higher percent of scheduled psychosocial services (72% vs. 30%, $p < .001$); adherence rates to scheduled psychiatrist appointments were similar across conditions (82% vs. 75%, ns). ROIC participants reported a greater reduction in GSI scores from baseline to month 3 than SOIC participants (7.60 vs. 3.68, $p < .10$).
Conclusions: These preliminary results suggest that contingency management approaches can improve utilization of psychiatric services scheduled within community-based drug abuse treatment programs, and may improve response to psychiatric care. These preliminary findings have important policy implications for the design of systems offering integrated substance use and psychiatric care.
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314

PHYSICAL HEALTH PERCEPTIONS OF WOMEN WITH COMORBID PTSD AND SUD.

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Aims: Individuals with comorbid post traumatic stress disorder (PTSD) and substance use disorders (SUD) are at greater risks for chronic health problems and report worse physical functional than individuals with SUD alone.It is unknown if treatment that addresses PTSD and/or SUD can impact these health concerns. The current study is a secondary analysis from a NIDA Clinical Trials Network study exploring the impact of two treatments for women with trauma and SUD on health status perception.
Methods: Women meeting criteria for PTSD and alcohol and/or SUD (N= 353) were randomized to either 12 biweekly group sessions of Seeking Safety, a trauma focused integrated SUD/PTSD treatment, or 12 biweekly group sessions of Women's Health Education, an intervention focusing on gender specific health issues. Women were assessed at baseline, 1, 12, 24 and 52 weeks post intervention on questions from the medical subscale of the addiction severity Index and five questions inquiring about health status perception. Multivariate analysis of variance was conducted to assess difference between study groups across time on measures of perceived physical health and whether women experiencing re-victimization had poorer health status perception.
Results: Forty six percent of women reported a chronic medical problem at baseline and 39% reported taking a prescribed medication for a medical problem. There were no main effects of time, group or time by group interaction on measures of perceived health or number of days experiencing medical problems. Across the follow-up visits, women who experienced re-victimization (25%) reported having significantly more days of medical problems and worse perceived health than those women who did not report trauma during the follow-up.
Conclusions: Women with PTSD and SUD have physical health concerns that were not differentially affected by study treatments. Treatment for SUD and PTSD may be improved by addressing health concerns, particularly in women who experience re-victimization post treatment.
Financial Support: This study was supported by NIDA grant U10 DA 13727-01 (Brady, PI)

315

FAMILY DRUG COURTS: FOCUSING ON THE CHILDREN.

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Aims: 1) Participants will gain an understanding of the impact of parental substance use and co-occurring mental health disorders and child development
2) Participants will learn strategies to address the needs of both the parent and the child
3) Participants will learn about the impact of court's decisions on the child
Conclusions: Often the focus in Family Drug Courts is on the parent and their treatment needs, with all partners assuming the needs of the child are being addressed elsewhere. Partners may also be operating under the misperception that if the parent's needs are being addressed and the home environment is stabilized, the child will be all right; when in fact, these children are at heightened risk for their own developmental, behavioral, mental health and substance abuse concerns. Responding to the needs of the child/family as well as the parent significantly increases the chances of successful reunification; decreases the risk of relapse and recurrence of maltreatment; and intervenes in the cycle of generational substance use and child abuse and neglect. This poster will focus on the impact of parental substance use and co-occurring mental health disorders and trauma on child development; the importance of and effective tools and strategies for addressing the needs of both the parent and the child; and, the role of the Family Drug Court team in identifying and meeting these needs. Whether you are creating a child-friendly environment in which children are welcome in court, or always keeping the face of the child in focus as you deal with the parent, Family Drug Courts play a critical role in ensuring not only safety and permanency, but a chance for these children to develop and even thrive.
Financial Support: Financial support for this project was provided by the Substance Abuse and Mental Health Services Administration and the Administration on Children, Youth and Families.

316

THE SHORT INVENTORY OF PROBLEMS - REVISED (SIP-R): PSYCHOMETRIC PROPERTIES IN ENGLISH AND SPANISH-SPEAKING POPULATIONS.

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Aims: This study sought to examine the psychometric properties of a revised version of the SIP (SIP-R) as a measure of adverse consequences for alcohol and drug users in both English and Spanish-speaking populations.
Methods: The English version was evaluated within a large population of alcohol and drug abuse treatment seekers (N=886) pooled from two national, multisite randomized trials. It was also translated into Spanish and evaluated in a large population of Spanish-speaking substance abuse treatment seekers (N=405) participating in a separate multisite randomized trial. All trials utilized a common assessment battery that included the ASI, the URICA, and a substance use calendar. Reliability and validity analyses included internal consistency, confirmatory factor analysis, and correlations. Differences in reported consequences were explored using ANOVA.
Results: For the English version, results supported the internal consistency (α=.95) and theoretical five-factor structure. Convergent validity was evident through strong correlations with the URICA (r=.61) and the drug composite score from the ASI (r=.48), whereas weak correlations with other composite scores (r=.07) provided evidence of discriminant validity. Results for the Spanish version were highly similar, with strong internal consistency (α=.96), factor structure, and a similar pattern of correlations with the ASI and URICA. In both the English and Spanish-speaking samples, baseline SIP-R total scores were higher for those not legally mandated to treatment and were associated with days retained in treatment.
Conclusions: This is the first study to evaluate the SIP-R within such a large, diverse sample of treatment seekers, including evaluation of a Spanish version. Both the English and Spanish versions of the SIP-R demonstrated strong psychometric properties and should be considered a valuable measure of adverse consequences associated with drug and alcohol use.
Financial Support: This study was supported in part by National Institute on Drug Abuse grants P50-DA09241, R37-DA 015969, U10 DA015831, and T32-DA007238.

317

CULTURALLY TAILORED NICOTINE DEPENDENCE TREATMENT FOR KOREAN IMMIGRANTS.

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Aims: The study was conducted to examine the relative effectiveness of cognitive behavior therapy with cultural tailoring interventions compared to brief counseling.
Methods: The study used a two-arm randomized controlled trial. The intervention condition received 8 weekly 40-min individualized counseling sessions of culturally tailored cognitive behavior therapy, while the control condition received 8 weekly 10-min individualized counseling sessions of medication management. Both conditions received nicotine patches for 8 weeks. Cultural tailoring interventions include (1) explanation of CO effects in an analogy of briquette gas poisoning in Korea, (2) information on smoking-related deaths among Korean celebrities in Korea, and (3) utilization of family members for medication adherence and emotional support. Data are collected at baseline and at four follow-up points (4 weeks, 3 months, 6 months, and 1 year post-quit). Treatment outcomes are presented as an intention-to-treat analysis.
Results: Seventy-seven Korean immigrants participated in the study. At 3-month follow-up (based on currently available data), 50.0% of participants in the intervention condition and 21.1% of participants in the control condition (odds ratio = 3.75, 95% confidence interval = 1.37–10.26, P = 0.01) had prolonged abstinence. Participants' self-reported abstinence is biochemically verified with exhaled carbon monoxide and salivary cotinine levels. A combination of the culturally tailored cognitive behavior therapy and nicotine replacement therapy had a better treatment outcome compared to brief counseling. Generalized estimating equations revealed that treatment condition ($z = 3.04$, $p = 0.002$) and self-efficacy ($z = 4.81$, $p < 0.000$) were the two significant correlates of abstinence over time.
Conclusions: Preliminary findings suggest that a need to test further the intervention with a larger sample and longer follow-up points before it can be utilized as evidence-based tobacco dependence treatment for Korean Americans.
Financial Support: The study was supported by National Institute of Drug Abuse (5K23 DA021243-02) to SSK.

318

IMPAIRED GO-NO GO PERFORMANCE ASSOCIATED WITH ALTERED BRAIN ACTIVATION IN CHRONIC ACTIVE CANNABIS USERS.

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Aims: Cannabis is the most abused illegal substance in the United States. Alterations in brain function, cognition, and behavior have been reported in chronic cannabis users, but the results have been variable. The current study evaluated behavioral inhibition in chronic active cannabis users and controls.
Methods: 30 cannabis users (18 males and 12 females) were compared to 30 control subjects (18 males and 12 females). All subjects were between 18 and 45 years old. Functional MRI was performed at 3 Tesla, using a Go-No Go task with letters (KX, KYX, and KYWX). The subjects pressed a button whenever they saw the letters, except when X is present. Each subject also performed the Stroop, Connors Continuous Performance, and Trial Making B tasks.
Results: Cannabis users performed the Stroop and Trail Making B tests slower than controls, and had higher perseveration scores in the Connors continuous performance test. In addition, cannabis users made fewer correct No Go responses than controls. Cannabis users also showed greater activation than controls in BA 7, BA 31, and BA 37 during the Go-No Go Task. As the task difficulty increased, with more letters, control subjects increased activation of the BA6 / 10, while cannabis users activated BA 3, BA 4 and BA 45.
Conclusions: Chronic active cannabis use is associated with failure to inhibit behavior, which may be related to their perseveration. The perseverative responding may reflect a difficulty in stimulus classification (i.e., is the letter a K or an X) as BA 7 is involved in visuospatial processing, and BA 37 is involved in within category identification. Thus, the performance of the cannabis users in these tasks may not reflect inhibitory failure, but rather may reflect stimulus classification failure.
Financial Support: This study is supported by: NINDS and NIDA (U54 NS56883-05, 2K24 16170), NCRR (G12RR003061 & P20RR11091), and the U.S. President's Office of National Drug Control Policy.

319

EFFECT OF HISTORY OF TASTE AVERSION CONDITIONING ON PLACE PREFERENCE LEARNING IN RATS.

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Aims: Drugs of abuse have both rewarding and aversive effects as indexed by the fact that they support both place preferences (reward) and taste aversions (aversive) even in the same animals trained concurrently in the two designs. Such results suggest that when exposed to the drug, both of these motivational effects can be recognized by an animal. Interestingly, experience with a specific motivational state has been reported to influence perception of reward or aversion on subsequent exposures to a drug. The current study explored whether having a history with taste aversion conditioning to a drug might preclude subsequent perception of the rewarding effects in the place preference preparation.
Methods: Sprague-Dawley male rats were habituated to restricted water access and then exposed to a conditioned taste aversion procedure in which a novel saccharin solution was followed by morphine (5 mg/kg; ip) for five conditioning cycles. Following this, place preference conditioning was initiated in which animals were injected with the same dose of 5 mg/kg morphine or equivolume saline and placed on one side of a two-chambered apparatus (saline was paired with the opposite side on alternate days). After two cycles, animals were tested for morphine-induced place preferences for the drug-paired side.
Results: Animals given saccharin-morphine pairings acquired an aversion to the morphine-associated taste, significantly decreasing saccharin consumption over repeated trials [$F(4,125)=12.8$, $p<.05$]. Animals with this history acquired morphine-induced place preferences to the same degree as animals without the taste aversion history (exposed to water alone with no morphine injections) [$F(1, 47)=.481$, $p>.05$].
Conclusions: The lack of differences in acquisition of place preference among groups in this study indicates that a history of taste aversion learning with morphine has no effect on the acquisition of place preferences. This further suggests that exposure to the aversive effects of morphine does not impact subsequent perception of the rewarding effects of the drug.
Financial Support: Supported by a grant from the Mellon Foundation to ALR.

320

DELIVERY OF INDIVIDUAL SUBSTANCE ABUSE COUNSELING USING A WEB-BASED VIDEOCONFERENCING PLATFORM: A RANDOMIZED STUDY.

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Aims: Web-based videoconferencing technology can improve delivery of evidence-based substance abuse treatment by allowing patients to access needed counseling services from their homes or other remote locations. Patients in methadone maintenance programs may benefit in particular because many experience obstacles to regular attendance of on-site counseling and are often poorly adherent. Improving the convenience of attending counseling services can improve adherence and allow more time to pursue other important rehabilitation activities.
Methods: The present study evaluates the efficacy of using eGetgoingTM - a web-based videoconferencing platform- to deliver individual counseling using delivery schedules routinely employed in community-based methadone clinics. Participants at a community-based methadone maintenance clinic with computer and Internet access (n = 80) are randomly assigned to receive individual counseling onsite or via the eGetgoing platform for 3 months. All participants report for methadone dispensing according to their routine treatment schedules.
Results: A total of 48 subjects have completed the study (eGetgoing=20; routine=28). Rates of attendance to individual counseling sessions were similar for the Routine, in-person group (67%) and the eGetgoing group (77%; p=ns). Treatment satisfaction as measured by the Client Satisfaction Questionnaire was high for both groups (Routine =3.65 and eGetgoing =3.76; p=ns). The strength of the therapeutic alliance as measured by the Helping Alliance Questionnaire patient assessment was also high (Routine =5.43 and eGetgoing =5.45; p=ns). Similar results were obtained for the HAQ therapist assessment (Routine =5.12 and eGetgoing =5.23; p=ns).
Conclusions: Results of preliminary analyses indicate that web-based counseling services can be integrated into a community-based opioid agonist treatment program while maintaining excellent patient satisfaction and treatment response.
Financial Support: NIH 1RC1DA028189

321

BARRIERS TO ENROLLMENT IN HIV CARE AMONG HIV-POSITIVE PWIDS IN ODESSA, UKRAINE.

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Aims: In Odessa, Ukraine, among PWIDs who know their HIV-positive status, the mean period between obtaining HIV test result and enrollment in HIV care was 3.2 times longer compared to non drug using populations (913 days in 1987-2009). Most of them postpone seeking medical care until their physical sickness became disruptive, and some die before obtaining any HIV treatment. We aimed to explore personal and system's barriers to enrollment in HIV care among PWIDs in Odessa Region, Ukraine.
Methods: We undertook qualitative face-to-face, semi-structured interviews (n=32) with PWIDs living in Odessa City and in nearby town of Illichivsk, in October 2011. All subjects had HIV+ status for 0.5–7 years, but never sought HIV medical care. Thematic analysis of interviews was conducted.
Results: The subjects living in Illichivsk stated the need to travel to Odessa City for HIV medical care and transportation cost as main barriers to their enrollment in care. Good state of health was another reason. They also would prefer to be accompanied by a social worker during their first visit to AIDS Center. However, the PWIDs who live in Odessa City and theoretically have better access to HIV services, stated known problems with ART availability as main discouraging factor. Another themes were feeling healthy, and fear of HIV status disclosure. Finally, in many cases, lifestyle of active drug user left no place for regular health care.
Conclusions: The results suggest the presence of internal and external barriers to PWIDs' enrollment in HIV care. The integration of substitution therapy into the complex of HIV services could increase the uptake of these services by PWIDs. Effective case management could be an additional facilitator. On the system level there is need in decentralization of services and in ensuring the availability of the comprehensive HIV care.
Financial Support: Supported by WHO CO Ukraine.

322

ADDICTION RISK IN MALES AND FEMALES: HIGHER-ORDER ITEM RESPONSE THEORY MODELING IN THE TRANSMISSIBLE LIABILITY INDEX.

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Aims: Transmissible Liability Index (TLI), quantifying transmissible component of the risk for substance use disorder (SUD), was derived in Center for Education and Drug Abuse Research (CEDAR).The purpose of this study is to examine a higher-order factor structure of TLI in multidimensional Item Response Theory (IRT) framework and estimate an overall TLI latent trait score in addition to subscales.
Methods: Indicators of cognitive, emotional, and behavioral domains of psychological functioning were assessed in a sample of 500 10-12 years of old CEDAR male subjects. The items were selected in the male sample based on their relationship with paternal SUD diagnosis. The 45-item TLI had an IRT-based reliability score of .93.
Results: A higher-order IRT model was tested using MPLUS using weighted least squares minimum variance estimation method. A reasonable model fit was obtained: chi-square/df=1.2, RMSEA=.015 (90% CI: .01, .02). Factor loadings were then transformed to IRT-based item location and discrimination parameters. A higher-order TLI discriminated individuals with and without paternal history of SUD for both sexes (ES=.47, p<.001). The TLI significantly predicted the SUD outcome at age 22 (OR=1.6, 95% CI: 1.21, 1.75).
Conclusions: The present study confirms that the TLI is based on higher-order IRT is applicable to identification of males at high risk for SUD. In addition, the results potentially have heuristic value for research aimed at elucidating the etiology of SUD.
Financial Support: This study was supported by the NIDA grants P50DA005605, K02DA017822.

323

PERSONALITY AND THE ACUTE SUBJECTIVE EFFECTS OF D-AMPHETAMINE IN HUMANS.

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Aims: Previously, our laboratory reported that healthy volunteers who scored high on the traits of reward sensitivity and physical fearlessness reported greater "positive" subjective effects after a single dose of d-amphetamine. Here, we replicate and extend these findings by examining personality measures in relation to acute amphetamine response using additional doses of d-amphetamine, in a larger sample of participants.
Methods: Healthy volunteers (N=286) completed the Multidimensional Personality Questionnaire Brief Form (MPQ-BF) and participated in four sessions during which they received oral doses of d-amphetamine (0, 5, 10, 20 mg). Subjective responses to the drug were measured using the Profile of Mood States, Addiction Research Center Inventory, and Drug Effects Questionnaire. Factor analyses were conducted to reduce the drug response data into a smaller number of higher-order drug effect factors ("euphoria," "arousal," "dysphoria"). Participants were rank ordered on the MPQ-BF scales; the top and bottom third on each trait were compared on the factors summarizing the drug responses.
Results: High trait physical fearlessness was significantly associated with greater amphetamine-related arousal, and high trait reward sensitivity was significantly associated with greater amphetamine-related euphoria. Additionally, high trait impulsivity was significantly associated with greater arousal and euphoria.
Conclusions: These results are consistent with previous data, and extend the evidence that individual differences in the subjective effects of d-amphetamine are partially explained by differences in personality.
Financial Support: Supported by DA002812 (HdW) and DA021336 (Abraham Palmer PI).

324

TWICE-STIGMATIZED: PROVIDER'S PERSPECTIVES ON DRUG-USING WOMEN IN THE REPUBLIC OF GEORGIA.

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Aims: Empirical data on drug use by women in the Republic of Georgia are non-existent. Anecdotal data suggests that drug-treatment-related and general medical services utilization by drug-using women is extremely low. The attitudes, perceptions, and treatment-related practices toward drug-using women on the part of the service providers are examined.
Methods: N=34 women-related health service providers completed semi-structured individual interviews. Service providers were drawn from staff of addiction clinics, OBG, neurologists, nurses, social workers, psychologists.
Results: Qualitative data analysis revealed several themes including the recognition that interpersonal violence is pervasive in drug-using women's lives. Women's drug use is less tolerated than men's drug use as drug use compromises women's abilities to perform their primary role of family care-giving. General beliefs indicate a worse profile in women compared to men including drug addiction develops more quickly, the course of the illness progresses with more severe symptoms, negative personality changes appear to be more lasting. There are opportunities for education regarding patient confidentiality and the rationale for and effectiveness of opioid agonist treatment on the part of non-addiction specialists.
Conclusions: 1. Confidentiality and treatment anonymity should be the major precondition for any intervention targeting drug-using women;
2. Non-addiction service providers would benefit from education regarding the principles of drug-addiction etiology, prevention, and treatment strategies;
3. Drug treatment and harm reduction programs should offer gender-specific services, with the development and implementation of women-specific treatment program as a priority.
Financial Support: Supported by NIDA grant R01DA029880

325

SOURCES OF OPIOIDS FOR NONMEDICAL USE BY FREQUENCY OF USE IN THE NSDUH SURVEY.

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Aims: Messages for safe opioid use directed toward patients and prescribers are often based on assumptions that most nonmedical opioid users acquire their drugs free from friends/relatives. This study examined how sources of opioids differ among experimental, occasional, and weekly nonmedical users.
Methods: The 2009 National Survey on Drug Use and Health was used to assess frequency of nonmedical opioid use, dependence, and source of opioid. There were 3845 individuals who reported nonmedical opioid use in the past year and source of opioid for last nonmedical use. Based on days of use in the past year, nonmedical users were categorized as experimental (≤2 days; n=750), occasional (≥3-51 days; n=2036), and weekly (≥52 days; n=1059) users. Opioid dependence was assessed using DSM-IV criteria (n=481).
Results: Purchasing opioids from a dealer, friend/relative increased as frequency of nonmedical use increased; 6% of experimental users, 13% of occasional users, and 25% of weekly users purchased opioids from dealers or friend/relative in the past year. Obtaining opioids free from friends/relatives decreased as frequency of nonmedical use increased; 66% of experimental, 59% of occasional, and 40% of weekly users reported being given an opioid free from friend/relative. Individuals diagnosed with opioid dependence were more likely to report purchasing opioids (37%) than obtaining them for free (31%). Approximately 20% reported one doctor as last source of opioid, regardless of frequency of use. Among those who reported nonmedical use of OxyContin® (oxycodone HCl controlled-release) Tablets, 21% of experimental users, 33% of occasional users, and 50% of weekly users purchased from a dealer, friend/relative.
Conclusions: Purchasing opioids from a dealer, friend or relative increased and obtaining opioids free from friends or relatives decreased as frequency of nonmedical use increased. Those with opioid dependence were more likely to purchase opioids than obtain them free. Interventions to prevent nonmedical use of opioids need to consider the heterogeneity in sources of procurement.
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326

MOTIVATION AND ENGAGEMENT AMONG ADULTS AND ADOLESCENTS: A COMPARISON OF CLIENTS IN SHORT-TERM RESIDENTIAL PROGRAMS.

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Aims: The importance of motivation in promoting treatment engagement among adults has been well documented, and similar research efforts have begun examining the issue with adolescents. While there is general consensus that motivation for treatment is lower among adolescents and that the engagement process is likely different among the two groups, direct comparisons are sparse. The purpose of this study is to compare motivation and engagement of adult and adolescent clients receiving treatment in short-term residential programs.
Methods: Data were collected from 546 adults in 2008 (mean age=36.4 years, 50% male); and 420 adolescents in 2011 (mean age=15.6 years, 80% male). In both samples, motivation measures were collected at admission and engagement measures at approximately 1 month. Motivation included Problem Recognition, Desire for Help, and Treatment Readiness. Engagement included Treatment Satisfaction, Counselor Rapport, Treatment Participation, and Peer Support. Scale scores ranged from 10 to 50.
Results: On average, adolescents scored 11 points lower on all motivation scales and 5 points lower on engagement scales (satisfaction was most comparable; peer support most dissimilar). Only one motivation-engagement relationship was consistent across both samples: clients with higher readiness reported higher counselor rapport. For adults remaining at month 1 (n=226), readiness was related to all aspects of engagement except satisfaction. For adolescents remaining at month 1 (n=213), readiness was related to satisfaction and rapport whereas desire for help was related to rapport and participation. Problem recognition was not related to engagement in either sample.
Conclusions: In general, motivation and engagement appear to be lower in adolescents compared with adults. While motivation is related to engagement in both samples, the specific patterns of associations differed across groups. Future work will examine gender issues and attempt to broaden the samples to include clients from a wider range of residential programs.
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327

EPIGENETICS OF MATERNAL CIGARETTE SMOKING DURING PREGNANCY AND CHILD NEUROBEHAVIORAL OUTCOMES.

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Aims: The period of in utero development is one of the most critical windows during which adverse exposures may both influence the growth and development of the fetus but also its future postnatal health and behavior. Maternal cigarette smoking during pregnancy remains a relatively common but nonetheless hazardous in utero exposure, and previous studies have associated it with reduced birth weight, poor developmental outcomes, and increased risk for diseases and behavioral disorders later in life. Current research suggests that many of the mechanisms whereby maternal smoke exposure may dysregulate key pathways crucial for proper fetal growth and development may include epigenetic modes of regulation.
Conclusions: Maternal cigarette smoking during pregnancy has been associated with aberrant DNA methylation, histone modifications, and dysregulated expression of microRNA, but a deeper understanding of the epigenetics of maternal cigarette smoking during pregnancy as well as how these epigenetic changes may affect later offspring health and behavior remains to be elucidated. This presentation seeks to explore many of the previously described epigenetic alterations associated with maternal cigarette smoking during pregnancy, assesses how such alterations may have consequences for both fetal growth and development as well as postnatal health, behavior and well-being, and recommends future directions for this new and exciting field of research.
Financial Support: Supported by: DA023134(VSK), T32 AA07459(MAM)

328

MODELING THE TRANSITION TO OFFERING MEDICATIONS IN PUBLICLY FUNDED SUD TREATMENT PROGRAMS.

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Aims: The majority of publicly funded substance use disorder (SUD) treatment programs have not adopted medication-assisted treatment (MAT). Few studies have measured program-level transition to MAT using longitudinal data. The aim of this study was to examine the associations between organizational characteristics and the odds of transitioning to offering MAT in a cohort of treatment programs.
Methods: In 2004-2006, baseline data were collected from administrators of 318 publicly funded treatment organizations. Follow-up data were collected from 86% programs still open in 2009-2010 (n = 250). Covariates measured at baseline included organizational characteristics, medical resources, funding, treatment culture, and detailing activities by pharmaceutical companies. Analyses focused on 190 programs that offered no SUD medications at baseline to model MAT adoption at follow-up.
Results: Of 190 programs offering no MAT in 2004-2006, 22.6% transitioned to offering at least one SUD medication in 2009-2010. Transition to MAT was associated with medical resources, funding, and pharmaceutical detailing. Specifically, the baseline numbers of physicians (odds ratio, OR = 1.63, $p<.05$) and nurses (OR = 1.35, $p<.05$) were positively associated with MAT adoption. Programs with a greater proportion of Medicaid clients were more likely to transition to offering MAT (OR = 1.02, $p<.05$). Pharmaceutical detailing at baseline was positively associated with transition to MAT at follow-up (OR = 1.37, $p<.05$).
Conclusions: Access to MAT has increased over time in publicly funded SUD treatment programs. The transition to offering MAT was associated with medical resources, Medicaid funding, and the efforts of pharmaceutical companies to market their products. Given the impending expansion of Medicaid under health care reform, patients served by publicly funded programs may gain greater access to medication-assisted treatment.
Financial Support: Supported by the Robert Wood Johnson Foundation's Substance Abuse Policy Research Program (65111) and the National Institute on Drug Abuse (R01DA014482).

329

AMYGDALA AND INSULA ACTIVITY DURING STRESS DIFFERS BY TREATMENT AND CORRELATES WITH LONG-TERM SMOKING OUTCOMES.

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Aims: Cigarette smoking is the leading preventable cause of disease and death in the US. Stress is a major trigger for smoking relapse and treatment failure. Mindfulness-based therapies are known to decrease stress and negative affect and we have recently shown that such mindfulness training is effective for reducing smoking (e.g., Brewer et al 2011). Here we assessed whether mindfulness treatment was associated with altered neural responses to stress, and whether these neural responses were related to smoking treatment outcomes.
Methods: We used Functional Magnetic Resonance Imaging (fMRI) to probe neural activity in 23 participants following a clinical trial in which they were randomized to receive Mindfulness Training (MT; N=10) or Freedom-From-Smoking (FFS; N=13). Participants were scanned during script-driven guided imagery of two individualized stress and two neutral-relaxing scenarios, presented in random order. Self-reported stress as well as neural activity were compared between groups, and correlated with % reduction in smoking. Neuroimaging results were familywise error corrected for multiple comparisons.
Results: Stress reports did not differ between groups. However, neural activity during stress revealed several significant between-group differences, including greater activity in dorsolateral prefrontal cortex in the FFS group, but lower amygdala and insula activity in the MT group. Importantly - across both groups - lower amygdala and insula activity was significantly correlated with greater reduction in smoking both immediately after treatment, as well as at 17 week follow-up.
Conclusions: These findings suggest that mindfulness treatment may be effective in part via reduction in neural responsivity to stress in amygdala and insula, which is related to improved smoking outcomes. In future samples, these regions may be used to predict treatment outcome directly.
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330

GABA-B RECEPTOR POSITIVE MODULATORS: ENHANCEMENT OF DISCRIMINATIVE STIMULUS EFFECTS OF GABA-B AGONISTS, AND EFFECTS WHEN GIVEN ALONE.

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Aims: The GABA-B receptor positive modulators CGP7930 and BHFF enhance in vivo effects of the GABA-B receptor agonist baclofen, assessed by loss of righting in mice. This study investigated their ability to enhance GABA-B receptor mediated discriminative stimulus effects in pigeons, and examined their effects when given alone.
Methods: Different groups of pigeons were trained to discriminate 7.5 mg/kg baclofen, 178 mg/kg GHB, or 100 mg/kg rac-BHFF from saline, using methods detailed elsewhere (Koek et al., JPET 317:409, 2006). All drugs were administered i.m., except the GABA-B receptor modulators, which were given p.o.
Results: In baclofen-trained pigeons, CGP7930 and BHFF substituted partially for baclofen (41 and 75% baclofen-appropriate responding, respectively). CGP7930 (100 mg/kg) and BHFF (32 mg/kg) shifted the dose-response curve of baclofen at least three-fold to the left, but did not shift the curve of GHB. In GHB-trained pigeons, CGP7930 and BHFF substituted partially for GHB (15 and 49%, respectively), and shifted the dose-response curve of baclofen at least two-fold to the left, but did not shift GHB. In BHFF-trained pigeons, baclofen and GHB substituted partially for BHFF (64 and 78%, respectively).
Conclusions: This study is the first to show that animals can discriminate a GABA-B receptor positive modulator from vehicle, and provides further evidence that the effects of BHFF are not identical to those of baclofen or GHB, consistent with the notion that selective enhancement of activated receptors has effects that differ from nonselective activation of all receptors. CGP7930 and BHFF enhanced the discriminative stimulus effects of baclofen, but not those of GHB, consistent with converging evidence that the mechanisms mediating the effects of baclofen and GHB are not identical. A better understanding of these mechanisms could lead to more effective medications.
Financial Support: DA15692 (WK) and DA17918 (CPF)

331

ADDITIVE EFFECTS OF SMOKING STATUS AND OBESITY ON DELAY DISCOUNTING AND SOCIAL DISCOUNTING.

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Aims: Delay discounting rate is known to be associated with smoking status and obesity in some populations. It is unknown, however, how these variables affect discounting for shared rewards (social discounting), or whether obesity and smoking status interact to have a greater effect on discount rate when combined.
Methods: The present study used a crowdsourcing service to collect discounting data, smoking status, height, and weight from 1181 individuals. Hypothetical delay discounting tasks included versions where all rewards were to be delivered to the participant, where all rewards were to be shared among 10 anonymous individuals including the participant, and where immediate rewards were to be delivered to the participant and delayed rewards were to be shared. Probability discounting was also assessed. Among those individuals that met various inclusion and data consistency criteria (n = 691), the effects of obesity (BMI ≥ 30), smoking status, and the interaction between smoking status and obesity were compared with 2x2 between-subjects ANOVAs. We hypothesized that smoking status and obesity would both contribute to delay discounting rates, although the precise nature of the relationship was unknown.
Results: Discount rates were found to be higher for all four discounting tasks among obese individuals, and were higher for the delay and social discounting tasks only among smokers. The interaction term was not significant for any of the discounting tasks, indicating that smoking status and obesity contribute to delay and social discounting rates additively.
Conclusions: These results extend the associations between delay discounting and smoking status and obesity to social discounting. Furthermore, these results indicate that smokers who are obese have higher delay and social discount rates than smokers or obese individuals alone.
Financial Support: Institutional start-up funds to WKB.

332

EFFECTS OF METHCATHINONE AND 3-CL-METHCATHINONE (PAL-434) IN ASSAYS OF COCAINE DISCRIMINATION AND SELF-ADMINISTRATION IN RHESUS MONKEYS.

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Aims: Monoamine releasers with varying selectivity for dopamine/norepinephrine and serotonin release are being investigated as candidate medications for cocaine abuse. Previous studies suggest that nonselective monoamine releasers or serotonin-selective releasers may be effective at reducing cocaine abuse and have low abuse liability. To assess this, the present studies compared methcathinone, a dopamine-selective releaser with low affinity for the serotonin transporter, with PAL-434, a methcathinone congener with equal potency for dopamine release (compared with methcathinone) but 10-fold higher potency for serotonin release, in drug discrimination and drug self-administration.
Methods: In drug discrimination studies, rhesus monkeys (N=3) were trained to discriminate cocaine (0.4 mg/kg, IM) from saline in a two-key, food-reinforced drug discrimination procedure. Another group of monkeys (N=3-4) was trained under a second order FR2(VR16) schedule of food and cocaine (0.01 mg/kg/inj) reinforcement. When responding was stable, methcathinone (0.1–0.32 mg/kg/hr, IV) or PAL-434 (0.56-1.0 mg/kg/hr, IV) was administered chronically (7-10 days) to assess selectivity of the effects on cocaine- versus food-maintained responding.
Results: In discrimination studies, cocaine and methcathinone dose-dependently increased responding on the cocaine-appropriate lever with equal potencies. Similarly, PAL-434 substituted for cocaine but was slightly less potent than cocaine and methcathinone. Further, both methcathinone and PAL-434 at the highest doses tested selectively reduced cocaine self-administration to about 50% of baseline with modest effects on responding for food.
Conclusions: These results suggest that in non-human primates, methcathinone and PAL-434 substitute for the discriminative stimulus effects of cocaine and selectively reduce cocaine self-administration. More studies to determine the abuse potential of PAL-434 are in progress.
Financial Support: NIH Grant DA02519

333

CHARACTERISTICS OF CIGARETTE USE BY YOUNG ADULTS DIAGNOSED WITH ADHD IN CHILDHOOD: RESULTS FROM THE LONGITUDINAL FOLLOW-UP OF THE MTA CHILDREN.

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Aims: To examine smoking quantity, nicotine dependence, quit attempts and craving among young adults diagnosed with ADHD as children compared to a demographically similar local normative comparison group (LNCG).
Methods: Individuals diagnosed with DSM-IV ADHD Combined Subtype in childhood (n=416) and a LNCG of classmates (n=220) completed the Substance Use Questionnaire and the Fagerstrom Test for Nicotine Dependence (FTND) 12 years after study enrollment (ages: 17-25).
Results: Compared to the LNCG, the ADHD smokers were significantly more nicotine-dependent as measured by the FTND (M=3.1 vs. 2.2; t=2.7, p<0.01). Moreover, among daily smokers (n=157 ADHD; n=40 LNCG), significantly more of the ADHD group reported smoking at least 1 pack of cigarettes/day compared to the LNCG (29.3% versus 7.5%, $\chi 2$=8.107, p<0.01). ADHD smokers reported starting regular smoking (>once weekly) at a younger age (16.1 yrs) than smokers in the LNCG(17.2 yrs; t=-3.2, p<0.01). Smokers in the ADHD group also reported significantly more quit attempts compared to the LNCG, regardless of success (1.7 attempts vs. 1.1 attempts; t = 2.37, p<0.05). During quit attempts, a significantly greater proportion of ADHD smokers reported moderate to severe levels of craving compared to the LNCG ($\chi 2$=18.4, p<0.001).
Conclusions: These findings from the MTA sample demonstrate prospectively for the first time that compared to their non-ADHD peers, smokers with ADHD histories smoke more cigarettes/day, are more nicotine dependent, and have more failed quit attempts, possibly due to increased craving. These findings suggest worse lifelong smoking-related sequelae for this population and, coupled with the earlier age of onset, should be considered when developing prevention and intervention efforts for this high-risk group.
Financial Support: K24DA023464 (Kollins); U01MH050467,N01MH12010,DA-8-5553 (Molina)

334

IMPLEMENTING ORGANIZATIONAL CHANGE STRATEGIES TO ADDRESS TOBACCO ADDICTION IN OUTPATIENT TREATMENT AGENCIES.

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Aims: Tobacco addiction continues to be very common amongst individuals with other addictions and/or psychiatric disorders, and is more frequent among staff employed at treatment facilities than in the general population. An increasing number of treatment agencies are focusing on ways to reduce tobacco use among patients and staff, promote recovery from this addiction alongside recovery from other substance addictions, and create tobacco-free environments through policies and other changes. Nevertheless, there exist many challenges to develop, implement, and sustain these efforts over time. Our goals are to a) describe the comprehensive Addressing Tobacco Through Organizational Change (ATTOC) approach, which allows to systematically address tobacco use within specific agency context and culture, and b) outline successful implementation of the ATTOC approach at four outpatient treatment agencies in the state of Connecticut.
Conclusions: A one-year intervention with the agencies included technical assistance and training, and promoted the development of leadership teams, site champions, and counselors providing tobacco addiction treatment. Two of the four sites become tobacco-free campuses and the other two sites developed increased restrictions on tobacco use. All four sites implemented tobacco addiction treatment for lower and higher motivated patients, started or made referrals to Nicotine Anonymous groups, trained providers to integrate medication treatment for tobacco addiction and to use carbon monoxide meters, began staff recovery initiatives, and made substantial improvements in health record documentation. This is one of the first reports documenting organizational change efforts to address tobacco in outpatient treatment settings. In addition to presenting main outcomes, we will specify lessons learned from implementing the ATTOC approach.
Financial Support: The organizational change intervention was funded by the Connecticut Department of Public Health.

335

A REVIEW OF CULTURALLY SENSITIVE TOBACCO INTERVENTIONS FOR ADOLESCENTS.

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Aims: Aim: Tobacco use rates among minority adolescents continue to be problematic; thus, identifying effective interventions is critical. The purpose of this review was to assess tobacco prevention and cessation interventions for minority adolescents published between 1990 and 2011.
Methods: Methods: Two independent reviewers identified 12 adolescent tobacco intervention studies and compared and contrasted them on demographic information, theoretical constructs, cultural components (surface and deep structure), and treatment outcomes.
Results: Results: Of the 12 studies, 5 focused on prevention, 4 on cessation, and 3 combined prevention and cessation. Nine were school-based, 2 were community-based, and 1 was school- and community-based. Diverse minority groups were targeted, with Hispanic group being the most examined (n = 6); other targeted ethnic/racial groups were, African American (n=3), Chinese American (n=1), American Indian (n=1) and Arab American (n=1). The most common theoretical construct was the Social Influence Model (n=5), and 6 included culture-specific components but the other 6 did not. The overall findings indicated that culturally tailoring cessation interventions did not improve tobacco quit rates among minority adolescents, but culturally tailoring prevention interventions produced lower tobacco initiation rates among all adolescents.
Conclusions: Conclusion: There is a critical need to develop a better understanding of cultural issues related to both cessation and initiation of tobacco use and develop improved interventions that are tailored for, or targeted to, minority adolescents.
Financial Support: T32 DA07238, P50DA09421, R01DA0264

336

INTENSIVE MOTIVATIONAL INTERVIEWING FOR METHAMPHETAMINE DEPENDENCE.

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Aims: Motivational interviewing (MI) is a short-term therapeutic intervention designed to increase readiness to change for drug and alcohol abusers. While this therapeutic approach has been used for many substance abusing populations, the efficacy of MI has not been examined for methamphetamine (MA) abusers. The present ongoing randomized clinical trial examines the efficacy of standard MI and intensive MI for patients meeting DSM criteria for MA dependence.
Methods: Study participants were randomly assigned to either a single 90 minute session of MI (n=58) or an intensive 9-session (60 minutes per session) MI intervention administered weekly (n=62). All participants received 12 weeks of outpatient group therapy and were followed for 2, 4, and 6 months. Data collection included days of drug use, and alcohol and drug use severity using the ASI.
Results: Both groups demonstrated significant decreases in the number of days using methamphetamine and ASI drug severity. While few significant overall differences between MI groups were observed, persons with lower MA severity at baseline attended more MI and outpatient sessions and reported fewer days of MA use. Additionally, women receiving intensive MI had significantly lower ASI alcohol scores at 6-month follow-up compared to those receiving only one session.
Conclusions: MA dependent individuals frequently present with serious medical and psychiatric conditions that complicate treatment efforts. The preliminary findings demonstrate MI combined with intensive outpatient group treatment is useful for MA abusers however, intensive MI may not be necessary to achieve improvement. Further investigation of ASI alcohol outcomes among women is merited. The current work focuses on substance use and severity outcomes but future study should encompass multiple areas (e.g., employment, social support) addressed in MI therapy that may work as moderators to successful recovery.
Financial Support: This work was funded by NIDA R01 DA024714.

337

ADVERSE PREGNANCY OUTCOMES AND CURRENT HEALTH STATUS IN WOMEN WITH PTSD AND SUD.

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Aims: The co-occurrence of post-traumatic stress disorder (PTSD) with substance use disorder (SUD) is a challenging clinical presentation with a complicated etiologic pathway. Women's reproductive history, especially adverse reproductive events, may represent an important set of factors predicting current health and health perceptions.
Methods: In the NIDA Clinical Trials Network, 'Women & Trauma Study', 353 women (age 18-65) with co-occurring PTSD and SUD were enrolled into a randomized controlled trial of 12 biweekly group sessions of either Seeking Safety, an integrated SUD/PTSD treatment, or Women's Health Education. Women were assessed at baseline, 1, 12, 24, and 52 weeks post intervention on measures of perceived health. We sought to characterize reproductive history in these women, and examine its association with current health problems. We employed generalized estimating equations (GEE) to account for the repeated health assessments.
Results: Of 328 women providing baseline reproductive history, 93.0% had ever been pregnant. Of these, 32 (10.5%) reported giving birth to a child who died, 154 (50.5%) reported an abortion, 119 (39.0%) reported a miscarriage, 13 (4.3%) reported stillbirth, and 71 (23.4%) reported a premature infant who survived. Overall, 206 (62.8%) reported at least one of these events, and 177 (54.0%) reported at least one other than miscarriage. At follow-up visits, these 177 women reported 3.1 more average days of medical problems in the last month (p=0.002), were more troubled by medical problems (p=0.003), more likely to report that they had been feeling bad lately (p=0.02), and rated current health status more poorly (p=0.03) than other women.
Conclusions: Our findings suggest that women with a history of adverse reproductive events may be at increased risk for poor perceived health status. Treatment of PTSD and SUD in these women may be improved by consideration of adverse reproductive history.
Financial Support: Support from U10DA013727

338

CONTINGENCY MANAGEMENT AND COGNITIVE BEHAVIORAL THERAPY FOR SMOKING CESSATION IN ADOLESCENT SMOKERS.

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Aims: Behavioral interventions that provide performance-contingent rewards can be used to motivate change in a variety of behaviors in adolescents including substance use. Pilot work from our group has shown that a novel high school-based intervention combining abstinence based, progressive ratio Contingency Management (CM) and Cognitive Behavioral Therapy (CBT) yielded robust end-of-treatment abstinence rates of 53-58%. However, evidence from these trials has raised questions about the utility of CBT in this intervention. The purpose of this trial was to examine the independent versus combined efficacy of CM for abstinence and CBT for smoking cessation.
Methods: 82 treatment-seeking adolescent smokers were randomized to receive weekly CBT alone, CM for abstinence alone or CM for abstinence with weekly CBT. All groups received a preparation to quit session 5-7 days before quit day and payments to complete weekly assessments. Abstinence was determined using NicAlert ITS (Jant Pharmacal) and reinforced on an escalating magnitude schedule.
Results: 67% of those randomized completed the treatment program and there were no significant differences in retention by treatment group. There was a significant decrease in cigarette use across treatment groups over time (RERM, effect of time, t=7.12, p <.00). ANOVA comparisons by treatment group indicated significant differences in abstinence rates (F=6.46, p <.05) over the treatment period with the CM alone group having better treatment outcomes than the CBT alone group (t=2.87, p<.05). Of the 55 participants who were retained at week 4, 7-day biochemically-confirmed point prevalence rates were 0% for the CBT alone group, 45% for the CM/CBT and 60% for the CM alone group (X2=14.96, p = .00).
Conclusions: These results support the utility of our intervention for smoking cessation in adolescents in a high school setting and question the utility of CBT in such interventions.
Financial Support: This study was supported by NIDA grant # P50 DA09421.

339

NALTREXONE FOR OPIOID DEPENDENCE: ORAL, IMPLANTABLE, AND INJECTABLE.

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Aims: The presentation will review results of five randomized double blind placebo controlled randomized clinical trials of different drug formulations of naltrexone we have been doing within the last 12 years: Oral, implantable and injectable.
Methods: 1st study: Double blind placebo controlled randomized clinical trial of oral naltrexone vs placebo. 2nd study: Four cell double blind double dummy placebo controlled randomized clinical trial of combination of naltrexone with fluoxetine vs. naltrexone, fluoxetine, and double placebo. 3rd study: Four cell double blind double dummy placebo controlled randomized clinical trial of combination of naltrexone with guanfacine vs. naltrexone, guanfacine, and double placebo. 4th study: Three cell double blind double dummy placebo controlled randomized clinical trial of naltrexone implant vs. oral naltrexone and double placebo (oral and implantable). 5th study: Double blind placebo controlled randomized clinical trial of injectable naltrexone vs. placebo.
Results: Oral naltrexone in Russia is more effective for relapse prevention and abstinence stabilization than placebo – basically due to family involvement in the control of compliance. Combining naltrexone with antidepressants or guanfacine does not improve outcome significantly. Long acting sustained release naltrexone formulations (injectable and implantable) are substantially more effective than oral naltrexone or placebo for relapse prevention in opiate addicts as they make control of compliance easier.
Conclusions: Extended release formulations of naltrexone are the most effective non-agonist pharmacotherapy formulations for opiate dependence.
Financial Support: NIDA: R01-DA-017317; K05-DA-17009; U10-DA-13043 (Woody, PI)

340

ENHANCED SENSITIVITY TO ATTENUATION OF METHAMPHETAMINE SEEKING BY THE MGLUR2/3 AGONIST LY379268 IN RATS WITH A HISTORY OF EXTENDED SELF-ADMINISTRATION.

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Aims: Recent findings implicate group II metabotropic glutamate receptors (mGluR2/3) in the reinforcing effects of psychostimulants and have identified these receptors as treatment targets for drug addiction. Here, we investigated the effects of mGluR2/3 stimulation on cue- and drug-primed reinstatement in rats with different histories of methamphetamine (METH) self-administration training.
Methods: ShA rats underwent 16 daily sessions of short-term (90 min) access, and LgA rats had 8 90-min sessions followed by 8 long-term (6 hr) sessions. Following self-administration and subsequent extinction training, rats were pretreated with the selective mGluR2/3 agonist LY379268 (LY; 0, 0.3, 1 or 3 mg/kg), exposed to METH-paired cues or a priming injection of METH (1 mg/kg), and tested for reinstatement of METH-seeking behavior.
Results: The LgA rats exhibited an escalated rate of METH intake during self-administration, but when pretreated with vehicle, ShA and LgA rats showed cue- and drug-primed reinstatement at equivalent response rates. However, LgA rats demonstrated greater sensitivity to mGluR2/3 stimulation with attenuated responding during cue-induced reinstatement after 0.3 mg/kg and higher doses of LY, whereas ShA rats decreased cue-induced reinstatement behavior following 1.0 mg/kg and 3.0 mg/kg LY. Additionally, both LgA and ShA rats exhibited decreased METH-primed reinstatement behavior at 0.3 mg/kg and higher doses of LY. A group of control rats was trained to self-administer sucrose pellets, and demonstrated attenuated sucrose-seeking behavior in cue-induced reinstatement testing following 1.0 mg/kg and 3.0 mg/kg LY.
Conclusions: Together, the results indicate that LY has drug-specific attenuating effects on cue-induced reinstatement behavior in rats with a history of escalated METH intake. LY treatment also attenuated drug-primed reinstatement of METH seeking, regardless of the different histories of METH intake during training.
Financial Support: This work was supported by DA025606.

341

SEX DIFFERENCES IN AMPHETAMINE-INDUCED BEHAVIOR ARE MEDIATED BY ORGANIZATIONAL EFFECTS OF ANDROGEN DURING PUBERTY.

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Aims: The goals of this study were: (1) to establish a behavioral rating scale for psychostimulant induced behavior in mice, (2) to determine if mice exhibit sex differences in amphetamine-induced behavior and (3) to evaluate the role of gonadal steroids in such differences.
Methods: Mice (C57Bl/6J) were treated sequentially with saline, amphetamine (1, 2.5 and 5 mg/kg i.p.) and behavior was measured both by an automated apparatus that quantitated locomotion and by a behavioral rating scale as follows: 1 = asleep or inactive 2 = light directed in-place behaviors 3 = normal exploratory behavior 4 = fast exploratory behavior 5 = in-place stereotypies 6 = patterned locomotion 7 = patterned rearing. Locomotion was analyzed by repeated measures ANOVA with time as the repeated measure. Behavioral rating distributions were evaluated by chi square. Brain amphetamine levels were measured by LC-MS at the University of Utah.
Results: Amphetamine caused a dose-related increase in locomotion by both methods. The lowest dose of amphetamine did not increase locomotion but caused stereotyped sniffing. The high dose caused high levels of patterned locomotion which were later interrupted by patterned rearing. Females exhibited higher levels of amphetamine-stimulated behavior than males. Neither ovariectomy nor castration affected behavior of adults, but pre-pubertal castration enhanced the behavioral responses of males. Brain amphetamine levels were slightly lower in females than in males.
Conclusions: These findings suggest that organizational effects of androgen contribute to the lesser locomotor activation by amphetamine in male mice compared to female mice.
Financial Support: This study was supported by NIDA Grant no. DA009079

342

CORRELATES OF ALCOHOL AND DRUG USE AMONG A SAMPLE OF COLLEGE STUDENTS WITH COMORBID SUDS AND GAMBLING PROBLEMS.

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Aims: Epidemiological trends indicate increasing non-medical use of prescription drugs (NMPD), particularly among adolescents/young adults with alcohol being the most frequently co-occurring substance. NMPD is higher among White students, Greek members, and those with lower GPA. Findings about gender differences are mixed. We evaluate gender differences in substance use, assess co-morbidity, and provide a more comprehensive picture of use based on severity of substance use.
Methods: Participants were college students from an online-survey to determine eligibility for a study of brief interventions for co-morbid SUDs and gambling. From a sample of 1930, 135 (7%) met criteria for high risk of developing dependence on a substance(s).
Results: ASSIST severity descriptives: Participants were Caucasian (70.4%), male (52.6%), and 20.1 (SD= 1.6) years old. They consumed an average of 19.2 (SD=14.6) drinks and reported drinking alcohol 3.6 (SD=1.7) days/week with 59.6% at high risk of dependence. Over 90% 'ever' smoked marijuana, and 46.7% were at high risk of dependence. Other drug percentages reported as ever used (and high risk of dependence %) were as follows: cocaine - 38.5% (5.8%); amphetamines - 55.6% (6.7%); sedatives - 46% (14.5%); and opioids - 41.5% (3.6%); Relationships between alcohol/drug use severity scores: There were significant and positive correlations for cocaine and amphetamine and all other substances' severity scores; Gender differences: Other than BAC, we did not find gender differences on any variables. Surprisingly, women's BAC (.23, SD=.09) was significantly higher than men's (.18, SD=.09), p =.001.
Conclusions: Our preliminary data suggests a high percentage of students may be at high risk for developing substance dependence. Those using either cocaine or amphetamines were also likely to report using other substances. Lastly, contrary to previous findings, women reported significantly higher BAC than men.
Financial Support: Financial support: NIDA RO1DA025051 (Larimer)

343

GESTATIONAL INTRAVENOUS NICOTINE INCREASES SENSITIVITY TO METHAMPHETAMINE REINFORCEMENT IN ADULT RAT OFFSPRING.

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Aims: Prenatal tobacco smoke exposure is correlated with low birth weight, ADHD, cognitive deficits as well as increased substance abuse in the human offspring. The purpose of the present study was to determine if prenatal low-dose, IV nicotine exposure would 1) increase sensitivity to methamphetamine (METH) reinforcement and 2) alter METH-induced conditioned taste aversion (CTA).
Methods: Pregnant dams were injected (3x/day) with 0.05 mg/kg nicotine (GN) or saline (GS) via jugular catheters on gestational days 8-21. For the self-administration experiment, animals acquired FR-3 responding for METH, 0.05 mg/kg/inj., and were tested on varying concentrations (0.0005, 0.0025, 0.005, 0.025, and 1.0 mg/kg/inj.) according to a FR-3 schedule. For the CTA experiment, separate GN and GS exposed offspring received three saccharin (CS) and METH (US; 0, 0.3, and 0.5 mg/kg, sc) pairings. Fourteen consecutive two-bottle (extinction) tests were conducted following conditioning. Male and female offspring were used in both experiments.
Results: The self-administration data revealed that GN and GS exposed offspring exhibited an inverted "U"-shaped dose response curve [$F(1, 32) = 39.6$, $P < .001$, quadratic]. GN animals exhibited a leftward shift in their dose-response curve, suggesting increased sensitivity to METH compared to controls; prenatal exposure X dose interaction [$F(1, 32) = 4.0$, $P = 0.05$, quadratic]. Acquisition of METH CTA occurred in a dose-dependent manner with no significant differences between groups; there were no significant differences between groups during extinction testing. Sex was not a significant factor in any analysis.
Conclusions: The present results indicate that prenatal IV nicotine did not reduce the aversive effects of METH as measured by CTA. However, GN exposure increased sensitivity to the reinforcing effects of METH, in adult offspring. That GN rats self-administered METH at higher rates for a lower dose relative to GS animals suggests that prenatal nicotine exposure, via maternal smoking, may produce increased substance use vulnerability in human offspring.
Financial Support: NIDA Grant DA 021287

344

WAVELET-TRANSFORMED REGIONAL FMRI SIGNAL COHERENCE CHARACTERIZES INDIVIDUAL DIFFERENCES IN CRAVING INHIBITION.

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Aims: Urine cocaine status at treatment entry has been a strong predictor of drug use outcome: patients with cocaine-negative entry urine (C-) have better outcomes than cocaine positive (C+) patients. However, the brain substrates underlying individual outcome variation are not yet known. We hypothesized that wavelet transform coherence (WTC) may reveal these substrates, with C- individuals having an inverse coupling (negative coherence) between an inhibitory region, dorsal anterior cingulate cortex (dACC), and a downstream motivational region, amygdala (amyg).
Methods: Treatment-seeking patients (C+: N=11, C-: N=8) were given an "inhibition of craving" training session during a stabilization week prior to fMRI. Scans were acquired on the last day of the stay. Patients were asked to "inhibit your cocaine craving" (by considering the negative consequences) while viewing a 5 min cocaine video. WTC was applied to the fMRI signals between dACC and amyg to capture the time and frequency-localized coherence between the 2 regions. "Coherence" measures the degree of coupling between the 2 regions. Bootstrapping was applied to test the statistical significance of individuals' WTC results.
Results: Inverse coupling, implicating an inhibitory connection, was found from all 8 C- patients, but from only 4 C+ patients. C- group showed a sustained inverse coupling for over half the video, but this sustained pattern was absent from C+ group ($p = 0.047$, independent t-test).
Conclusions: WTC reveals a potential imaging biomarker: a difference in the brain connection for "good prognosis" C- patients, as compared to patients who are more likely to fail. Lack of inverse coupling in "poor prognosis" C+ patients may help explain their struggle to inhibit cocaine craving states – a deficiency that may lead to relapse. This deficiency may be a novel treatment target.
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345

HIV-1 MOLECULAR EPIDEMIOLOGICAL PROFILE DIFFERENCES AMONG TAIWAN DRUG ABUSERS.

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Aims: Human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) epidemic among drug users is a global health threat, especially the viral genotypic variation affecting the spreading of the virus. The purposes of this study were to investigate the molecular epidemiology of HIV infection among injecting drug users (IDUs).

Methods: Based on the partial env nucleotide sequence information, the phylogeny and epidemiological profile of 66 HIV strains circulating among IDUs in HIV surveillance database in Taiwan were analyzed. This HIV surveillance database was established during 2007-2009 in accordance to IRB rules. Using genotype classification of HIV as a molecular marker, the origin and the genesis of HIV epidemic were investigated.

Results: The phylogenetic analysis showed two viral strains, CRF07_BC (80.3%) and CRF01_AE (19.7%) subtypes circulating among Taiwan IDUs during 2007-2009. Three routes were identified in CRF07_BC transmission and only one transmission chain was found in CRF01_AE spreading through the Bayesian tree analysis. The evolution rates which represent the transmission efficiency were also different between CRF07_BC and CRF01_AE viruses, 1.16×10^{-2}, 2.82×10^{-3} respectively. The transmission entry to IDUs population for both viruses could be traced back to the year 2002 by using coalescent theory approaches. But, the human genomic COMT Val158Met polymorphism frequency, which is associated with the drug abuse behavior, was not different between these two subtypes of the infection population.

Conclusions: HIV-1 CRF07_BC and CRF01_AE subtypes infection among Taiwan IDUs had different molecular epidemical profiles. CRF07_BC virus had multiple transmission routes and circulated among IDUs with greater efficiency than CRF01_AE virus. But, the human genomic COMT polymorphism showed that the genetic behavior phenomenon still were similar between these two infection groups.

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346

EFFECTS OF D-AMPHETAMINE ON BRAIN ACTIVATION OF COCAINE-DEPENDENT SUBJECTS DURING A GO/NOGO TASK OF INHIBITORY CONTROL.

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Aims: Cocaine dependence is marked by high levels of state and trait impulsivity, and this outcome may be related to dysfunctional dopamine transmission. Dopamine-enhancing agents have shown some efficacy in reducing cocaine-positive urines, and in reducing impulsivity on laboratory behavioral tasks. The effect of dopamine enhancing drugs on brain function in cocaine dependent subjects during performance on laboratory impulsivity measures has not been examined. The purpose of this study was to determine the effects of acute administration of d-amphetamine on brain function during a Go/NoGo task in cocaine dependent subjects.

Methods: Following informed consent, 10 non-treatment seeking cocaine dependent subjects underwent two separate fMRI scans during performance on a Go/No-Go paradigm with two levels of difficulty (Easy, Hard). Subjects were administered 20mg of d-amphetamine on one of the scans and placebo on the other scan. Dosing was counterbalanced and double blind.

Results: On correct Easy NoGo trials (e.g., successful inhibition of the response), there was significantly greater activation in prefrontal, striatal, and thalamic regions under placebo compared to d-amphetamine. On correct Hard No-Go trials, placebo showed significantly greater activation compared to d-amphetamine in parietal and occipital cortex (FWE corrected $p<0.05$). For the behavioral performance measure of discriminability (detecting Go from NoGo targets and executing the proper (non)response) there was a drug (plc, d-amph) x trial type (Easy, Hard) interaction ($p < .04$). D-amphetamine improved discriminability on Easy No-Go trials and decreased discriminability on Hard NoGo trials.

Conclusions: The findings are consistent with enhancement of monoamines in cocaine users leading to changes in brain activation in brain regions known to subserve response inhibition.

Financial Support: NIDA Grants P50DA009262, K02DA00403, P50DA018197

347

RELATIONSHIP BETWEEN WEIGHT STATUS AND RISKY SMOKING BEHAVIORS IN A NATIONAL SAMPLE OF ADOLESCENT FEMALES.

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Aims: The need for smoking cessation intervention efforts within childhood obesity treatment programs have been strongly recommended by the Expert Committee on Childhood Obesity (Barlow et al., 1998). Moreover, while adolescent females have reported increased use of smoking cigarettes when attempting to lose weight, adolescent males have reported decreased use of cigarettes (Ryan et al., 1998; Strauss & Mir, 2001). However, little research has examined the effect of female weight status on smoking patterns during adolescence.

The current study examined the relationship between female adolescents' weight status to cigarette smoking. It was hypothesized that higher weight perceptions (ie. overweight, obese), greater BMI, and the desire to lose weight would be associated with the endorsement of risky smoking patterns.

Methods: The study utilized the data obtained by the Center for Disease Control (CDC) 2009 Youth Risk Behavior Surveillance System (YRBSS), sampling 196 schools, 9th-12th grades (N = 16,410). However, the present study only examined females (N = 7,816).

Results: Regression analyses revealed, as hypothesized, that higher perceptions of weight (B = .161, $p < .001$) and greater BMI (B = .008, $p < .001$) predicted ever having smoked a cigarette. Moreover, compared to adolescent females unconcerned with their weight status, those attempting to lose weight were twice as likely to report smoking cigarettes (B = .608, $p < .001$, Odds Ratio = 1.837). As hypothesized, higher perceived weight, greater BMI, and desire to lose weight significantly predicted ($p < 0.01$) age of first cigarette (B = -.115, -.006, -.325), days smoked per month (B = .086, .004, .221), and number of cigarettes smoked per day (B = .069, 0.003, .194), respectively.

Conclusions: These findings indicate a concerning relationship between weight status and cigarette smoking patterns in adolescent females. It is vital for future research efforts targeting prevention and intervention efforts towards smoking cessation to account for both gender and weight status when working with adolescents.

Financial Support: No financial support.

348

CHARACTERIZATION OF ANATABINE: AN UNDERSTUDIED ALKALOID WITH POTENTIAL BENEFITS.

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Aims: Anatabine is an alkaloid found in Solanaceous plants considered to have few significant biological effects. Recent evidence suggests that anatabine may be helpful in reducing cigarette cravings in smokers, although the mechanism is not understood. We conducted studies to characterize anatabine's pharmacological and toxicological profile, including preclinical tests of abuse potential.

Methods: A complete set of GLP toxicology studies included repeat dose toxicity, genotoxicity, and teratogenicity. Receptor binding assays evaluated binding to and activation of three cloned human nicotinic receptor (nAchR) subtypes in mammalian cells. Preclinical behavioral assays included acute behavioral disruption, effects on nicotine withdrawal, drug discrimination, and self-administration.

Results: Toxicology results indicated that anatabine had no adverse effects at the usual human exposure of 0.06 mg/kg/day, and most tests were negative at doses up to 6 mg/kg/day. Anatabine acted as an agonist at the nAchR subtypes tested, but was much less potent than nicotine. Anatabine was less potent at disrupting behavior than nicotine, with a longer duration of action. Anatabine failed to significantly reverse nicotine withdrawal, was not self-administered at rates higher than saline, and was much less potent in producing nicotine-like interoceptive effects than nicotine (relative potency: 0.006).

Conclusions: Anatabine is a minor tobacco alkaloid that is similar in structure but very different pharmacologically than nicotine. Although less potent than nicotine, anatabine acts as an agonist at relevant nAchR subtypes, has a longer half-life, is safe in high doses, and does not have discernible abuse potential. Anatabine may be a useful compound to study in models of disease or drug dependence in which nAchRs are implicated or thought to play a role.

Financial Support: This work was funded by Rock Creek Pharmaceuticals, Inc., Gloucester, MA.

349

TRENDS IN ILLICIT DRUG USE IN AUSTRALIAN CORRECTIONAL CENTRES.

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Aims: This paper examines trends in illicit drug use while in prison in New South Wales (NSW), Australia. It is well recognized that drug markets are dynamic and that changes in drug markets have implications for treatment providers. There has been no research considering how drug markets within a prison system might change, and what this may mean for drug treatment programs in prisons.
Methods: Data were obtained from three waves of the NSW Inmate Health Survey (IHS), conducted in 1996, 2001 and 2009. The IHS uses a random sample of inmates, stratified by age, sex and Indigenous status. Self-report data regarding use of illicit drugs while in prison were collected, as were data on participation in the prison opioid substitution treatment (OST) program. Data were analysed in SAS using survey analysis procedures to account for the survey sampling design, clustering and missing data.
Results: The proportion of respondents with a history of illicit drug use who reported having used an illicit drug in prison decreased from 67% in 1996 to 56% in 2009. The proportion of inmates reporting that it is 'easy' or 'very easy' to obtain drugs in prison also decreased. The proportion of heroin users receiving OST has increased over time; in 2009, 43% of respondents with a history of heroin use were in OST.
Considering injecting drug use specifically, the proportion of injecting drug users who have injected in prison fell from 53% in 1996 to 44% in 2009. There have been clear changes in the types of drugs injected; most notably, a decrease in the prevalence of heroin injecting and an increase in injecting of methamphetamine, methadone and other opioids.
Conclusions: Notwithstanding the limitations of self-report data, it appears that the use of illicit drugs while in prison is decreasing in NSW. Coverage of OST has improved and has been accompanied by a decrease in heroin injection; however, some of this decrease has been offset by an increase in the injection of methadone and other opioids. Increased methamphetamine use in prison is a challenge for drug treatment providers in a system oriented towards pharmacotherapy for heroin dependence.
Financial Support: Justice Health and NSW Health

350

MILITARY LIFETIME BEHAVIORAL HEALTH UTILIZATION IN DEPLOYED ARMY SERVICE MEMBERS BY SUBSTANCE ABUSE AND NON-SUBSTANCE ABUSE GROUPS.

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Aims: In recent years, alcohol dependence has been one of the top mental health diagnoses among active duty service members who have been hospitalized, and substance abuse-related hospitalizations have increased by 72% since 2006 (Armed Forces Health Surveillance Center, 2010). Little is known about pre-deployment behavioral health (BH) utilization in military personnel with substance abuse problems. Using a cohort of Army active duty service members (AADSMs) returning from deployment in FY2010, we compared the military lifetime history (FY2002-2010) of BH-related service utilization [i.e., BH, substance abuse (SA)] in those with and without SA problems.
Methods: Military health system administrative data were analyzed using a retrospective, longitudinal design of non-equivalent groups (SA vs. non-SA groups). We identified cases of possible SA problems (based on utilization) during military lifetime history and report BH utilization rates, adjusting for lifetime military months of service.
Results: In this 2010 cohort of AADSMs (n=152,447), 17% had SA utilization during their military lifetime. AADSMs in the SA group were significantly younger, had fewer lifetime military service months, and were lower ranking than those in the non-SA group. During their lifetime military service, the SA group was also significantly more likely to have serious wounds (i.e., amputations, traumatic brain injury) and use inpatient mental health services. During the year prior to deployment, more than twice as many Army personnel in the SA group than in the non-SA group had BH utilization (39% vs. 14%).
Conclusions: Findings underscore the need to identify substance use problems in primary care and explore behavioral health referral and intervention opportunities with active duty Army personnel prior to military deployments.
Financial Support: This work was supported by the National Institute on Drug Abuse (NIDA) Grant #R01DA030150.

351

ALCOHOL AND TOBACCO USE IN A RURAL DISTRICT IN NEPAL.

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Aims: Alcohol and tobacco use are associated with serious health risks. In Nepal, studies of substance use are scarce or are carried out in the Kathmandu Valley, neglecting rural areas. Aims: To assess the prevalence and patterns of alcohol and tobacco use in the Manang District and health problems in households (HH)in the Manang district.
Methods: Data were obtained from the Himalayan Family Healthcare Project, conducted to assess the health needs of Manang District residents. Purposive sampling was used in a cross sectional design. HH heads (N=204) were interviewed using a standardized instrument, representing 1,108 people. HH heads reported the tobacco use among members of their household, including the number of cigarettes smoked and hours spent smoking for each member. Alcohol use measures included HHs quantity and frequency of consumption, type, and source of alcohol. HH heads also identified the desire for alcohol treatment within their HH.
Results: More than one-third (34%) of HHs had at least one male smoker; 8% of females smoked. Forty seven percent of men (44% of women) smoked 6-10 cigarettes a day; 22% smoked 16-20. None of the women smoked 10 or more cigarettes. HHs reported that 64% of men used alcohol compared to 9% among women. In HHs where alcohol was used, 41% of men and 39% of women drank nearly every day. Among men, 68% had 4 or more glasses daily, as did 6% of women. The alcohol used was largely homebrewed. Forty-three percent of HH's reported that at least one HH member needed or wanted alcohol treatment.
Conclusions: While the prevalence of alcohol use was not as high as expected,the quantity of alcohol consumed was found to be substantial among men in the Manang District. The desire for alcohol treatment was also high. Treatment services for substance use problems are a serious public health priority in this poor, rural area of the world.
Financial Support: Fogarty International Center ICOHRTA Training Program in Behavioral Disorders (Grant No. D 43-TW05811; Sonam Ongmu Lasopa, Fellow; LB Cottler, PI)

352

THE RELATIONSHIP BETWEEN DRUG USE STIGMA AND DEPRESSION.

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Aims: The current study sought to examine the relationship between drug use stigma and depression in an inner-city sample with high rates of drug use. We assessed the relationship between drug use, drug use stigma/discrimination and depressive symptoms.
Methods: The current analyses are cross-sectional from the CHAT study. "CHAT" was an acronym for a set of communication skills, taught in a social network based HIV/STD prevention intervention for women and their social network members. Participant were recruited through street outreach, referrals, and word-of-mouth in inner-city Baltimore, MD, USA.
The stigma/discrimination scale was comprised of 8 items, such as "How much do you feel ashamed of using drugs", "how much do you feel people avoid you because you use drugs", and "how much do you fear you will lose your friends because you use drugs." Depression was assessed with the Center for Epidemiological Studies, Depression Scale (CES-D). The two standard cutoff points of 16 and greater and 20 and greater were used to create the outcome variables.
Results: Overall, 49.25% of the participants had CES-D scores of 16 or greater and 36.87% had CES-D scores of 20 or higher. Female gender, homelessness, drug stigma, larger size of drug network, current use of heroin, cocaine, and crack were all significantly associated with high levels of depressive symptoms. In the multivariate analysis, only drug use stigma remained associated with depression in both models. In the CESD≥20 model female gender remained significantly associated with depression ($p<.01$, OR=2.89).
Conclusions: The results of these findings suggest that depression is linked to both drug use and drug use stigma and that active drug use does not explain the association between drug use stigma and depression. Drug treatment programs and other service providers to drug users should consider addressing issues of self-stigma and programs for family members of drug users should also address stigma and discrimination by significant others of drug users.
Financial Support: Funded by NIDA

353

PREVALENCE OF CHRONIC CONDITIONS AND IMPACT ON FUNCTIONING AMONG PERSONS IN ADDICTION RECOVERY: OPPORTUNITIES UNDER HEALTH CARE REFORM.

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Aims: Health care reform (HCR) will have a widespread impact on substance use disorder (SUD) services and presents opportunities for persons recovering from chronic SUD. Especially relevant are parity and the integrated (physical and behavioral health) chronic care model. We examine (a) The prevalence of chronic physical and mental health conditions (PH and MH) in SUD persons at various recovery stages; (b) The association among comorbidities; and (c) The impact of comorbidities on care utilization and on key areas of functioning relevant to recovery – e.g., employment, a priority at all recovery stages.
Methods: Data from two NYC samples of predominantly ethnic minorities with a long, severe history of polysubstance dependence are used: An outpatient treatment sample (N = 314) and one of community-based persons whose abstinent recovery at intake ranged from one month to >10 years (N = 356).
Results: [Similar trends in both samples. Community sample presented here only for concision] The sample was 53% male, mean age = 43; 53% had a chronic PH condition, 72% reporting more than one: heart and respiratory disease, HIV/AIDS and diabetes were most frequent; 38% had a chronic MH condition - 55%, depression. Having an MH diagnosis doubles the odds of having a PH condition. Having a chronic PH condition is associated with significantly (<.05) more doctor visits and hospitalizations in the past year, with lower employment rates (31% vs. 49%) and higher stress levels. MH conditions are also associated with lower employment (29% vs. 43%), higher stress and with lower quality of life satisfaction, both predictors of subsequent relapse.
Conclusions: The prevalence of chronic comorbid PH/MH conditions among persons in recovery from chronic SUD is very high and associated with high costs, economically - services utilization, unemployment- and clinically (stress and quality of life). HCR's integrated chronic care model for underserved populations, many with multiple comorbidities, holds great promise to reduce healthcare costs and to promote SUD recovery.
Financial Support: NIDA grants R01 DA14409 and R01 DA015133

354

ACUTE BINGE COCAINE INDUCES OPPOSING AND REGION-SPECIFIC EFFECTS IN THE STRIATUM OF D1 AND D2-EGFP MICE.

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Aims: Cocaine addiction is a chronic relapsing disorder consisting of genetic, neurologic and environmental components. Our lab and others have shown that D1-like (D1-r) and D2-like (D2-r) dopamine receptors may differentially modulate the effects of cocaine administration on drug-seeking behavior in humans and rodents. To identify cocaine-induced alterations in D1 versus D2 expressing cells during the early stages of addiction, we asked to what extent are either cell-type altered by acute binge cocaine exposure.
Methods: We used BAC-eGFP transgenic mice, to distinguish between D1-r and D2-r neuronal subpopulations. Heterozygotes from each line were bred from a single breeder pair, (given to our lab from the GENSAT core). To mimic early stage cocaine use, we administered acute binge cocaine or saline to D1 and D2 mice (n=6-8 per group), and sacrificed mice at 30 minutes and 24 hours after their last injection. Cell number alterations in the striatum were determined from stereological counts using confocal microscopy and Visiopharm© software.
Results: Compared to controls, D2-r mice administered cocaine and sacrificed 30 minutes after their last injection, had fewer cells in the dorsolateral striatum (DLS) and nucleus accumbens core ($p<0.05$). D2-r mice did not differ from controls after 24 hours. In contrast, D1-r mice administered cocaine and sacrificed 30 minutes post-injection had a greater number of cells in the DLS compared to controls ($p<0.05$). The D1-r increase was also present in mice sacrificed 24 hours after their last injection ($p<0.01$).
Conclusions: These results suggest that acute binge cocaine administration may induce region specific alterations in the striatum that have opposing patterns in D1-r versus D2-r expressing cells. These data also support the development of therapeutics targeted at differential striatal circuitry to treat early stage addiction.
Financial Support: NIH: NIDA P60-DA05130, NIDA T32 DA007274; The Gary R. Helman Postdoctoral Fellowship; The Weill Cornell Traveler's Summer Research Fellowship Program

355

LONGITUDINAL STUDY OF THE ASSOCIATION BETWEEN IMPULSIVITY AND TOBACCO USE AMONG YOUNG ADULTS.

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Aims: Impulsivity is a risk factor for tobacco use initiation as well as the development of tobacco dependence. However, it is not known whether the effects of impulsivity on tobacco dependence reflect an influence of impulsivity on transitioning from initiation to regular tobacco use or a consequence of tobacco use. This study will determine if 1) impulsivity confers vulnerability to escalating tobacco use, and 2) behavioral inhibition changes as a consequence of escalating tobacco use.
Methods: Young adults (N=400) were repeatedly assessed across their first three years of college (data collection will be completed in December 2011). Measures included self-reported (UPPS-P) and performance-based (cued go/no-go, BART, MCQ) indices of impulsivity, and self-reported (Life History Calendar) tobacco use. Group trajectory modeling will examine whether dimensions of impulsivity influence trajectories of smoking behavior, and linear mixed models will determine whether behavioral impulsivity changes as a function of tobacco use. It is hypothesized that a bi-directional relationship will be identified in that baseline impulsivity will predict tobacco use escalation, and behavioral impulsivity will increase as a function of nicotine exposure.
Results: A cross-sectional analysis of baseline data indicated that scores on UPPS-P negative urgency were significantly greater in daily smokers compared to intermittent smokers (2.7 + 0.08 vs. 2.4 + 0.07, mean + SE), while BART inflations were greater among intermittent smokers compared to non-smokers (34.4 + 1.1 vs. 31.2 + 0.5). Scores on all dimensions of the UPPS-P were greater in daily smokers compared to non-smokers.
Conclusions: Cross-sectional baseline data analyses were consistent with initial hypotheses in that trait impulsivity was greater among smokers than non-smokers and that behavioral measures of impulsivity varied as a function of prior tobacco exposure. Longitudinal data analyses will be presented to inform the directional relationships among these variables.
Financial Support: DA-05312

356

RELATIONSHIP BETWEEN HIV TESTING FOLLOWING INCARCERATION AND PARTICIPATION IN WAYSAFE.

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Aims: The TCU Disease Risk Reduction (DRR) Project tested an intervention, WaySafe, designed to increase positive decision-making skills among offenders for healthy living, including skills for reducing disease risk behaviors. WaySafe focused on improving problem recognition, commitment to change, and strategies for avoiding behavioral risks of infections. The current study compares offenders who participated in WaySafe versus treatment as usual (TAU) during re-entry into the community.
Methods: A total of over 170 offenders who participated in the DRR study and who returned follow-up surveys after release from incarceration were included. Differences at follow-up between offenders who completed WaySafe and those receiving TAU were examined as well as relationships between post-WaySafe measures taken before release and follow-up outcomes. Participating offenders were randomly assigned to the DRR Waysafe intervention or TAU. At the completion of the six-week Waysafe curriculum, all participating offenders completed the post-test survey.
Results: Offenders who completed the WaySafe intervention were more likely than offenders who received TAU to report getting tested for HIV after release from prison. Results also showed that participants who had higher post-test scores on HIV Knowledge Confidence, Risky Sex and Drug Use Avoidance, Risk Reduction Plans, and Prevention Skills were more likely to report getting tested for HIV after release.
Conclusions: Emphasis has been placed on increasing HIV testing rates for offenders getting released from prison who are at increased risk for HIV infection by way of risky sex and/or drug use activities. Results of this study demonstrated that offenders who completed WaySafe while incarcerated were more likely than others to report getting tested for HIV in the community and that getting tested was positively associated with decision-making skills that are the focus of WaySafe.
Financial Support: Funding was provided by the National Institute on Drug Abuse, National Institutes of Health (NIDA/NIH) through a grant to Texas Christian University R01DA025885.

357

THE EFFECTS OF ACUTE AND CHRONIC METHADONE ADMINISTRATION ON MEMORY RETRIEVAL IN RATS.

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Aims: Although widely prescribed to treat opioid addiction, little is known about possible side effects of methadone on memory functions. The objective of this study is to compare the effects of acute and chronic methadone on memory retrieval in rats, and explore the selectivity of possible deficits.
Methods: Administration of acute (0, 1.25, 2.5 and 5 mg/kg SC) and chronic steady-state methadone (0, 10, 30 and 55 mg/kg/day) was tested on recall of three different types of information: stimulus-reward (10-arm parallel maze), stimulus-response (8-arm radial maze), and stimulus-stimulus (Barnes maze). Acute and chronic steady-state methadone doses were also compared on tests of locomotor activity, swimming behaviour, and acoustic startle reactivity.
Results: In the stimulus-reward task, acute methadone impaired performance as a result of severe depression of locomotion. This motor deficit, however, was modulated by the motivational valence of environmental stimulation. In fact, acute methadone did not eliminate forced swimming behaviour. In the stimulus-response and stimulus-stimulus tasks, accuracy was impaired independently of direct motor deficits. But, rats were hyper-reactive to aversive stimulation and, in fact, 5 mg/kg enhanced acoustic startle. Importantly, chronic steady-state methadone did not affect accuracy on memory retrieval, did not depress motor or swimming activity, and did not change startle reactivity.
Conclusions: Only acute methadone impaired accuracy and/or performance on three tests of memory retrieval. These findings in rats suggest that memory deficits reported in methadone-maintained individuals may not be directly attributable to maintenance on methadone.
Financial Support: Supported by the Natural Sciences and Engineering Research Council of Canada (NSERC).

358

CHANGES IN PRESCRIPTION AND OXYCONTIN® DRUG ABUSE PATTERNS IN A RURAL KENTUCKY COUNTY.

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Aims: Appalachian Kentucky has a history of distilling corn to alcohol as well as conflicts about alcohol and marijuana. More recently the popular press highlighted the area as a national leader in prescription drug abuse and misuse, particularly OxyContin®. This study examines routes of administration and abuse patterns of drug misuse before and after the August 2010 introduction of a new tamper–resistant formulation of OxyContin®.
Methods: Quantitative interviews with 192 OxyContin® abusers and in-depth qualitative Interviews with 25 OxyContin® abusers were conducted. Participants were age 18 or older, were misusing Oxycontin® and resided in one rural county. Interview data included demographics, drug use and routes of administration.
Results: Participants were male (54.2%) and white (97.9%) with a median age of 32. 80.7% reported lifetime injecting and 96.1% of injectors injected prescription opioids. When past 30 day use was examined before and after the new formulation there were, as hypothesized, significant decreases at <0.001 for days snorted (5.88 vs. 3.29) and days injected (8.46 vs. 3.60) for the original formulation. Less than one day on average was reported for snorting (0.17) and injecting (0.005) the new formulation. However, snorting, injecting and swallowing increased at the <0.001 level for other oxycodone formulations and swallowing hydrocodone. No other differences in prescription drug use patterns emerged.
Conclusions: The new formulation of OxyContin® decreased snorting and injecting of OxyContin®. However, snorting and injecting of other oxycodone formulations increased. Recommendations include increasing physician pain management education, interstate prescription monitoring, and access to drug abuse, mental health and pain treatment to reduce misuse. The increased rural injecting is alarming and underscores the need for interventions targeting injectors.
Financial Support: Supported by Purdue Pharma, Inc. L.P.

359

GENDER DIFFERENCES IN MENTAL HEALTH-RELATED QUALITY OF LIFE AMONG CANNABIS USERS.

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Aims: The aim of the present study was to assess self-reported mental quality of life (QoL) among cannabis users and individuals with cannabis use disorders (CUD) in a large representative sample.
Methods: We analyzed data from the National Epidemiological Survey of Alcohol and Related Conditions (NESARC,n=43,093). Mental health related QoL was assessed using the Mental Component Summary (MCS) score of the Short-Form 12-Item Health Survey (SF-12). The contribution of cannabis use and CUD to SF-12 scores was assessed using multiple linear regressions models and controlling for sociodemographic variables and mental illness.
Results: The prevalence of cannabis use and CUD in the last 12 months was 4.1% and 1.5%, respectively. Mean MCS scores were significantly lower among female (n=607) and male (n=996) cannabis users compared to non-users (by 0.6 standard deviations (SD) and 0.3SD, respectively), and by females (n=174) and males (n=386) with CUD compared to those without CUD (by 0.9SD and 0.4SD, respectively). Each joint smoked daily was associated with a greater decrease in MCS scores in females (0.1SD) compared to males(0.03SD).
Conclusions: Cannabis use and CUD were associated with lower self-reported mental QoL. Specifically, our findings showed that cannabis use and CUD have a more significant effect on self-reported mental health QoL among female users. Using functional and emotional outcomes may particularly aid in detecting the impact of cannabis use and cannabis use disorders on mental health among females.
Financial Support: Dr Lev-Ran receives funding through the Social Aetiology of Mental Illness (SAMI) CIHR program. Drs. Lev-Ran, Rehm and Le Foll receive salaries from the Centre for Addiction and Mental Health.

360

VENLAFAXINE TREATMENT LOWERS ABSTINENCE RATES IN MARIJUANA-DEPENDENT ADULTS WITH DEPRESSION.

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Aims: Venlfaxine-ER (Ven-ER) has been shown to be an effective treatment for depression. We hypothesized that VEN-ER would be an effective treatment of depression in cannabis-dependent adults with concurrent depressive disorders and that it will positively impact marijuana use.
Methods: A randomized, 12-week, double-blind, placebo-controlled trial of adult outpatients meeting DSM-IV criteria for cannabis dependence and major depression or dysthymia was conducted. Ven-ER was titrated to 225 mg/day and subsequently raised to 375 mg/day if depressive symptoms persisted. The primary outcomes were 1) at least a 50% reduction in depressive symptoms or clinical remission of depressive symptoms based on Hamilton Depression (HAM-D) score and 2) the achievement of two consecutive weeks of abstinence. Logistic regression was used to analyze all dichotomous outcomes and mixed effect models with appropriate link functions was employed to analyze all longitudinal continuous outcomes.
Results: One hundred and three participants were randomized to placebo (n=52) or Ven-ER (n=51). Overall, the majority of both treatment groups had a clinically significant mood response (> 50% decreased in HAM-D score from baseline), with no significant difference between the 2 treatment arms. Notably, the Ven-ER group had significant greater marijuana withdrawal symptoms and significantly lower rates of abstinence than the placebo group (11.8% vs 36.5%, p=0.0063). Reduction in marijuana use was significantly associated with lower mood ratings in the placebo arm but not the Ven-ER group.
Conclusions: Ven-ER was not superior in reducing depressive symptoms or marijuana use. Instead, it was less likely to promote abstinence. Although these data are preliminary, Ven-ER may be contraindicated in depressed marijuana abusers.
Financial Support: NIDA grants: R01DA15451, K23 DA21209, K24 DA029647

361

COGNITIVE CONTROL AND GENDER-SPECIFIC NEURAL PREDICTORS OF RELAPSE IN COCAINE DEPENDENCE.

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Aims: Deficits in cognitive control are implicated in cocaine dependence. Previously, combining functional magnetic resonance imaging (fMRI) and a stop signal task (SST), we demonstrated altered cognitive control in cocaine dependent individuals. However, the clinical implications of these cross-sectional findings and, in particular, whether the changes were associated with relapse to drug use, were not clear. The current study aimed to address this issue, focusing specifically on error processing during cognitive control.
Methods: We recruited 97 treatment-seeking individuals (37 women) with cocaine dependence (CD) to perform the SST during fMRI and participate in follow-up assessments for 3 months, during which cocaine use was evaluated with time line follow back. Brain images underwent standard pre-processing with SPM8. Using voxelwise analysis with logistic and Cox regressions, we identified brain activations of cognitive control that predict relapse and time to relapse. We used receiver operating characteristic analyses to describe the accuracy of these predictions and a stratified scheme to validate these predictors.
Results: In women, decreased error-related activations of the thalamus and dorsal anterior cingulate cortex (dACC) predicted relapse and an earlier time to relapse. In men, decreased error-related activations of the dACC and left insula predicted relapse and an earlier time to relapse. These regional activations were validated with data re-sampling and predicted relapse with an average area under the curve of 0.849 in receiver operating characteristic analyses.
Conclusions: These findings provide direct evidence linking deficits in cognitive control to clinical outcome in a moderate-sized cohort of cocaine dependent individuals. These results may provide a useful basis for future studies to examine how psychosocial factors interact with cognitive control to determine drug use and to evaluate the efficacy of pharmacotherapy in remediating deficits in cognitive control in cocaine addicts.
Financial Support: This study was supported by NIH grants R01DA023248 (Li), K02DA026990 (Li), P50-DA16556 (Sinha).

362

WOMEN-ONLY TREATMENT, SERVICE SYSTEM EXPOSURE, AND DRUG USE ABSTINENCE AMONG MOTHERS 10 YEARS AFTER SUBSTANCE ABUSE TREATMENT.

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Aims: Specialized substance abuse treatment for parenting women is thought increase utilization of health and social services, thereby improving treatment outcomes, but research on its long-term impacts is limited. We examine service system exposure and drug use outcomes among mothers approximately 10 years after admission to women-only (WO) or mixed-gender (MG) treatment.
Methods: Participants (n=713) were recruited at admission to 44 treatment programs in 13 California counties during 2000-2002 and completed a 10-year follow-up interview in 2010-2011. 53% received WO treatment. Addiction severity index was administered at intake and follow-up. Exposure to health, social services, and criminal justice systems during the 10 years following baseline was obtained from administrative data systems.
Results: Preliminary analysis showed that at baseline, mothers' mean age was 31.7 + 7.3; race/ethnicity was 53% white, 23% Hispanic, 16% African American, and 7% other; 35% lacked a high school education; 32% was employed; 44% received public assistance; 18% were married; and 43% reported methamphetamine as the primary drug problem. 82% had dependent children, with a mean of 2.3+ 2.0 children per woman. At the follow-up, 52% of mothers were drug abstinent. Multiple logistic regression analysis indicated that WO treatment increased the odds of drug use abstinence, even after controlling for individual-level characteristics. Future analyses will explore whether the effects of WO treatment on drug use abstinence is mediated by exposure to health, social services, and criminal justice systems.
Conclusions: Mothers who receive substance abuse treatment exhibit severe problems in many domains that may be best treated by specialized care. More research is needed to understand associations between specialized care, service system exposure, and treatment outcomes.
Financial Support: Supported by NIDA R01DA021183, P30DA016383, & K05DA017648 (PI: Hser)

363

ANALYSIS OF GENETIC EFFECTS AND HERITABILITY OF SNPS AND THEIR INTERACTIONS IN TWO ETHNIC POPULATIONS FOR SMOKING DEPENDENCE.

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Aims: With genome-wide and candidate gene-based association studies, numerous single nucleotide polymorphisms (SNPs) from different candidate genes are reported to be associated with nicotine dependence (ND). However, the contribution of each SNP and/or of interacting SNPs to ND is rarely addressed.
Methods: To determine the genetic contribution of each associated SNP and significant interacting SNPs to ND, we estimated genetic effects and heritability of SNPs that were reported to be associated with ND in our earlier studies and of significantly interacting two- and three-SNP combinations detected by generalized multifactor dimensionality reduction based on an exhaustively searching all possible two- and three-SNP combinations of 252 SNPs in 30 candidate genes.
Results: We revealed 9 SNPs in 5 genes (i.e., CHAT, CRHR1, GABBR2, NRXN1, and TAS2R16) have significant genetic effect on at least one ND measure in both AA and EA samples; 12 SNPs in 11 genes (i.e., ANKK1, CHRNA3, CHRNA4, CHRNA5, DRD2, DRD3, GABBR2, GRIN3A, NRXN1, SHC3, and TAS2R38) show significant effect on ND in the AA sample, and 5 SNPs in 4 genes (i.e., DLG4, DRD2, GABBR2, and NRXN1) show significant effect on ND in the EA sample, respectively. Further, we found that 10 two-interacting SNPs and 8 three-interacting SNPs also contribute significantly to ND.
Conclusions: We found these identified individual and interacting SNPs account 0.42, 0.58 and 0.57 of heritability for SQ, HSI and FTND, respectively. We conclude these detected significant individual SNPs and interacting SNP combinations account for about 2/3 and 1/3, respectively, of the detected heritability for these three ND measures.
Financial Support: Supported by NIH grants DA-12844, DA-13783, National Basic Research Program of China (2011CB109306) and Key Technologies R&D Program in China (2009ZX08009-004B).

364

ALKS 33 REVERSES FENTANYL-INDUCED RESPIRATORY DEPRESSION IN DOGS: A MECHANISTIC PK/PD MODEL.

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Aims: The purpose of this study was to develop a mechanistic PK/PD model to investigate the action of ALKS 33, a novel μ-opioid antagonist, to reverse fentanyl (FEN) induced respiratory depression and sedation in the dog.
Methods: Dogs (N=6) were administered FEN (0.36 to 0.48 mg/kg) via IV infusion for up to 12 hours. ALKS 33 (0.1 mg/kg or 0.2 mg/kg; IM) was administered 1.5 hours after the initiation of FEN infusion. PD response was assessed through objective (pO_2/ pCO_2; breaths per minute) and subjective (sedation score) measures. Serial plasma samples were analyzed for ALKS 33 and FEN via a validated LC/MS assay. A compartmental model was used to characterize ALKS 33 and FEN PK data. A mechanistic, time-independent, receptor-competitive PK/PD model was developed to investigate opioid agonist–antagonist interaction. The PD responses of pCO_2 and sedation score were analyzed across both ALKS 33 dose levels. Compartmental data analysis was conducted using WinNonlin v5.2.
Results: A one-compartment model best described ALKS 33 PK across both dose levels (R^2= 0.99); parameter estimates [Mean(CV)] of V/F, k_{01} and k_{10} were 29(16)L, 31.14(6)hr^{-1} and 0.6(18)hr^{-1}, respectively. The infusion FEN has a lower clearance (24.1 L/hr) compared to iv bolus FEN clearance (44.00 L/hr). A multiple compartment PK/PD model characterized the maximum reversal of FEN induced pCO_2 increase achieved at both 0.1 mg and 0.2 mg ALKS 33. Model estimates of k_{on} (48.9hr^{-1}) and k_{off} (0.081hr^{-1}) of ALKS 33 were derived from reversal of FEN-induced pCO_2 increase.
Conclusions: A mechanistic, opioid agonist-antagonist, competitive, PK/PD model was developed to describe the ability of ALKS 33 to reverse FEN-induced respiratory depression and sedation in dogs. These results demonstrate that ALKS 33 is a potent and long acting μ-opioid antagonist.
Financial Support: Alkermes, Inc.

365

ZOLPIDEM-SSRI INTERACTIONS: IMPLICATIONS FOR TREATMENT OF COMORBID DEPRESSION AND INSOMNIA?

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Aims: Sleep disturbances are a primary symptom in depression and upwards of one third of depressed patients taking selective serotonin reuptake inhibitors (SSRIs) also take prescription sleep-aids. Although SSRIs are known to affect the pharmacokinetic profile of sedative/hypnotics, no empirical evidence exists demonstrating a pharmacodynamic interaction between SSRIs and the short-acting benzodiazepine-like hypnotic zolpidem.
Methods: The present study used proton magnetic resonance spectroscopy at 4T to investigate the effects of zolpidem on brain chemistry in male and female volunteers maintained on stable SSRI treatment for major depressive disorder but who were otherwise healthy. Participants (n= 6) underwent scanning following acute oral administration of a therapeutic dose of zolpidem (10 mg) in a within-subject, single-blind, placebo-controlled study. In addition to neurochemical measurements from voxels positioned within the anterior cingulate (ACC) and thalamus, a series of questionnaires was administered periodically throughout the experimental session to assess subjective mood states associated with the treatment.
Results: Preliminary results indicate that while the depressed individuals exhibited higher baseline GABA levels in the ACC and thalamus compared to previously reported data from healthy volunteers ($p < 0.001$), levels of GABA in the thalamus were increased further by zolpidem ($p < 0.05$). Unlike the healthy cohort who exhibited a decrease in GABA related to zolpidem-induced increases in self-reported ratings of dysphoric effects, the depressed individuals reported only trend-level increases in "dizzy" ($p = 0.06$) relative to placebo. However, the depressed cohort also reported trending increases in "high" ($p = 0.07$).
Conclusions: These preliminary data hint at a zolpidem-induced interoceptive state specific to SSRI-maintained individuals that may be indicative of a pharmacodynamic interaction. Effects could be related to the unusual behaviors described in a number of case reports.
Financial Support: Brain & Behavior Research Foundation (The Oxley Foundation) and NIDA K01 DA023659

366

ROLE OF NITRIC OXIDE SIGNALING IN STRESS-INDUCED REINSTATEMENT OF COCAINE-INDUCED CONDITIONED PLACE PREFERENCE.

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Aims: Nitric oxide (NO) signaling pathways play an integral role in regulating synaptic plasticity and the formation of long-term memory. Stress serves as a trigger for relapse to drug use. However, the relationship between stress, NO signaling and drug-associated memory is unknown. The present study investigated the effects of the selective neuronal nitric oxide synthase (nNOS) inhibitor S-methylthiocitrulline (SMTC) on stress-induced reinstatement of cocaine place preference.
Methods: Male C57BL/6 mice were first conditioned with ascending doses of cocaine (3, 6, 12, 24mg/kg) over 4 days. CPP was extinguished by reconditioned with saline (confinement; 4 days) and mice were tested on the following day. Then, mice were divided into two groups: one group was re-exposed to the training context for 3 additional days, while the other group was not. On the following day mice received SMTC (100mg/kg; IP) or saline 30 min prior to administration of 6 footshocks. CPP was monitored immediately following the footshock.
Results: The effect of SMTC was dependent on the frequency of exposures to the training context. SMTC prevented the stress-induced reinstatement of cocaine CPP in the group that received multiple exposures to the training context. On the contrary, SMTC significantly reinstated CPP following footshock stress in the group that received a single exposure to the training context.
Conclusions: Results suggest that repeated exposures to the training context render the subject sensitive to NO signaling-dependent stress-induced reinstatement. On the other hand, a single exposure to the training context does not render the mice sensitive to stress-induced reinstatement; however, blockade of nNOS by SMTC might have impaired reconsolidation of the extinction memory, allowing the shock to reinstate CPP. Hence, NO signaling has a role in reinstatement of cocaine seeking behavior.
Financial Support: Supported by R01DA026878 and R21DA029404

367

PHARMACOKINETIC AND PHARMACODYNAMIC EFFECTS OF SUPRA-THERAPEUTIC Δ9-THC DOSES IN CANNABIS USERS.

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Aims: The purpose of the present study was to characterize the pharmacokinetic and pharmacodynamic effects of oral Δ9-THC in cannabis users at doses higher than those tested previously in humans.
Methods: Dose escalation procedures were used to assess increasingly larger doses of Δ9-THC, up to a maximum of 90 mg or until side effects occurred that contraindicated the administration of higher doses. We hypothesized that peak Δ9-THC concentrations and time would vary considerably within and across subjects; that Δ9-THC would have a flat dose-effect function on cannabinoid-sensitive measures; and that Δ9-THC would be well tolerated in cannabis users. Seven subjects who reported at least weekly cannabis use participated in session activities from 1600-2300 h and remained in the hospital overnight; sessions were separated by at least 72 h. Data were collected prior to, and hourly for 6 h following drug administration. Blood was drawn at these times, and also 12 h post-dose.
Results: Five subjects received all doses, and two subjects were discontinued after experiencing adverse GI effects. Data were analyzed using linear mixed models. Plasma Δ9-THC concentrations were generally a function of dose, but a wide range of Cmax values were observed across subjects for a given dose (e.g., 9.0 vs. 127.1 ng/mL at 90 mg). Peak plasma levels for both cannabinoids emerged at 4 h post-dose on average, but Tmax ranged from 1-12 h. The behavioral effects of Δ9-THC increased as a function of dose and blood concentration at low doses, but were not consistently related to dose or blood concentration at higher doses. Further, peak abuse-related self-reported effects occurred at low Δ9-THC plasma concentrations.
Conclusions: These data demonstrate the variable pharmacokinetic profile of oral Δ9-THC, are consistent with a partial agonist classification, and demonstrate that acute doses of Δ9-THC higher than those tested previously can be safely administered to cannabis users.
Financial Support: NIH grants DA025605, DA018772, DA005312 and RR015592, and a grant from the UK Center for Clinical and Translational Science.

368

THE RELATIONSHIP BETWEEN CHILDHOOD TRAUMA AND SUBSTANCE USE IN DOMESTIC VIOLENCE SURVIVORS.

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Aims: Recent research suggests that there is a bidirectional relationship between the risk of substance abuse and trauma (National Child Traumatic Stress Network, 2008). Specifically, trauma survivors are at risk of using substances to cope with trauma-related emotions and symptoms, and people who abuse substances are more likely to engage in high-risk behaviors that increase vulnerability to trauma. The Urban Resource Institute's Evaluation Unit has developed a research program that has demonstrated high rates of childhood trauma among domestic violence survivors (Griffing et al., 2006a, 2006b).
The aim of this study is to extend this research to examine associations between different forms of childhood trauma and substance abuse in 111 women recruited from domestic violence shelters in New York City.
Methods: Participants completed semi-structured interviews which included measures of substance abuse, childhood abuse, and questions about other adverse childhood experiences (witnessing domestic violence, foster care placement).
Results: Thirty-one percent (n=34) of participants identified as having a history of substance abuse. A series of chi-square analyses yielded significant associations between prior trauma and substance abuse. As expected, domestic violence survivors with a substance abuse history were significantly more likely to report exposure to severe childhood sexual abuse (47% vs. 29%, $X2=3.24$, $p<.05$), maternal domestic violence (55% vs. 30%, $X2=5.33$, $p<.01$) and foster care placement during childhood (38% vs. 19%, $X2=4.39$, $p<.05$). There were no significant between-group differences in the experience of physical or emotional abuse or neglect (p values >.05).
Conclusions: In conclusion, these findings underscore the importance of integrated and coordinated intervention services to address both trauma and substance abuse in domestic violence survivors.
Financial Support: Funded by Urban Resource Institute's program operation funding

369

BEHAVIORAL TREATMENT ADDED TO PHARMACOTHERAPY WITH BUPRENORPHINE FOR OPIOID DEPENDENCE.

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Aims: Evidence confirms the effectiveness of buprenorphine pharmacotherapy for the treatment of opioid dependence, and physicians must include or provide referrals to behavioral treatment when treating opioid-dependent individuals. No study has examined the efficacy of combining buprenorphine with different psychosocial treatments. The current study is a recently completed randomized controlled trial that compares 4 behavioral treatment conditions provided with buprenorphine and medication management for the treatment of opioid dependence.
Methods: After a 2-week buprenorphine induction and stabilization phase, 202 participants were randomized to 1 of 4 behavioral treatment conditions provided for 16 weeks with buprenorphine and medication management: 1) Cognitive Behavioral Therapy (CBT), 2) Contingency Management (CM), 3) CBT and CM (CBT+CM), and 4) No behavioral treatment (MM).
Results: Baseline group comparisons indicate a significant difference only in Clinical Opiate Withdrawal Score (p = 0.05; CBT = 3.6 (3.5), CM = 2.3 (2.7), CBT+CM = 1.7 (2.3), and MM = 2.1 (2.7)). Collapsing across groups, mean age = 37.0 years, 69% = males, and 52.5% = White, 20.3% = Hispanic, 10% = Black. Using the Treatment Effectiveness Score (TES) to computes a percentage of opioid-negative urine results over the total number of urine tests possible, no significant difference in opioid use was found (p = 0.44; CBT = 0.52, CM = 0.56, CBT+CM = 0.63, and MM = 0.53). No significant differences were found for any of 3 retention measures, withdrawal symptoms, craving, or adverse events across the treatment duration by treatment group.
Conclusions: These results suggest that providing weekly guidance such as that offered in the medication management condition included in this study, may be sufficient to optimize treatment outcomes. The MM condition, however, provides a higher level of care that that typically provided in private practice and clinic settings.
Financial Support: NIDA DA020210

370

CONCENTRATED SUBSIDIZED HOUSING AND ITS IMPACT ON THE HOUSING INSTABILITY OF CURRENT AND FORMER INJECTION DRUG USERS IN BALTIMORE.

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Aims: Housing instability, a determinant of poor health outcomes, can result from eviction, job loss, and lack of affordable housing. The purpose of this study was to: (1) assess the association between concentrated subsidized housing (CSH) and housing instability among persons with a history of injection drug use (IDUs); (2) explore perceptions of housing instability and subsidized housing among IDUs.
Methods: We assessed the longitudinal association between CSH and housing instability among 1373 IDUs in follow-up 2006-2010. Participants were geocoded to the census block group (CBG) of their reported residence. Logistic regression with random intercepts was used to assess the association between CSH (percentage of subsidized housing per CBG in 2006) and housing instability (moving at least once within six months). Analysis was stratified by status of injection drug use. Nineteen of the 1373 participants participated in in-depth interviews exploring neighborhood conditions in East Baltimore. In-depth interviews were analyzed using constant comparison methods.
Results: The median percentage of CSH was 22.6 (IQR:7.8,58.5). Housing instability was reported in 25% of observations (n=8547). Among non-injectors, living in a CBG in the highest quartile of CSH, as compared to living in the lowest, was associated with a 36% reduction in the odds of housing instability [AOR=0.6, 95% CI(.4,1.0)]. There was no statistically significant association between CSH and housing instability among active injectors [AOR=1.3, 95%CI(0.7,2.3)]. In-depth interview respondents indicated that status of drug use impacts housing stability and access to subsidized housing is constrained by structural barriers.
Conclusions: Subsidized housing programs may positively impact marginalized populations. Strategies are needed to increase access to subsidized housing and strengthen housing stability among drug users.
Financial Support: NIDA DA12568,DA04334

371

RCT CROSS-OVER TRIAL COMPARING BUPRENORPHINE-NALOXONE TABLETS TO FILM.

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Aims: Suboxone film was introduced in 2011 in Australia as an alternative to tablets. This study compared the 2 formulations on dose effects and equivalence, adverse events, patient satisfaction, time required for effective supervised dosing, and impact upon treatment outcomes (drug use, psychosocial function).
Methods: Multi-site outpatient double-blind double-dummy parrallel group RCT of 92 long-term Suboxone tablet patients over 31-day period. Patients randomised to either remain on tablets or cross over to film, without dose changes.
Results: No significnat differences between 2 groups regarding subjective dose effects (sedation, withdrawal), plasma BPN or nor-BPN trough levels, adverse events, drug use or psychosocial function over study period. Film took significnatly less time to dissolve than tablets (173 ± 71 v 242 ± 141 sec, p=0.007, F=7.67). Mucoadhesion assessment indicated minority of patients could remove at 30 or 60 sec after dosing. A majority of subjects preferred the film to tablets
Conclusions: The study demonstrated dose equivalence and comparable clinical outcomes between the buprenorphine-naloxone sublingual film and tablet preparations, whilst also showing improved dispensing times and patient ratings of satisfaction with the film.
Financial Support: Investigator-led project with financial support from Reckitt Benckiser.

372

EFFECTS OF ESCITALOPRAM ON ATTENTIONAL BIAS TO COCAINE WORDS IN COCAINE-DEPENDENT SUBJECTS.

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Aims: Cocaine-dependent subjects express attentional bias (AttnBias) to cocaine-related stimuli. Our group showed that citalopram, a selective serotonin transporter inhibitor (SSRI), reduced cocaine positive urines compared with placebo. The purpose of the present study was to investigate whether the SSRI escitalopram will suppress AttnBias to cocaine words in cocaine-dependent subject using cocaine-word Stroop task for measuring AttnBias.
Methods: A double-blind placebo-controlled design was used for the study. Cocaine-dependent subjects received placebo (n=12) or escitalopram (n=11) orally once daily for 4 weeks. The dose of escitalopram started at 10 mg (days 1 – 3), increasing to 20 mg (day 4 – 25) and then 10 mg (day 26-28). The cocaine-word Stroop task was performed at baseline (4 days before medication start), days 1 and 4 (5 hrs after placebo or escitalopram), days 11, 18 and 25 (30 min after placebo or escitalopram). Since escitalopram reaches peak levels in blood about 5 hrs after oral administration, the acute effects of escitalopram were measured on days 1 and 4 and chronic effects on days 11, 18, and 25. The AttnBias was defined as the difference between the reaction time to indicate color of cocaine words vs. that of non-cocaine words.
Results: No significant difference of baseline AttnBias was found between the 2 groups. Two way repeated measure ANOVA analysis showed a significant treatment * time interaction ($p < 0.05$) but not a main effect of treatment or time for the AttnBias change from baseline. Post hoc comparison showed that AttnBias decrease from baseline in the escitalopram group was significantly bigger than in the placebo group on day 1 ($p < 0.05$) but not on days 4, 11, 18, 25.
Conclusions: The results that acute administration of escitalopram decreases AbbnBias to cocaine words in cocaine-dependent subjects suggest that acute administration of escitalopram may be useful for controlling cocaine cue-induced response in cocaine dependence treatment.
Financial Support: NIDA Grants P20 DA024157 (Cunningham) and P50 DA009262(Moeller)

373

THE EVALUATION OF TWO FIRST-GRADE PREVENTIVE INTERVENTIONS ON CHILDHOOD AGGRESSION AND ADOLESCENT MARIJUANA USE: A LATENT TRANSITION LONGITUDINAL MIXTURE MODEL.

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Aims: This study evaluates the impact of two first-grade universal interventions (classroom-centered and family-school partnership) on the development of aggression in early childhood (grades 1-3) and marijuana use in adolescence (grades 8-12).
Methods: The sample consists of 605 predominately minority (87%) and low SES (70%) youths (53% were male) who participated in the Johns Hopkins University Prevention Intervention Research Center (JHU PIRC) Second Generation Intervention Trial. A latent transition longitudinal mixture model (LT-LMM) is used to analyze the data.
Results: Despite the strong proximal impact of the classroom-centered intervention on trajectory class membership of early childhood aggression as well as the significant association between aggression trajectory class membership and marijuana use longitudinal latent class membership found for males, the predicted probabilities of being in the high frequency marijuana use class did not differ significantly by intervention status, though in the expected direction. Associations for females are limited to proximal impact of the classroom-centered intervention on trajectory class membership for aggression.
Conclusions: This study extends the prior work of Petras, Masyn, and Ialongo (2011) by considering that aggressive, disruptive behavior during early childhood is linked to not only adolescent aggressive, disruptive behavior (i.e., homotypic continuity) but also to adolescent marijuana use (i.e., heterotypic continuity) and by considering that an early intervention may influence later non-targeted behaviors through these heterotypic developmental pathways. Implications to developmental theories and substance abuse prevention are discussed.
Financial Support: National Institute of Mental Health T32 training grant (MH18834; PI: Nicholas Ialongo).

374

SUBSTANCE USE AND PROBLEM AWARENESS AMONG DRUG-INVOLVED PRISONERS IN NORWAY.

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Aims: This cross-sectional survey assessed drug use and alcohol consumption, problem awareness, ambivalence and treatment readiness among prisoners.
Methods: A sample of 123 prisoners filled in three questionnaires: The AUDIT for alcohol consumption, the DUDIT for drug problems level and the DUDIT-E for type of substances used, drug-related beliefs and treatment readiness. Drug-involved offenders were compared regarding their problem scores indicating occasional, harmful or highly problematic use. The level of drug problems was related to use of hard drugs (amphetamines, cocaine or heroin), prescription drugs and cannabis.
Results: Of the 110 drug-involved offenders, 63% reported hazardous alcohol consumption and 47% reported highly problematic drug use. The strongest predictor of highly problematic drug use was frequent use of hard drugs with an OR of 6.8 (95% CI 2.43 to 19.03). Highly problematic users reported more problem awareness such as drug effects damaging their family life, finances and social relations and they scored higher on cognitive dissonance. Treatment readiness was rated higher by problematic users compared to users reporting less problems.
Conclusions: In light of higher levels of cognitive dissonance and more treatment readiness among highly problematic users, opportunities for substance use treatment in prisons should be increased. Drug-involved prisoners should be identified systematically including assessment of alcohol consumption. The influence of prison environment on ambivalence to change and beliefs related to drug effects needs to be studied longitudinally during and after imprisonment.
Financial Support: This study was supported by the Research Council of Norway and the Norwegian Centre for Addiction Research. The authors have no conflict of interest.

375

RELATIONSHIP BETWEEN AMOUNT OF OPIOID USED, OPIOID WITHDRAWAL AND PAIN SEVERITY IN PRESCRIPTION OPIOID-DEPENDENT ADULTS.

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Aims: Prescription opioid (PO) dependence is a significant public health problem in the U.S. This study aimed to: 1) characterize PO dependent adults on an array of measures, and 2) assess the impact of amount of opioid used on opioid withdrawal (OW) and bodily pain severity.
Methods: PO-dependent, healthy adults (n=48) enrolled in an inpatient study evaluating the efficacy of a novel agent for treating OW. Screening measures included demographic questionnaires, the Addiction Severity Index, a 30-day time-line follow-back of PO use (TLFB), and the McGill Pain Inventory. Prior to randomization (PTR), all subjects were experiencing OW as assessed by several OW measures. Daily oral morphine equivalents (ME) were calculated using the TLFB among a subsample (n=26) that used only oxycodone (OXY) in the 14 days PTR. Correlational analyses evaluated the relationship between ME and pre-randomization OW and pain scores (collected after a minimum of 15.7 hrs inpatient).
Results: Subjects (n=48) were 58% male and mostly Caucasian (98%) with a mean age of 29.4 yrs and 6.1 yrs of regular (>2-3x/week) PO use. Many (42%) endorsed bodily pain during screening. In the last 30 days, OXY was the most frequently used opioid. Immediate release OXY was the PO of choice for most (81%). Various POs were injected (e.g., OXY, oxymorphone); however, hydrocodone injection was not reported. In the subsample (n=26), a mean of 746 mg of ME were used in the 4 days PTR. There were significant positive correlations (r values: ~0.4-0.5) between total ME used in the 4, 7, and 14 days PTR and the affective component of pain measured during OW. There was no significant relationship between ME and OW scores.
Conclusions: The association between affective pain and OW highlight the emotional aspects of both pain and OW. The lack of relationship between ME and OW was unexpected and may be due to differing intervals between last opioid use and OW assessment.
Financial Support: NIDA R01 DA027068(MRL), T32DA007304-14 and UK CTSA(UL1RR033173)

376

EXPLORING THE DIFFERENTIAL IMPACT OF ANXIETY SENSITIVITY AND IMPULSIVITY ON PPI-I AND PPI-II FACTORS OF PSYCHOPATHY IN A SUBSTANCE-ABUSING POPULATION.

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Aims: To examine the emotional correlates of PPI-I and PPI-II traits of psychopathy in a sample of substance users by considering the unique contributions of several theoretically relevant variables such as anxiety sensitivity (AS) and impulsivity
Methods: One hundred participants at a residential drug treatment center, receiving treatment primarily for problems with heroine and cocaine use, completed several self-report and interview assessments during their treatment. Assessment measures were chosen based on existing theory regarding the core components of Factor I and Factor II psychopathy and included the Psychopathic Personality Inventory, Anxiety Sensitivity Index, Difficulties in Emotion Regulation Scale, Behavioral Inhibition Scale, Multidimensional Personality Questionnaire and the Structured Clinical Interview for DSM-IV.
Results: We conducted a regression analysis predicting PPI-I and PPI-II scores, using AS, impulsivity, emotion regulation, and negative affect as predictors. In a regression predicting PPI-I, low anxiety sensitivity (AS) was a robust predictor ($Sr2 = -.279$, $p < .01$). A higher level of emotional regulation also was a significant predictor ($Sr2 = -.341$, $p < .01$). In a regression predicting PPI-II, high impulsivity was a robust predictor ($Sr2 = .258$, $p < .01$). Greater negative emotionality ($Sr2 = .281$, $p < .01$) and poorer emotional regulation ($Sr2 = .168$, $p < .05$) were also significant predictors. A diagnosis of antisocial personality disorder (APD) was only related to PPI-II traits and not PPI-I traits ($p < .05$). The relationship with PPI-II was no longer significant when taking into account the contributions of impulsivity, negative emotionality, and emotion regulation.
Conclusions: Impulsivity and AS play distinct roles in PPI-I and PPI-II traits. Taken together with past research that has demonstrated the links between AS and impulsivity and substance use disorders (SUDs), our findings indicate that individuals with low PPI-I scores and high PPI-II scores may form a group that is especially vulnerable to SUDs.
Financial Support: R01DA19405

377

CHARACTERIZING THE RELATIONSHIP BETWEEN SMOKING STATUS AND BREASTFEEDING AMONG NEWLY POSTPARTUM WOMEN.

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Aims: There is a strong association between smoking status and breastfeeding, with smokers weaning earlier than non-smokers. The purpose of the present study was to provide a fine-grained characterization of the relationship between smoking status and breastfeeding among women who quit smoking during pregnancy. We hypothesize that abstainers will breastfeed longer than women who relapse.
Methods: Study participants were 116 women who were participating in clinical trials on preventing postpartum relapse to smoking. They received incentives contingent on sustaining abstinence or independent of smoking status through 12-wk postpartum. The incentive intervention did not significantly change relapse rates and thus data are combined across treatment conditions. All women were biochemically verified as being abstainers or smokers at 2-, 4-, 8-, 12-, and 24-weeks postpartum (PP). Self-reported breastfeeding status was also collected at these time points. Breastfeeding rates between smokers and abstainers were completed using chi-square analysis.
Results: The percent of women breastfeeding at week 2, 4, 8, 12 and 24 weeks PP were 81, 72, 59, 50 and 30 among abstainers compared to 4, 4, 4, 6 and 11 among smokers ($p<.05$ for 2-12 weeks and $p=.07$ at 24 weeks). Logistic regression revealed that in addition to smoking status, maternal education (> 12 yrs) predicted a significantly greater likelihood of continuing to breastfeed through 24 weeks PP, and in addition to breastfeeding, older age and fewer depressive symptoms predicted a greater likelihood of sustaining smoking abstinence through 24 weeks PP.
Conclusions: This study confirms prior observations regarding a robust relationship between cigarette smoking and premature weaning that is evident within 2 weeks through 24 weeks PP. Younger, more depressed women are more likely to resume smoking and discontinue breastfeeding. Higher education appears to be a protective factor for continuing breastfeeding. Improved interventions to prevent relapse back to smoking are likely to also increase breastfeeding.
Financial Support: R01DA14028 and T32DA007242

378

ABNORMALITIES IN THE CINGULATE ARE CORRELATED WITH AGE OF ONSET OF MARIJUANA USE IN ADOLESCENTS.

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Aims: The time frame of frontal neural circuit development has been implicated in the onset of substance use. This study examined the cingulate in light versus heavy smoking adolescent users to determine if there are differences in cingulate volumes associated with heavier smoking and if changes in cingulate volume are associated with clinical variables of MJ use.
Methods: Thirty-nine adolescents with MJ use (aged 18.0±2.2 years), and 38 HC (18.0±0.9) had MRI scans on a 3T scanner. The MJ sample was divided into 2 groups: adolescents who had 1) number of lifetime smokes greater than 1250 (n=19) and 2) number of lifetime smokes less than 1250 (n=20). Volumetric segmentation was performed with the FreeSurfer. Volumetric data for anterior (ACC) and posterior (PCC) cingulate regions were extracted and univariate analyses were performed covarying for sex and intracranial volume (ICV). MJ use indices were correlated with significant cingulate regions.
Results: Youths with greater than 1250 lifetime smokes had smaller left rostral ACC volumes ($p = 0.01$), and smaller right ($p = 0.01$) and left ($p = 0.01$) PCC volumes compared to HC. There were no significant differences between youths who had smoked less than 1250 lifetime smokes and either HC or youths with greater than 1250 lifetime smokes. For MJ users who smoked more than 1250 lifetime smokes, positive correlations with left rostral ACC ($r = 0.44$, $p = 0.06$) and negative correlations with right PCC ($r = -0.53$, $p = 0.02$) and age of onset were seen. A negative correlation with total lifetime MJ use and left PCC ($r = -0.47$, $p = 0.04$) was seen.
Conclusions: The finding of smaller cingulate volumes in our heavier MJ smoking adolescent group suggests distinct differences exist in this group as compared to HC and the lighter smoking MJ group. These results are consistent with other neuroimaging modalities that have reported abnormalities in the cingulate and suggest both neurodevelopmental and neurotoxic effects may influence cingulate morphometry.
Financial Support: NIMH: 1 K23 MH087831-01A1 & NIH: 1 R01 DA020269-01.

379

NONMEDICAL USE OF PRESCRIPTION DRUGS AMONG SCHOOL ADOLESCENTS IN BOGOTA, COLOMBIA.

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Aims: Nonmedical Use of Prescription Drugs (NMUPD) is about to exceed the use of illicit street drugs worldwide, and the existence of unregulated markets in many countries, particularly in developing countries, poses a threat for youth. This study aims to determine the incidence and predictors of NMUPD among school adolescents in Bogota, Colombia.
Methods: A longitudinal study was conducted among 2279 8th-10th grade students in 23 schools in Bogota, selected in a stratified multistage probability sample (Wave1). Wave 2 data was collected one year later from 1455 students (attrition rate=71.7%) who had not reported NMUPD at Wave 1. Binary logistic regression analyses were carried out to determine incidence and predictors of NMUPD.
Results: Overall, 5.3% of students initiated NMUPD between Wave 1 and Wave 2. At Wave 1, 16.8% reported positive NMUPD intentions, of whom 27.8% initiated NMUPD by Wave 2. Significant sex differences were noted in NMUPD intentions - 18.5% and 15.0% among girls and boys, respectively ($p<0.05$), however no sex differences were noted in NMUPD incidence (girls 6.3% and boys 4.2%, $p=0.085$). Positive NMUPD intentions predicted NMUPD incidence among boys (age-adjusted Odds Ratio=2.7, 95%CI=1.2,6.3), but not among girls (age-adjusted OR=1.5, 95%CI=0.8,3.1). Other predictors of NMUPD incidence in the whole sample include peer drug use and degree of problematic behavior.
Conclusions: NMUPD incidence is higher than marijuana or cocaine incidence in this sample. Extrapolating the observed incidence using school census data, approximately 25,000 of 8th to 10th grade school students in Bogotá will initiate NMUPD every year. Stricter supervision of tranquilizer and sedatives supply should become a national priority.
Financial Support: Milstein Doctoral Scholarship to C L-Q

380

SEX DIFFERENCES IN THE PURCHASING AND USE PATTERNS OF HEROIN AND COCAINE.

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Aims: Animal laboratory studies have demonstrated sex differences in drug self-administration. However, clinical studies have not systematically investigated with behavioral economic methods whether the acquisition and use of drugs like heroin and cocaine differ by sex; such differences may have implications for estimating costs to individuals, families, and society. The aim of this study is to examine the purchasing and use patterns of heroin and cocaine among non-treatment-seeking females and males.
Methods: In two parallel human behavioral pharmacology studies, primary heroin- or cocaine-dependent research volunteers were interviewed at screening about their past-month income sources, and patterns of purchasing and consumption of heroin (males N=94; females N=34) or cocaine (males N=52; females N=16) and other expenditures.
Results: Among heroin abusers, females (vs. males, respectively) reported purchasing more heroin per buying episode (Ms = $52.00 vs. $27.41, $F[1,126] = 7.25$, $p < .01$) and consumed more $10-equivalent bags daily (Ms = 5.7 vs. 4.0, $F[1,126] = 7.45$, $p < .01$), despite having less employment income (Ms= $262 vs. $720, $F[1,126] = 10.29$, $p < .01$). There were sex differences in circadian heroin use: Females consumed more heroin from 6pm to midnight ($F(1, 126) = 4.98$, $p < .05$) and midnight to 6am ($F(1, 126) = 10.06$, $p < .01$). Among cocaine abusers, females used significantly higher dollar amounts of cocaine per day (Ms= $28.48 vs. $8.29, $F(1, 57) = 6.32$, $p < .05$), but the sexes did not significantly differ in their income or cocaine-acquisitive patterns.
Conclusions: These results indicate sex differences in purchasing and use of illegal drugs. Notably, females use larger daily amounts of heroin and cocaine than males, a pattern unrelated to extra income. Greater drug use by females is consistent with extant preclinical studies. Future research should identify the environmental conditions that support greater use by females, toward developing sex-specific treatments.
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381

CORRELATES OF NON-PARTNER VIOLENCE AGAINST WOMEN WHO USE METHAMPHETAMINE.

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Aims: Most research regarding violence against women who use drugs focuses on intimate partner violence. However, social marginalization and poverty among inner-city drug-using women also makes them susceptible to other forms of violence. This presentation examines correlates of non-partner violence among women who use methamphetamine(meth) in San Francisco, CA.
Methods: A community-based sample of women who use meth was recruited from 2007-2009 (N=322. Eligibility criteria included meth use past 30 days and at least one male sexual partner past six months. "Non-partner violence" (NPV) was defined as physical or sexual assault in the past six months by a person who was not a current or former boyfriend/spouse/partner.
Results: Over a quarter (28%) of participants experienced NPV in the past six months. NPV was not associated with the mean frequency of meth use past 30 days (18.5 days among those who experienced NPV and 17.6 days among those who did not [one-sided t test = 0.289]. Nor was it associated with use or frequency of use of other drugs, such as crack cocaine or injection heroin. Using Gelberg's Competing Priorities Scale, we found that 33% of women who reported frequent subsistence difficulty were victims of NPV, compared to 13% of women who didn't report frequent subsistence difficulty (p<.001. In multivariate analysis, women who traded sex for money or drugs had over twice the odds of experiencing NPV (AOR= 2.27; 95% CI=1.3, 4.1), as did women with frequent subsistence difficulty (AOR=2.43; 95% CI=1.3, 4.6). Having a steady male partner was not protective for NPV(AOR 0.66; 95% CI 0.4, 1.1).
Conclusions: NPV should not be overlooked among women who use drugs. The prevalence of NPV in this study is similar to levels of intimate partner violence reported in the literature. Efforts to improve women's ability to meet their basic needs may concurrently make them less vulnerable to NPV.
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382

PROBABILITIES AND PREDICTORS OF LONG-TERM CONTINUING ABSTINENCE FOR HEROIN AND METHAMPHETAMINE USERS.

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Aims: Abstinence is considered to be a critical component of recovery from substance use disorders. To better understand abstinence stability, we examined the conditional probability of continuing abstinence given increasing durations of preceding abstinence and predictors of these probabilities.
Methods: Data were obtained from two studies: 1) n=341 heroin users who were sampled from methadone treatment in the 1970s and completed a 25-year follow-up; and 2) n=351 methamphetamine users who were treated for substance abuse in the mid-1990s and completed 3 follow-ups (up to 15 years). Both longitudinal studies conducted Natural History interviews with participants on their drug use, treatment, and criminal behavior. Duration of abstinence from the study's primary drug was measured for the first period of abstinence of at least one year. ROC curves were used to examine probability of achieving a subsequent year of abstinence given the preceding years of continuous abstinence from designated drug. Logistic regression was used to examine predictors of each additional year of abstinence.
Results: Probabilities of continued abstinence were similar for both samples, increasing steeply to .84-.85 through 3 years of abstinence, then tapering off and rising to .94 (heroin) and .91 (meth) by year 6. For heroin users, employment during the prior period of abstinence was the only consistently significant predictor of the 2nd to 6th year of continuing abstinence; older age was a significant predictor for another year of abstinence after 1, 2, or 6 preceding years. For meth users, participation in treatment or self-help during the 1st year of abstinence was a significant predictor of the 2nd year of abstinence, but was not significant in subsequent years.
Conclusions: Attaining at least 3 years of continuous abstinence substantially decreases the likelihood of relapse for both heroin and methamphetamine users, with some variations in specific predictors across groups.
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383

SMOKING OLFACTORY AND VISUAL CUES ACTIVATE DIFFERENT BRAIN REGIONS AS MEASURED VIA BOLD FMRI.

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Aims: Nicotine dependence is currently the most common form of chemical dependence in the world. Quitting smoking can be very difficult for most people and usually involves many attempts because relapse rates are so high. Historically, visual, auditory, and tactile cues have been studied individually to better understand the causes of relapse. To date, no known studies have used odor stimuli to study relapse despite the olfactory system's known close links with centers of emotion, learning, and craving. We hypothesized that visual cues would lead primarily to an activation of visual cortex, and olfactory cues to a deactivation of frontal brain regions to coincide with the strong direct connections between olfaction and these brain areas.
Methods: Twelve healthy adults (7M/5F) diagnosed with nicotine dependence (SCID-R) participated in two 4-hour sessions. Before one session, subjects were able to smoke ad lib for 2.5 hours until they were scanned while the second scan (visit) was conducted under mild abstinence. During the scan, individuals wore a nasal cannula through which plain air, fresh cigarette smoke odor, or phenylethyl alcohol (rose scent) were delivered. Both cigarette-related and neutral (matched for content) pictures were presented along with the odor presentation, all synchronized with fMRI acquisition. A visual analog scale questionnaire was given pre and post scanning to assess cigarette craving ("desire to smoke").
Results: The data demonstrated that cigarette pictures activated both visual and prefrontal cortex while the cigarette odor deactivated regions of the executive control network. Subjects also significantly rated their "desire to smoke" much higher during the scan performed after the abstinence session.
Conclusions: The results of this study show that the introduction of cigarette-related odor cues affects regions of the brain that may be linked to self-control, craving and learning and thus may play a more direct role in the relapse process.
Financial Support: NIDA grants to SBL and SEL

384

EXTENDED ACCESS TO METHAMPHETAMINE SELF-ADMINISTRATION ALTERS DOPAMINE SYSTEMS IN RATS.

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Aims: Rats given extended access to methamphetamine self-administration (SA) display an escalation of drug intake as compared to rats given limited access to this drug. This study compared changes in dopamine systems in rats allowed extended versus limited access to methamphetamine SA.
Methods: Adult rats were given either extended (6 hour/day) or limited (1 hour/day) access to intravenous SA of methamphetamine (0.05 mg/infusion) for 30 days. Control rats received surgical implantation of jugular catheters. All rats were sacrificed 72 hours after the final SA session. All groups were compared with respect to striatal dopaminergic function (Tyrosine hydroxylase, TH and dopamine transporter, DAT) using western-blot and immunocytochemistry procedures.
Results: Rats given extended access to methamphetamine SA displayed an escalation of drug intake during the first hour of each session, and this effect was absent in limited access rats. Despite this behavioral difference, the largest changes in dopamine systems were observed between naïve controls versus rats that were exposed to methamphetamine SA. Both groups of methamphetamine SA rats displayed a decrease in striatal TH immunoreactivity and an increase in DAT levels versus controls. The immunocytochemistry analysis was consistent with the latter results throughout the striatum.
Conclusions: Our results reveal that dopamine systems in the striatum are altered 72 hours after methamphetamine SA. Ongoing studies are examining whether these changes in dopamine systems are related to compensatory changes or neurotoxicity produced by methamphetamine and withdrawal from this drug.
Financial Support: This study was funded by: R24 DA029989, G12 RR008124, and 2T34GM008048.

385

LIFE-COURSE SOCIAL STATUS AND SMOKING/HEAVY ALCOHOL USE IN ADULTHOOD.

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Aims: During the transition from adolescence into adulthood, the effects of social status on smoking/alcohol behaviors are mixed. This may be due to the varying role of social status across the life course or the multidimensional aspect of social status. This study examines the effects of social status across the early life course on smoking and alcohol behaviors. The construct of "life-course" social status will capture the ebb and flow of socioeconomic advantages or disadvantages from adolescence into early adulthood. The main hypothesis is that lower life-course social status will be associated with higher risk for smoking and higher life-course social status will be associated with higher risk for heavy episodic drinking.
Methods: Respondents with Waves 1, 3, and 4 data were used from the National Longitudinal Study of Adolescent Health (n=9,421). Using latent class analysis, social status is operationalized as latent constructs of economic, human, and social capitals from measures in adolescence (W1), young adult (W3), and adulthood (W4). Outcomes are adult smoking and alcohol behaviors. Analyses are conducted in Mplus and account for survey weights.
Results: 23% of respondents reported daily smoking in the past 30 days in adulthood, and 8% met criteria for lifetime nicotine dependence. 34% reported heavy episodic drinking in the past 30 days in adulthood, and 25% met criteria for lifetime alcohol dependence. Results from latent class analyses identify four distinct classes: persistent advantage (35%), upward mobility (20%), downward mobility (28%), and persistent disadvantage (17%). Preliminary findings show higher daily smoking among the most disadvantaged group. Heavy episodic drinking is highest among the most advantaged group and the downwardly mobile group.
Conclusions: These findings highlight the complex role of social status on risky substance use behaviors during the early part of the life course and can help to identify optimal times for intervention.
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386

BRAIN ACTIVATION ASSOCIATED WITH ATTENTIONAL BIAS IN SMOKERS IS MODULATED BY A DOPAMINE ANTAGONIST.

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Aims: Attentional bias is the tendency of smokers to automatically direct their attention to smoking cues and is known to influence smoking behaviour. FMRI studies have shown that attentional bias in smokers is associated with activation in brain regions involved in cognitive control. It has been suggested that attentional bias emerges as a consequence of dopaminergic firing when smokers encounter smoking related cues. The current fMRI study employed a dopaminergic challenge in order to test whether dopamine modulates brain activation associated with attentional bias in smokers.
Methods: 25 smokers were compared with 24 controls. Participants were scanned twice while performing the attentional bias line counting task. Haloperidol (2mg), a selective D2/D3 dopamine antagonist, or placebo was orally administered four hours before each scanning session in a double-blind randomized cross-over design.
Results: After placebo, smokers showed enhanced brain activation relative to controls in the anterior cingulate cortex, dorsolateral prefrontal cortex and superior parietal lobe implying that these regions are involved in attentional bias. However, these differences in brain activation between smokers and controls disappeared after haloperidol, suggesting a normalization of brain activation in smokers.
Conclusions: The current results provide evidence for the role of the dopamine system in attention bias. Brain activation in smokers did not differ from controls when dopaminergic firing was reduced by a dopamine antagonist, whereas the expected attentional bias related brain activation in smokers was observed after placebo in brain regions involved in cognitive control. These findings suggest that a reduction of dopaminergic firing when smoking cues are presented is able to normalize brain activation in smokers.
Financial Support: This study was supported by a grant of the Netherlands Organization for Scientific Research (NWO; VIDI grant number 016.08.322).

387

FEMALE PARTNERS OF OPIOID-INJECTING MEN IN THE REPUBLIC OF GEORGIA.

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Aims: HIV is strongly related to injection drug use in the Republic of Georgia. The vast majority of Georgian men with HIV are injection drugs users. Little is known about the female partners of opioid-injecting men in the Republic of Georgia, many of whom may not be using drugs. However, these women are at high risk of being infected by HIV and Hepatitis C from their partners.
The aims of the present study were to describe the prevalence of HIV and Hepatitis C among non-drug using female partners of men receiving treatment for opioid injection drug use in the Republic of Georgia.
Methods: The study population consisted of 40 non-drug-using female partners of opioid-injecting men in the Republic of Georgia. The women were interviewed using a modified version of the Baltimore Risk Assessment Battery and a Partner Support Questionnaire. All women received cash equivalent of $18 US for participating. Descriptive analysis using SPSS was conducted.
Results: The sample had a mean age of 32 (SD = 7) years, mean years of education were 16 (SD = 2) and 48% were currently employed. At the interview, 1 woman reported being HIV-positive, 20 reported being HIV negative, and 15 women refused to answer this question. Regarding reports on Hepatitis C status, 3 women were positive, 24 were negative and 9 refused to answer. Only 10% reported usually using condoms while having sex. Over half (52%) were not at all worried about getting infected with HIV. Physical abuse by their partner during the last year was reported by 42%, and 48% reported feeling unsafe in their current relationship.
Conclusions: Drug-free female partners of injection-drug-using men are at high risk for HIV and Hepatitis C. There is an urgent need for interventions targeting injection drug users and their partners to prevent the spread of HIV and hepatitis C. Moreover, drug treatment represents an important time to intervene with both perpetrators and subjects of interpersonal violence.
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388

PLACEBO-RESPONDING IS ASSOCIATED WITH FAILURE TO DISCRIMINATE ACTIVE THC FROM PLACEBO THC CIGARETTES.

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Aims: To investigate whether cannabis dependent individuals able to discriminate active THC from placebo THC cigarettes differ from those unable to learn the discrimination in demographic variables, marijuana and other drug use, and physiological and subjective responses to THC and placebo cigarettes.
Methods: A total of 24 healthy individuals who met DSM IV criteria for cannabis dependence were enrolled in a 3-wk inpatient, marijuana discrimination study. Participants who did not meet criteria for learning the discrimination were discharged from the study after 6 days. Thus, analyses were restricted to the first 6 days. Each participant completed 2 sessions per day. In each session, participants smoked 3 puffs from a placebo (0.02% THC) or an active (2.9% THC) cigarette, in counterbalanced order, for a total of 6 placebo THC and 6 active THC sessions. Physiological and subjective effects measures were collected for 4 hr after each smoking bout. Peak effects from each session were used in the analyses.
Results: Discriminators (n=17) and non-discriminators (n=7) did not differ in age, sex, race, BMI, estimated IQ, or pre-experimental depressive symptoms, marijuana or other substance use. Repeated measures ANOVAs indicated that compared to discriminators, non-discriminators reported greater "High", "Drug Liking", "Good Drug Effect" and "Strength of Effect" following placebo THC smoking. They also reported greater "Urge to Use Marijuana" across drug conditions and sessions compared to discriminators. Heart rate was significantly increased ($p<.001$) following active THC smoking compared to placebo across groups and sessions.
Conclusions: Non-discriminators reported similar subjective effects when smoking placebo and active cigarettes, and this pattern of "placebo-responding" was evident in the first exposures. These data demonstrate that non-discriminators can be identified very early in drug discrimination studies, thus reducing the cost of otherwise expensive inpatient studies.
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389

ABUSE AND HARASSMENT OF FEMALE IDUS BY POLICE IN ST PETERSBURG, RUSSIA: SYRINGES AND SEX.

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Aims: Repressive law enforcement strategies, such as unjustified arrest and planting evidence, have emerged as a primary theme in qualitative research studies exploring Russian injection drug users' (IDUs) experiences of living with HIV. Anecdotal evidence suggests that sexual violence against female IDUs is an issue in Russia. We sought to measure interactions between police and female HIV-infected IDUs in St Petersburg, Russia.
Methods: We describe reported police involvement of 228 women with a history of injection drug use from the HERMITAGE study, a behavioral intervention trial to reduce risky behaviors among 700 HIV-infected Russian drinkers with recent unprotected sex.
Results: Among all participants, 44.3% (95% confidence interval, 37.9%, 50.8%) reported having had syringes taken from them by the police, 36.8% (30.6%, 43.1%) reported having been arrested for carrying a syringe, and 37.7% (31.4%, 44.0%) reported having been arrested after the police 'planted' syringes or drugs on them. 36.8% (30.6%, 43.1%) decided not to go to a pharmacy to buy clean syringes because they were afraid of being confronted by police officers, and 66.7% (60.6%, 72.8%) reported having been forced to give money to the police to avoid arrests. Almost a quarter of all women (24.1%; 18.6%, 29.7%) reported having been forced to have sex with a police officer.
Conclusions: In this sample of Russian female HIV-infected IDUs, abuse and harassment from police, including unjustified arrests and coerced sex, were commonly reported. These findings raise both human rights and public health concerns. This study's results might inform advocacy efforts to promote partnerships between public health and public policy in Russia. Policy change towards evidence-based drug policing, proven elsewhere an effective HIV prevention strategy, might contribute to reducing IDU risk behavior and addressing Russia's HIV epidemic.
Financial Support: Supported by the National Institute of Alcohol Abuse and Alcoholism (NIAAA; R01AA016059 and K24-AA015674).

390

CROSS-CULTURAL ADAPTATIONS OF CRA FOR SUBSTANCE USE DISORDERS.

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Aims: There is a burgeoning interest in cross-cultural adaptations of substance use treatment, yet contention about whether treatments found to be efficacious with predominantly non-Hispanic White participants should be assumed to be efficacious with other diverse populations. In the present study, academic and community researchers partnered to adapt the community reinforcement approach (CRA) for use with Southwestern American Indians (AIs) with substance use disorders.
Methods: Two AI counselors attended an unadapted CRA workshop. Separate meetings were held with an internationally known CRA trainer and the project team to adapt CRA modules and the forms.
Results: Most of the attention was directed to the forms for surface level adaptations. Other adaptations to forms included changing the name of forms, and adding specific categories such as traditional artwork and AI spirituality. Regarding the CRA modules, possible modifications in communication styles for drug refusal skills and assertiveness were suggested for this particular tribe where directly refusing substances would be viewed as rude. As would be true for anyone using CRA, brainstorming culturally and individually appropriate reinforcers to compete with substance use is crucial. These adaptations have been formalized using forms from both the Project COMBINE manual and the Clinical Guide to Alcohol Treatment (Smith & Meyers, 1995). Currently the randomized controlled trial is recruiting participants to test this adapted version of CRA as compared to TAU.
Conclusions: Cultural adaptations have been included in treatment outcome research yet only recently have RCTs been employed to test the efficacy of these adaptations. Future research into mechanisms of change will be crucial to guide effective cultural adaptations to address health disparities for diverse populations.
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391

SEX AND HORMONAL INFLUENCES ON MOTIVATION FOR COCAINE AT DIFFERENT STAGES OF ADDICTION: NEUROBIOLOGICAL MECHANISMS.

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Aims: While evidence demonstrates sex and hormonal modulation of mesolimbic DAergic signaling following initial cocaine exposure, little information is available on their effects at later stages of addiction or on glutamatergic signaling. Here we examined the contribution of DA versus glutamate signaling in the nucleus accumbens on motivation for cocaine in both males and intact and OVX females with and without estradiol replacement at different stages of cocaine addiction (i.e., following short access (ShA) versus extended access (ExA) cocaine self-administration).
Methods: Male (N=30) and intact (N=28) and OVX female rats with (N=11) and without (N=16) estradiol replacement were trained to self-administer cocaine (FR1, 1.5 mg/kg, 20 infusions maximum), and once acquired, they were given either ShA (3 additional fixed ratio 1 sessions) or ExA to cocaine (24-hr access, discrete trial procedure, 4 trials/hr, 10 days). Following 14 days of abstinence, motivation for cocaine was assessed under a progressive-ratio (PR) schedule, and once stable, the effects of intra-accumbens infusions of the DA D1 receptor antagonist SCH23390 (0, 0.3, 1.0, 3.0 μg/side) or the glutamate AMPA/KA receptor antagonist CNQX (0, 0.01, 0.03, 0.1 μg/side; intact males and females only) were determined.
Results: Motivation to obtain cocaine was higher following ExA versus ShA self-administration in females with estradiol, but not in males or females without estradiol. Intra-accumbens infusion of SCH23390 dose-dependently decreased PR responding for cocaine after ShA self-administration, particularly in females with estradiol, but was not effective following ExA self-administration. In contrast, CNQX dose-dependently reduced PR responding for cocaine after ExA, but not after ShA self-administration; its effects did not differ by sex.
Conclusions: These findings suggest that estradiol interacts with D1 DA signaling to influence sex differences in vulnerability during early, but not later stages of the addiction process.
Financial Support: This research was supported by grants from NIDA (R01-DA024716 and R01-DA024716-S1-WJL).

392

NEUROPSYCHOLOGICAL CORRELATES OF RISKY ALCOHOL USE BY YOUNG ADULTS.

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Aims: Traits of impulsivity, reward sensitivity and disinhibition have been linked to risky alcohol use in young adults, suggesting that inherent deficiencies in frontal lobe function increase alcohol-related risk. This notion was examined in the present study.
Methods: A community sample of young adult social drinkers (n = 47) was divided into Low Risk, Hazardous, and Harmful drinkers based on Alcohol Use Disorders Identification Test (AUDIT) scores.
Results: MANCOVA controlling for age and gender revealed a significant overall effect of AUDIT group on three well-known neuropsychological tests of frontal lobe functioning: the Wisconsin Card Sorting Test (WCST), the Iowa Gambling Task (IGT) and the Tower Test of the Delis-Kaplan Executive Function System (D-KEFS), $F(8, 32) = 2.72$, $p = .02$, partial $\eta 2 = .41$, observed power = .86. Individual effects were significant for total IGT gambling money earned, $F(2, 18) = 4.21$, $p = .03$, partial $\eta 2 = .32$, observed power = .66, and for the Tower Test total achievement score, $F(2, 18) = 5.15$, $p = .02$, partial $\eta 2 = .36$, observed power = .76. WCST-CV perseverative error scores approached significance ($p < .10$).
Conclusions: These three neuropsychological tests can reliably distinguish patients with focal lesions of the frontal lobes from those with lesions of posterior regions as well as controls, thus our results in a non-clinical sample are especially striking. As participants were all social drinkers from the community who reported never being in treatment for any alcohol or drug related problem, with no history of head injury or neuropsychological or psychological disorder, the findings are consistent with our hypothesis that a significant portion of the executive function deficits reported in alcoholic samples may reflect premorbid traits rather than neurotoxic sequelae of chronic alcoholism. Such premorbid executive function deficits are likely to predispose to risky or problematic alcohol use via mediating traits such as impulsiveness, disinhibition and reward sensitivity.
Financial Support: This research was supported by a grant from the Alcohol Education and Rehabilitation Foundation.

393

SIGNIFICANT ASSOCIATIONS OF CHRNA2 AND CHRNA6 WITH NICOTINE ADDICTION IN EUROPEAN-AMERICAN AND AFRICAN-AMERICAN POPULATIONS.

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Aims: The direct physiological effects which promote nicotine dependence (ND) are primarily mediated by nicotinic acetylcholine receptors (nAChRs). Previously, we have shown that variants within several nAChR subunit genes, including CHRNA4, CHRNA5/CHRNA3/CHRNB4 gene cluster, CHRNB1, and CHRM1, contribute to the etiology of ND in European Americans (EA) and/or African-Americans (AA). In this study, we aimed to determine whether variants in CHRNA2 and CHRNA6 on chromosome 8 play any role in the etiology of ND.
Methods: An expanded family sample set was used in this study, which includes 1728 EAs with 495 families and 1881 AAs from 423 families. Three quantitative measures of ND were assessed: Smoking Quantity (SQ), Heaviness Smoking Index (HSI), and Fagerström Test for ND (FTND).
Results: Using a family-based association test, we found nominal associations for all seven SNPs of both genes with at least one ND measure in the EA population, and for two SNPs in CHRNA2 in the AA population. Of these, associations of SNPs rs3735757 with FTND ($P = 0.0068$) and rs2472553 with all of three ND measures (with a P value being 0.0043, 0.0032, and 0.00086 for SQ, HSI, and FTND, respectively) continued to be significant in the EA population even after correction for multiple tests. Furthermore, we found several haplotypes which are significantly associated with ND in the EA population on CHRNA6, and in both the EA and AA populations on CHRNA2.
Conclusions: These findings indicate that both CHRNA2 and CHRNA6 may play a significant role in the development of etiology of ND in both AA and EA smokers and further replication is thus warranted in additional independent samples.
Financial Support: This project was in part supported by NIH grant DA-012844.

394

SPON2 EXPRESSION IN CIGARETTE SMOKE-EXPOSED AND VITAMIN D-DEFICIENT MICE.

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Aims: Nicotine dependence and cigarette smoke exposure (CSE) remain relatively common and hazardous worldwide, and the CDC predicts that cigarette smoking (CS) will cause 8 million deaths annually by 2030. CSE is a risk factor for vitamin D deficiency (VDD), lung infections, and bladder cancer, three growing public health concerns, especially in the developing world where prevalence of smoking and nicotine dependence is increasing. Coupled with VDD and infection, CSE is a leading risk factor for bladder cancer. Preliminary data collected by our group suggested that a suite of genes have differential expression in bladders and lungs of mice in a chronic CSE system. Aim: We hypothesized that CSE and VDD would alter gene expression and epigenetic profiles in lung and bladder, thereby making these tissue sites more susceptible to disease progression, including lung infections or cancer of bladder or lung.
Methods: Mice on a VDD or control diet were exposed to CS or filtered air for a 14-week exposure period and organs were harvested at term.
Results: Spondin-2 (Spon2), a gene involved in microbial infection response and tumorigenesis, was downregulated in the lungs and bladders in CSE mice compared to controls ($p<.001$). Furthermore, Spon2 was downregulated in the lungs of mice with CSE and VDD compared to controls ($p<.05$). miRNA target prediction analysis predicts that mmu-miR-19b-1-5p and mmu-miR-19b-2-5p may be negative regulators of Spon2.
Conclusions: Future investigations into possible epigenetic mechanisms may further reveal pathways dysregulated by CSE and VDD leading to a compromised immune system, cancer progression, and overall increased morbidity.
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395

REAL-TIME MANAGEMENT AND SHARING OF FMRI ANALYSES USING A CUSTOM WEB-BASED NEUROINFORMATICS SYSTEM.

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Aims: Recent studies suggest that real-time fMRI neurofeedback may be of therapeutic benefit for substance abuse patients by training individuals to self-modulate craving circuitry and/or maintain executive function in the face of drug-related distraction cues. While advances in computing power have led to these real-time processing capabilities, they have also introduced new data management challenges, as vast quantities of 4-dimensional (spatiotemporal) fMRI data are generated during the course of even routine scan sessions. The purpose of this work was to develop a user-friendly web-based system of neuroinformatics featuring automated management, visualization, image processing, and sharing of fMRI data, particularly in the context of real-time addiction research.
Methods: A custom framework for web-based management of fMRI data was developed using C++, the Qt4 GUI toolkit, and a system of plugins for data visualization and processing. Once imported into the system's database (at the time of the scan), data are available for interactive visualization (and processing) from any computer via a secure web-browser interface.
Results: The system has thus far accommodated raw fMRI data from more than 200 scans across multiple real-time studies. Including processing results, this amounts to a database of thousands of individual array objects (3D and 4D), together with relevant metadata required for reproducing processing results. Furthermore the system takes advantage of computational benefits of cloud-style computing, with a powerful central computing engine, expandable to cluster or grid-computing.
Conclusions: By allowing remote interaction with results only moments after acquisition, our system has enabled the efficient pursuit of a therapeutic protocol with optimized parameters for real-time studies. The system is in active use by addiction researchers at our institution to collaboratively manage, process, and visualize fMRI data from real-time and other addiction-related studies.
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396

DELAY-DISCOUNTING OF FOOD AND REMIFENTANIL IN RHESUS MONKEYS RESPONDING UNDER A FOOD VS. DRUG CHOICE PROCEDURE.

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Aims: This experiment used a delay-discounting procedure to examine the relationship between delay and reinforcing effectiveness of food and the μ-opioid receptor agonist remifentanil.
Methods: Three rhesus monkeys lever-pressed under a concurrent FR 5 FR 5 schedule of reinforcement in which responding on one lever resulted in delivery of one food pellet and responding on another lever resulted in an i.v. infusion of remifentanil.
Results: Increasing the unit dose of remifentanil dose-dependently shifted response allocation from near-exclusive responding on the food lever at 0.032 μg/kg/infusion to near-exclusive responding on the drug lever at 0.32 μg/kg/infusion. When monkeys chose between immediate delivery of food and delayed delivery (15-300 s) of 0.32 μg/kg/infusion remifentanil, the number of choices for drug decreased with increasing delay. When monkeys chose between immediate delivery of a dose of remifentanil that initially did not maintain responding (0.032 or 0.1 μg/kg/infusion) and delayed delivery of food, the number of choices for drug increased with increasing delay to food.
Conclusions: These results (1) demonstrate that response allocation under a drug-versus-food choice procedure is sensitive to changes in the dose of remifentanil, (2) provide clear evidence that responding for each reinforcer type is sensitive to delay (i.e., delay-discounting curves were obtained for each reinforcer type), and (3) show that reinforcing effectiveness is impacted by the magnitude (e.g., dose) and availability (e.g., delay) of concurrently available reinforcers. That is, as the delay to food increased, monkeys increasingly responded for a dose of remifentanil that otherwise did not maintain behavior, suggesting that the absence of immediately available alternative sources of reinforcement might contribute to the development and maintenance of drug self administration.
Financial Support: Supported by USPHS Grants R01DA029254, K05DA017918 (CPF), and T32DA031115 (DRM).

397

STRUCTURAL EQUATION MODELING WITH CROSS-LAGGED PATHS TO EVALUATE ALCOHOLICS ANONYMOUS' EFFECTS ON DRINKING: PRELIMINARY RESULTS.

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Aims: To determine whether participation in Alcoholics Anonymous (AA) appears to be causally related to changes in drinking behavior using panel analysis.
Methods: The study is a secondary analysis of the Project MATCH dataset, which was a national alcoholism treatment trial conducted in the early 1990s. Study subjects were recruited at primary outpatient programs (N=952) and in-patient treatment aftercare programs (N=774); 90% were diagnosed as alcohol-dependent. The variables measured for each 3-month follow-up interval were: percent of days attended AA and percent of days abstinent (PDA) from alcohol (arc-sin transformed). The structural equation model (SEM) consists of the first-order cross-lagged regression paths between AA and PDA over 5 time periods and the adjacent regression paths (auto-regressions) among AA and PDA. Control variables were: readiness for treatment, taking steps to change, social support for recovery and living with spouse. Missing data were handled by FIML and M-Plus software estimated the model.
Results: For the outpatient sample, all four first order cross-lagged paths from AA to PDA were statistically significant ($p < .01$), with directionality indicating that more frequent AA attendance in a given period is associated with greater alcohol abstinence in the next period. Three of the four cross-lagged paths from PDA to AA were significant ($p < .05$), with directionality indicating that less abstinence in a given period is associated with greater AA attendance in the next period. The results were similar for the aftercare sample.
Conclusions: Cross-lagged SEM is a potentially useful technique for identifying and disentangling causal relationships among intervention and outcome variables that are changing over time. The method provided evidence of a reciprocal but also asymmetrical relationship between AA participation and drinking behavior. The magnitude and directionality of the regression paths may help explain why only modest correlations are found between AA and drinking in cross-sectional studies.
Financial Support: R21 AA017906.

398

LIFETIME STRESS IS ASSOCIATED WITH ELEVATED ADDICTION SEVERITY INDEX SCORES IN METHAMPHETAMINE-DEPENDENT PARTICIPANTS.

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Aims: The goal of this project is to evaluate the relationship between lifetime stress, addiction severity, and drug use in methamphetamine-dependent participants.
Methods: Participants answered questionnaires, including the Life Stressor Checklist (LSC), Addiction Severity Index (ASI), and Demographic/Drug use assessments.
Results: The sample (N=94, to date) includes methamphetamine-dependent volunteers who are primarily Caucasian males aged 34.7±8.5 (mean ± S.D.) years. Participants reported using 1.0±0.70 grams of methamphetamine/day for 11.4±8.1 years. They reported frequent use, 17.6±9.1 days out of the last 30 days. A majority were cigarette smokers (80%), who had been using nicotine for 17.4±9.4 years and were currently smoking 12.6±8.0 cigarettes/day. Using the LSC, participants were separated into those with high lifetime stress (HIStress; 12.9±3.1) or low lifetime stress (LOStress; 5.8±1.7) scores based on median split ($F1,92=179.1$, $p<0.0001$). ANOVA revealed significantly higher ASI total scores among those in the HIStress (1.4±0.6) group compared to those in the LOStress (1.1±0.5) group ($F1,92=5.8$, $p<0.02$). In addition, ANOVA revealed significantly higher ASI Psychiatric composite scores among those in the HIStress (0.2±0.2) group vs. the LOStress (0.1±0.1) group ($F1,92=9.8$, $p<0.002$).
Conclusions: The results indicate that methamphetamine-dependent individuals with higher lifetime stress exhibit elevated total ASI and psychiatric composite scores. Data acquisition is continuing and final outcomes will be presented at the conference.
Financial Support: This study is sponsored by NIH via support to RDLG (DA023964, DA027134) and TFN (DA024756, DA023468).

399

DROJNET 2: THE INTEREST OF INFORMATION AND COMMUNICATION TECHNOLOGIES (ICT) IN PREVENION AND HARM REDUCTION LINKED TO DRUG USE.

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Aims: Drojnet 2 is a project between transboarder communities and associations from Spain and France: Aragon, La Rioja, Cataluña (Spain) and Bizia Association (Bayonne, France). It has begun in December 2009.
The goal of Drojnet 2 is to use ICT in the fields of drug prevention and harm reduction, thus allowing young people to be part of the drafting of messages. The ICT used were mostly SMS, MMS, curts, social networks and discussion forums.
Methods: Common actions have been developed in this purpose: experiences exchanges between partners and implementation of actions in educational field (technical colleges mostly) and festive field: monthly contest for the best SMS/MMS. Specific actions have also been developed by each partner, programs "Drug and Curts" and "Drogomaton" in Cataluña, "Piensa la Noche" en La Rioja, photo contest in Aragon and development of a web site and a forum in 3 languages dedicated to the transboarder area of the Bask Country.
Results: Several indicators will be use to assess the project: number of participants to the different contests, number of visits on the web site, number of new products realized (animation shorts, SMS ...)
Conclusions: ICTs seem to be a major tool for preventing and reducing harms linked to drug use in young people. The fast evolution of the type of tool allows the implementation of new projects in these fields
Financial Support: None

400

ASSOCIATION BETWEEN N-ACETYLCYSTEINE MEDICATION COMPLIANCE AND HOMOCYSTEINE LEVELS.

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Aims: Homocysteine levels were examined in cocaine-dependent individuals receiving either placebo or N-Acetylcysteine (NAC). It was expected that those receiving the higest dose of NAC and who showed the highest levels of compliance would show the greatest reductions in homocysteine levels.
Methods: Homocysteine levels were collected at baseline and during the 4th study week from 66 cocaine-dependent participants receiving placebo (n=24), 1200mg (n=23) or 2400mg (n=19) of NAC during an 8-week double-blind trial. Riboflavin levels were collected weekly from each participant. Participants with riboflavin levels exceeding 1500ng/ml during a given week were considered compliant for that week. Percent compliance was calculated by dividing the participant's number of compliant weeks by the participant's total number of riboflavin samples collected. Homocysteine change scores were calculated by subtracting baseline values from Week 4 values.
Results: A regression analysis testing the effects for treatment group, %compliance, and the interaction of the two revealed a signficant overall effect, R^2=.26, $F(3,65) = 7.1$, $p < .001$. The group effect was significant, β=2.7, t=2.8, p<.01, as was the group x %compliance interaction, β=-.04, t=-3.7, p<.001. Separate correlations between compliance and homocysteine change scores were conducted within each group, with Pearson r's equal to .37, -.28, and -.55, for placebo, 1200mg, and 2400mg groups, respectively. Corresponding p values were .07, .19, and .02, respectively. A follow up ANCOVA that examined dose-related reductions in homocysteine and using compliance as a covariate was significant overall, $F(3,62)=3.1$, p<.05, with a trend towards significance for the group effect, $F(2,62)=2.9$, p<.059. The 2400mg group showed a trend towards being significantly lower than placebo, p<.058, and was significantly lower than the 1200mg group, p<.05.
Conclusions: As predicted, greater reductions in homocysteine levels were associated with higher compliance levels with the high dose NAC group.
Financial Support: DA019903

401

MOTIVATIONAL INTERVIEWING REDUCES SMOKING IN WOMEN LIVING WITH HIV/AIDS.

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Aims: Smoking among people living with HIV, particularly women living with HIV, is associated with a number of negative health consequences as well as heightened mortality rates when compared to non-smoking individuals with HIV. The overall aim of the current study was to test the efficacy of a brief motivational interview for smoking cessation with HIV+ women smokers.
Methods: Thirty HIV+ women smokers were recruited from an HIV primary care clinic in an urban safety-net hospital in San Francisco. Participants were were randomized to receive a single session of Motivational Interviewing (MI) or Prescribed Advice (PA). Both conditions were designed to reduce smoking and encourage abstinence from tobacco.
Results: Participants were an average age of 48.87 years (SD=5.78). Many (67%; n=20) reported an annual income of less than $10,000. At baseline, participants reported smoking an average of 16.13 (SD=9.82) cigarettes per day. There was a significant within-groups difference from the baseline to the one-month follow-up interview in the average number of cigarettes that participants reported smoking per day ($F(1, 26) = 7.89$, $p=.009$). The interaction between treatment condition and average cigarettes per day was also significant, ($F(1, 26) = 5.39$, $p=.028$) with participants in the MI condition reporting a significantly greater reduction in cigarettes smoked per day at the one-month follow-up.
Conclusions: Few interventions have directly targeted smoking cessation among women living with HIV/AIDS. Preliminary findings from this small pilot study suggest that Motivational Interviewing is more effective than Prescribed Advice in reducing smoking behavior reported by women living with HIV/AIDS and deserve further study.
Financial Support: NIH T32DA07250 and UCSF's Center for AIDS Prevention A105651.

402

PILOT TRIAL OF GABAPENTIN FOR THE TREATMENT OF BENZODIAZEPINE ABUSE OR DEPENDENCE IN METHADONE-MAINTENANCE PATIENTS.

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Aims: The primary aim of this project was to evaluate gabapentin for the treatment of benzodiazepine abuse or dependence in methadone maintenance patients.
Methods: This was an eight-week randomized double-blind placebo-controlled outpatient pilot trial. Participants were using benzodiazepines at least 4 days per week. All participants received weekly manual-guided supportive psychotherapy aimed to promote abstinence. Study medication was titrated over a two-week period to a maximum dose of gabapentin 1200 mg or placebo three times a day. Benzodiazepine use was assessed using urine toxicology confirmed self-report.
Results: Nineteen participants were enrolled into the trial and 16 participants (11 males) had post-randomization data for analysis. Six participants were assigned to gabapentin and 10 to placebo. Retention at week eight was 50%. There were no significant differences between gabapentin and placebo in changes in benzodiazepine use. Over the study period, participants in the gabapentin group increased their abstinent days per week from 0.0 to 2.0 (SD=3.1;p=.16) and decreased their daily use of benzodiazepine by 4.0 mg per day (in lorazepam equivalents)(SD=4.0; p=0.03), a 77% reduction. One participant in the gabapentin group discontinued study medication because of peripheral edema. Two participants in the placebo group sought admission for inpatient detoxification treatment.
Conclusions: No between group differences were detected. Gabapentin in doses of 3600 mg daily was well tolerated by methadone maintenance patients with benzodiazepine abuse or dependence. Participants assigned to gabapentin demonstrated significant reductions in daily amounts of benzodiazepine used. An adequately powered double-blind trial is required to further evaluate the utility of gabapentin in treating benzodiazepine dependence.
Financial Support: NIDA grants: K23 DA21209, P50-DA09236, K24 DA022412
& K24 DA029647

403

MARIJUANA USE AND ITS RELATIONSHIP TO PROBLEMATIC DRINKING IN YOUNG ADULT MARIJUANA STUDY VOLUNTEERS.

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Aims: Marijuana is the most widely used illegal substance, and its use may increase as legislation decreases barriers to access. The relationship between marijuana use and problematic alcohol drinking and psychiatric symptoms was examined in a general healthy population of young adult marijuana users recruited from the local community. We hypothesized that marijuana abuse would be associated with problematic alcohol drinking.
Methods: Young adult marijuana users (N=70) reporting good physical and mental health were assessed using the SCID Screen Patient Questionnaire-Extended, the Beck Depression Inventory and a DSM-IV based symptom checklist for Attention Deficit Hyperactivity Disorder. Level of caffeine, tobacco, alcohol and marijuana use was also reported.
Results: Preliminary analysis of 37 subjects (25 males, 12 females; mean age 21.6 ± 3.2) revealed the following substance use: 10.3 ± 7.2 episodes of marijuana use/month: 1.2 ± 2.4 cigarettes/day; 144.93 ± 162.3 mg caffeine/day; and 8.5 ± 9.7 alcoholic drinks /week. A chi-square was performed to examine the relation between symptoms of cannabis abuse and problematic alcohol drinking. At least one symptom of cannabis abuse was reported by 41% of the subjects. Subjects who reported symptoms of cannabis abuse were significantly more likely to report symptoms of alcohol abuse $\chi 2$ (2, N = 37) = 11.01, p <.001 and dependence $\chi 2$ (1, N = 37) = 3.73, p <.05; as well as symptoms of cannabis dependence $\chi 2$ (1, N = 37) = 6.44, p < .01. Reports of driving under the influence of cannabis was associated with drinking and driving $\chi 2$ (1, N = 37) = 6.12, p < .01.
Conclusions: Nearly half of a healthy population of young adult marijuana users recruited from the local community reported one or more symptoms of marijuana abuse. Those reporting marijuana abuse were more likely to report symptoms of alcohol abuse and dependence, suggesting that modest symptoms of marijuana abuse are not benign.
Financial Support: DA-05312

404

CONTINGENT VOUCHERS FOR SMOKING IN SUBSTANCE ABUSERS AS ADJUNCT TO NICOTINE PATCH.

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Aims: Adults with substance use disorders (SUD) have low smoking cessation rates. The aim of this study is to determine whether contingent reinforcement for smoking abstinence (CM), compared to noncontingent reinforcement (NR), increases the effectiveness of brief counseling and transdermal nicotine replacement (NRT) on short-term smoking outcomes for smokers with SUD receiving smoking treatment.
Methods: In a 2-group design, substance abusers in a residential program for SUD who smoke 10 or more cigarettes per day received Brief Advice (4 sessions) and free NRT (8 weeks), and were randomized to 19 days of CM for smoking vs. a matched NR condition. The CM intervention included a 5-day reduction phase to shape initial abstinence and a 14-day abstinence phase. During the abstinence phase reinforcement was based on twice daily carbon monoxide (CO) readings levels <6 ppm. The Brief Advice was adapted for sobriety settings. Subjects did not need to be motivated to quit smoking to participate. Point prevalence smoking abstinence, substance use and other outcomes were assessed at 1 and 3 months after starting study treatment.
Results: During the CM phase, groups did not differ in the number of days of NRT use or the number of counseling sessions competed. Groups did differ in the percentage of participants whose CO samples demonstrated complete abstinence throughout the 14 day abstinence phase (22% for CM vs. 6% for NR; p < .05). At 1 and 3 months after the start of treatment the CM group had fewer smoking days and fewer cigarettes smoked per day (p < .05). The trend for group differences in point prevalence abstinence)verified with CO or cotinine) was not significant.
Conclusions: This short-term CM intervention is effective at reducing smoking among people with SUD and can be readily combined with pharmacological treatment for smoking cessation.
Financial Support: This research was supported by a grant from NIDA (R01DA023995 – PI Rohsenow) and by a Senior Research Career Scientist Award from the Department of Veterans Affairs

405

EARLY ADOLESCENT ONSET OF GAMBLING AND PSYCHIATRIC HEALTH AND BEHAVIORS AMONG EARLY ADULTHOOD GAMBLERS.

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Aims: Gambling opportunities are becoming more common among US youth and youth are beginning to be involved in gambling activities at younger ages. We explore whether there is more involvement in gambling and drug use behavior and several other mental health problems by age 21 among those who initiated gambling at an earlier age (Early-onset gambling = before age 14) than those who start gambling at or after age 14 (Later-onset gambling).
Methods: Among a cohort of young adults who began their education in an inner-city public school system, 188 gamblers were identified. On an annual basis, participants have been self- reporting gambling and drug using behaviors. Other items assess several psychiatric disorders. The mean age at the last interview was 22.3 years and any behavior or disorder noted during interviews collected between the ages of 17-21 was included in this analysis. Contingency tables and logistic regression models (adjusted for demographics) estimated associations.
Results: Thirty percent of the sample (n=57) were Early-onset gamblers. Compared to later-onset gambling, early-onset gambling was associated with gambling more frequently (91% of early-onset gamblers gambled weekly versus 72% of later-onset gamblers, p=0.04) and more gambling-related problems (79% of early-onset gamblers had problems versus 47% of later-onset gamblers, p=0.001), higher prevalence of any anxious or depressive disorder (18% versus 9%, p=0.1), twice the proportion of antisocial personality disorder (32% vs. 15%, p=0.03); and more illegal drug use (79% versus 55%, aOR:3.11[1.08-9.01], p=0.04). No differences were seen for alcohol and tobacco use.
Conclusions: Gambling onset before age 14 is associated with more severe psychiatric problems in young adult gamblers. Prevention strategies should target elementary school children before they reach an age in which they have access to gambling opportunities.
Financial Support: NICHD grant RO1HD060072 (P.I. Martins) and NIDA grant RO1 DA11796 (P.I. Ialongo).

406

STIMULANT AND NON-STIMULANT EFFECTS OF MEPHEDRONE, MDPV, METHYLONE, AND OTHER "BATH SALT" COMPONENTS ON OVERT BEHAVIOR IN RODENTS.

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Aims: Synthetic drugs commonly sold as "bath salts" and used for their stimulant properties are an emerging abuse problem in the U.S. Reports of human use have shown psychotic behavior, paranoia, delusions, and self-injury. In vivo research has shown that rats will self-administer mephedrone, and that mephedrone increases locomotor activity. The purpose of the present study was to evaluate in vivo effects of synthetic cathinones found in bath salts, and compare these effects to those of cocaine (COC) and methamphetamine (METH).
Methods: Acute effects of methylenedioxypyrovalerone (MDPV), mephedrone, methylone, methedrone, 3-fluoromethcathinone (3-FMC), 4-fluoromethcathinone (4-FMC), COC, and METH were examined, with dose-effect curves determined for each drug. Effects of these drugs were examined in male Sprague-Dawley rats on locomotor behavior, prepulse inhibition, and tail flick analgesia, and in male ICR mice on locomotor behavior, rotorod, and a functional observational battery (FOB).
Results: Methylone, MDPV, COC and METH produced significant increases in locomotor behavior in rats. In mice, all drugs examined increased locomotor activity. 3-FMC and methylone also produced significant decreases in performance on the rotorod. Results of the FOB showed that in addition to typical stimulant induced effects, some synthetic cathinones produced ataxia, convulsions, self injury, reactions to stimuli not present, and retropulsion.
Conclusions: Synthetic cathinones produced many behavioral effects that resemble those of known stimulants of abuse, but some also disrupted motor coordination and induced behaviors that were not typical of known stimulants. Due to the recent DEA ban on MDPV, mephedrone, and methylone, it is likely that bath salts now contain other synthetic cathinones examined here. These newer synthetic cathinones appear to share pharmacological properties with the ones that have been banned, suggesting that they may be just as behaviorally toxic.
Financial Support: RTI International internal research and development funds.

407

THE KYNURENINE 3-HYDROXYLASE INHIBITOR RO 61-8048 BLOCKS THC-INDUCED ACTIVATION OF GLUTAMATERGIC AND DOPAMINERGIC SIGNALING IN THE VENTRAL TEGMENTAL AREA AND NUCLEUS ACCUMBENS SHELL IN RATS.

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Aims: Alpha 7 nicotinic acetylcholine receptors (α7nAChRs) modulate neurochemical effects of delta-9-tetrahydrocannabinol (THC), the main psychoactive ingredient of marijuana. Kynurenic acid (KYNA), a neuroinhibitory and neuroprotective agent in mammalian brain, is an astrocyte-derived endogenous antagonist of α7nACh receptors. Here we investigated whether kynurenine 3-hydroxylase inhibition by Ro 61-8048, which markedly increases brain KYNA levels, modulates THC's effects on the mesolimbic brain reward system in rats.
Methods: We conducted *in vivo* microdialysis experiments on freely moving Sprague-Dawley male rats.
Results: THC (3 mg/kg, i.p.) significantly increased both extracellular dopamine and glutamate levels in the ventral tegmental area (VTA) and nucleus accumbens shell and these increases were prevented by Ro 61-8048 (100 mg/kg, i.p.), which markedly increased KYNA levels in both areas. Blockade of THC's effects by Ro 61-8048 were reversed by galantamine, a positive allosteric modulator of α7nAChRs.
Conclusions: Up-regulation of brain KYNA levels reduces activity of α7nAChRs and, thus, markedly attenuates THC-induced activation of the mesolimbic dopamine system suggesting that kynurenine 3-hydroxylase is a promising new target for development of medications for the treatment of cannabis abuse
Financial Support: Supported in part by the Intramural Research Program of NIDA, NIH, DHHS and in part by the Department of Psychiatry, University of Maryland School of Medicine.

408

REGIONAL REDUCTIONS IN BRAIN MYO-INOSITOL LEVELS ARE ASSOCIATED WITH COGNITIVE IMPULSIVITY IN MARIJUANA-DEPENDENT YOUNG MEN: PRELIMINARY EVIDENCE FROM MRSI AT 4T.

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Aims: Long-term marijuana (MRJ) use functionally alters brain activation during cognitive task performance, however the effects of chronic MRJ use on neurochemistry are not well characterized. Previously, altered global myo-Inositol (mI) concentrations and distribution in white matter (WM) were found to be associated with impulsivity and mood symptoms in young MRJ-dependent men. Thus, the current study objective was to examine the potential regional specificity of metabolite levels in brain regions densely packed with cannabinoid receptors, as well as possible associations with clinical measures.
Methods: The study included MRJ-using (n=13) and healthy non-using (NU; n=10) men. Proton metabolite data were acquired at 4.0 Tesla from the medial temporal cortex (MTL) using 2D J-resolved magnetic resonance spectroscopic imaging (MRSI). Spatial and spectral localization afforded the opportunity to investigate high-quality proton metabolites, individually quantified from regions of interest, including the left and right thalamus, left and right temporal lobe, and parieto-occipital cortex.
Results: Consistent with previous global findings, reduced mI (mI/Cr) levels ($p \leq 0.01$) were observed in the MRJ group relative to the NU group, however reductions were regionally specific to the left thalamus (lThal). In addition, reduced lThal mI levels were significantly associated with elevated cognitive impulsivity ($r=-0.49$, $p=0.04$), but not with clinical state measures or marijuana use indices.
Conclusions: The current findings extend previous work, indicating that reduced mI levels are specific to the lThal in individuals with MRJ dependence. Furthermore, findings suggest that mI and the lThal uniquely contribute to heightened impulsivity, possibly reflecting a neurobiological basis of cognitive alterations that develop as a result of long-term MRJ use.
Financial Support: Supported by K01 grant AA014651 (MMS) and R01 grants DA020269 and DA12483 (DYT).

409

TRAUMATIC EVENTS, PTSD AND SUBSTANCE USE AMONG ADULTS IN AN URBAN EMERGENCY DEPARTMENT.

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Aims: Prior research has documented exacerbated rates of violence exposure and post-traumatic stress disorder (PTSD) among adults residing in urban/poor communities. This study examined rates and correlates of exposure to traumatic events and PTSD in relation to substance use among adults in an urban ED.
Methods: Adult (18-60) ED patients self-administered a computer survey (e.g., demographics, illicit and non-medical prescription drug use, alcohol use, and PTSD). Participants screening positive for drug misuse (ASSIST score >4) completed a baseline assessment (i.e., depression, social influences, and community violence). Multinomial logistic regression analyses (for screening and baseline, controlling for demographics) were used to predict PTSD groups: no traumatic event (NTE), traumatic event/PTSD- (TE), traumatic event/PTSD+ (PTSD).
Results: Among the screening sample (n=1617), 67% reported NTE, 17% reported TE, and 16% reported PTSD. Logistic regression analyses showed that those in the screening sample with PTSD were more likely than the NTE group to report marijuana use (AOR=1.70) and prescription drug use (AOR=2.28). Among the baseline sample (n=269), 55% reported NTE, 21% reported TE, and 24% reported PTSD. Participants with PTSD in the baseline sample were more likely to report depression and community violence than the other groups. Logistic regression analyses examining drug misuse variables showed that those with PTSD in the baseline sample were more likely that the NTE group to report prescription drug misuse (AOR=2.79).
Conclusions: Given rates of PTSD and associated substance use and depression, ED screening and referrals appear warranted. Prescription drug misuse was a robust correlate of PTSD. Future studies are needed to determine whether these drugs are being used to cope with PTSD or if users of these drugs who witness traumatic events are more likely to develop PTSD.
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410

MOTIVATIONAL-ENHANCED CASE MANAGEMENT FOR HEPATITIS CARE COORDINATION IS ASSOCIATED WITH REDUCED ALCOHOL USE.

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Aims: Drug users (DUs) have a high prevalence of chronic hepatitis C (HCV) and many are not engaged in hepatitis care. Progression of liver disease can be accelerated by alcohol intake. We conducted a randomized trial to examine the impact of a motivational -enhanced case management (ME-CM) intervention on engagement of DUs in HCV care and HAV/HBV vaccination and found that the intervention significantly increased vaccination and engagement in HCV evaluations. Here we examine the impact of ME-CM on illicit drug and alcohol use and risky injection drug use.
Methods: 489 participants were randomized to either the control (n = 245) or the enhanced arm (n = 244). We examined the impact of the ME-CM intervention on days of illicit drug use and alcohol use and any risk injection drug use in the past 30 days at 3, 9, and 12-months post-randomization. A repeated measures zero-inflated Poisson regression model was used to compare illicit drug and alcohol use between treatment groups controlling for treatment arm, age, gender, race/ethnicity, HIV status, homelessness, and recruitment site. Logistic regression analysis controlling for the same covariates was used to compare the effect of treatment condition on any risky injection drug use.
Results: Fifty-eight percent (286 out of 489) were HCV anti-body positive. Modeling revealed no significant treatment effect on any of the drug use variables or injection risk behavior but a significant positive treatment effect on days of alcohol use ($z = -2.317$, $p = 0.021$) over the 12-month study period.
Conclusions: The ME-CM intervention was associated with reductions in alcohol use which is particularly important in a population with a high prevalence of HCV. It did not, however, have positive impacts on ongoing illicit drug use or injection risk behaviors.
Financial Support: Supported by: National Institute on Drug Abuse, R01DA020781, R01DA020841, P30DA 011041, P50DA009253 and U10DA015815.

411

EFFECTS OF BENZODIAZEPINES ON MORPHINE-INDUCED HYPERLOCOMOTION ACCOMPANIED BY THE CHANGES OF KCC2 IN THE NUCLEUS ACCUMBENS.

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Aims: Benzodiazepines have been used as a sedative, sleeping, and anti-anxiety drug. Benzodiazepines are believed to be relatively safe, because of fewer side effects compared with barbiturates. However, benzodiazepines induce some serious adverse effects (e.g. drug dependence by long-term use). Even thought, drug dependence is considered to be related to the neuroplastic changes in the mesolimbic dopaminergic system, underlying mechanisms of drug dependence induced by benzodiazepines is not fully understood. So, we investigated effects of benzodiazepine on the activation of mesolimbic system.
Methods: We examined the effect of benzodiazepines on the morphine (10 mg/kg s.c.)-induced hyperlocomotion after treatment with diazepam (10 mg/kg i.p.) for 7 days in mice. In addition, we also examined the role of GABAARα1 on the morphine-induced hyperlocomotion using the GABAARα1 agonist zolpidem (30 mg/kg i.p.).
Results: Chronic treatment of diazepam and zolpidem enhanced the morphine-induced hyperlocomotion. Furthermore, 1h or 24h pretreatment with zolpidem did not enhance the morphine-induced hyperlocomotion, indicating that chronic treatment owithbenzodiazepines, but not acute treatment, are required to induce the behavioral change by morphine. It is known that potassium chloride cotransporter 2 (KCC2) plays an important role in the Cl- homeostasis. Here, we found that chronic treatment with zolpidem could increase the KCC2 levels in the nucleus accumbes. Furthermore, KCC2 inhibitor frosemide (30 nmol/mouse i.c.v.) reversed enhancing effects of zolpidem on the morphine-induced hyperlocomotion.
Conclusions: These results suggest that the chronic activation of GABAARα1 causes the change of KCC2 levels in the nucleus accumbens, and these changes can influence the activation of mesolimbic dopaminergic system induced by morphine.
Financial Support: The Supported Project for Creating a Strategic Research Infrastructure in Private Universities of the Ministry of Education, Culture, Sports, Science and Technology of Japan.

412

METHAMPHETAMINE SELF-ADMINISTRATION IN RATS LEADS TO INCREASED SYSTEMIC AND NEURAL INFLAMMATION.

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Aims: An important route of HIV infection is by needle sharing during the use of drugs like methamphetamine (meth). HIV disease progresses more rapidly in meth abusers. The aim of this study was to determine whether meth use increases inflammatory cytokines which could explain HIV and meth co-morbidity.
Methods: Rats were trained to self-administer meth for 14 days and sacrificed on day 15 with harvest of blood, spleen, and brain tissue. Yoked controls received saline according to the infusions of self-administering rats. We compared serum levels of pro-inflammatory cytokines, interferon-γ (IFNγ), tumor necrosis factor α (TNFα), interleukin-6, and the anti-inflammatory cytokine IL-10, by ELISA. Splenocyte production of IFNγ and TNFα was assessed by flow cytometry. TNFα levels in the striatum were determined via Western blot.
Results: Rats trained to self-administer meth had a signficantly greater number of IFNγ producing CD8+ T cells per spleen than saline controls. Serum cytokine levels of some proinflammatory cytokines were also higher in meth than in saline-treated rats. TNFα expression was ~10% higher in the striatum of rats trained to self-administer meth than in saline controls.
Conclusions: HIV disease progress is measured by decreases in CD4 T cells and increases in inflammatory markers. Our data suggests that meth use increases pro-inflammatory cytokine production, which could exacerbate inflammation caused by HIV infection and lead to more rapid disease progression. Chronic meth self-administration also results in increased expression of TNFα and neuroinflammatory responses in the brain that leads to meth-neurotoxicity which parallels the neuropathology seen with HIV infection.
Financial Support: Chicago Developmental Center for AIDS Research P30AI082151, DA024923, and Rush Univ Center for Compulsive Behavior and Addiction.

413

SUBSTANCE USE AMONG YOUNG ADULTS WITH MOOD DISORDERS IN DRUG TREATMENT DIFFERS BASED UPON HISTORY OF BEING PRESCRIBED MOOD DISORDER MEDICATION.

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Aims: Mental health problems are common among young adults in substance abuse treatment. We examined the relationship between medication treatment for mood disorders and rates of substance use in a sample of 12-25 year olds who had been diagnosed with a mood disorder and were receiving substance abuse treatment. Following from the self-medication hypothesis, we expected that medication treatment of mood disorders would be associated with reduced use of substances.
Methods: We surveyed 1,860, 12-25 year olds at substance abuse treatment entry. Of these, 726 self-identified as having ever been diagnosed with depression or bipolar disorder. We compared the substance use patterns of those who had been prescribed medication for their mood disorder to those who had not. When differences were observed between the two groups, we further explored this relationship using logistic regression.
Results: Medicated and non-medicated clients had similar rates of non-prescription drug abuse. A significantly higher proportion of the medicated clients had ever used alcohol to intoxication and prescription pain relievers and stimulants. Similar results were observed for past year use. In multivariate models, having been medicated significantly increased the odds of ever having used prescription stimulants but was not associated with any other substance use indicator.
Conclusions: Contrary to the self-medication hypothesis, young people prescribed medications for a mood disorder may be at increased risk for alcohol and prescription drug abuse. Medication treatment for mood disorders may reduce negative perceptions toward prescription drugs and their illicit use, increasing consumption. Longitudinal study of these relationships is needed before this conclusion can be fully endorsed.
Financial Support: This research was supported by NIDA grant 1R01DA024658.

414

MINIMIZING THE UNINTENDED CONSEQUENCES OF OPIOID TREATMENT: DEVELOPMENT OF A DRUG BEHAVIOR SCALE FOR USE IN AUSTRALIA.

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Aims: To develop and validate a brief 'aberrant' opioid behavior scale for use in Australian clinical and research settings. Based on the US literature, the project aims to develop an instrument that will identify patients who would benefit from clinical review (i.e. it is not prescriptive), and is also able to measure changes over time (3 months).
Methods: A self-complete patient survey was developed based on the existing literature, key expert and advisory committee input and administered to N=427 chronic opioid patients in treatment for chronic pain (n=222) or opioid dependence (n=205). The survey included 40 items on 'aberrant' and related behaviors/issues, rated in terms of frequency. Item and scale psychometrics were employed to refine items to a brief scale.
Results: Following removal of problematic items (due to poor retest-reliability or wording, independence, collinearity or rarity) iterative exploratory factor analytic procedures identified a 10-item unifactorial scale that achieved criteria for good model fit (CFI, TLI >0.95; RMSEA <0.05) in both chronic pain and opioid dependence patient groups. These items provided good discrimination between groups, demonstrated acceptable test-retest reliability and had strong face validity among advising clinicians.
Conclusions: The opioid-related behavior scale has sufficient reliability and validity as a one-factor structure containing 10 items, and is suitable for use across a variety of opioid patient groups (chronic pain, addiction medicine).
Financial Support: Funded by Reckitt Benckiser through an untied educational grant.

415

CONFIDENCE, TEMPTATION AND CALLOUS-UNEMOTIONAL TRAITS AMONG ADOLESCENT SUBSTANCE USERS IN RESIDENTIAL TREATMENT.

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Aims: Adolescents represent approximately 1/3 of all admissions to substance use treatment facilities in the US. Residential substance use treatment settings often provide services to the most impaired adolescents, who are at risk of poor treatment outcomes.

Adolescents high in callous and unemotional (CU) traits show elevated rates of substance abuse problems and exhibit poor response to treatment and premature dropout. Findings suggest the need to understand the impact of CU traits on clinical process variables.

This aims of this study were 1) to examine the relationship between CU traits, situational temptations (ST, the intensity of desire to use in the presence of substance-related cues) and situational confidence (SC; a person's perception of his/her own ability to maintain abstinence in the face of various temptations) and and 2) to examine the moderating effect of CU on the relationship between ST and SC.
Methods: Participants were 200 adolescent substance users recruited from 2 residential treatment facilities. Upon admission, participants completed self-report measures of CU traits, ST and SC. ST and SC ratings were examined for positive affect/peers, negative affect, and need/urge.
Results: CU traits were associated with decreased confidence across all situations (ps<.001), but were not associated with elevated temptations. Results revealed that the relationship between ST and SC was moderated by CU. Specifically, across situations, the negative relationship between ST and SC was robust for those low in CU traits, p <.01, but this relationship was not significant for adolescents high in CU traits, ps >.4.
Conclusions: CU traits were associated with decreased confidence, but not with temptation intensity. Adolescent substance users high in CU traits experienced a dissociation of ST and SC, suggesting that they have low self-efficacy to remain abstinent even in low temptation situations. Findings will be discussed in terms of treatment implications.
Financial Support: No financial support for preparation of abstract.

416

MEDICATION-ASSISTED THERAPY (MAT) IN THE CRIMINAL JUSTICE SYSTEM: A NATIONALLY REPRESENTATIVE SURVEY OF DRUG COURTS.

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Aims: To determine the need for, availability of, and barriers to the use of MAT for opioid addiction in drug treatment courts in the United States.
Methods: Using a database from the National Drug Court Institute (NDCI), we stratified courts by urbanicity, state, and need (courts in areas where prescription opioids or heroin use was prevalent were oversampled). Administrators of the selected drug courts (n=186) were sent an online survey to assess the prevalence of and barriers to MAT. Respondents were offered the option to receive a $20 gift card as an incentive.
Results: Respondents (n=103) estimated their drug court census range from <10 to >400 clients with a median of 26-50. Ninety-nine percent of courts estimated that at least some of their clients were opioid-addicted in 2010. Prescription opioids were more frequently cited as the primary opioid problem than heroin (65% vs. 35%). Overall, 64% of opioid-addicted drug court clients were receiving MAT; 36% methadone, 46% buprenorphine, and 27% naltrexone. The two most frequent reasons why buprenorphine was not offered in a drug court were opposition to its use from the drug court judge (54%) and/or from state, county, or municipal government (54%); the two most frequent reasons why methadone was not offered were that the drug court policy did not permit it (56%) and that the drug treatment provider did not recommend or provide methadone (54%).
Conclusions: Despite evidence of the safety and efficacy of MAT (especially agonist medications) to improve outcomes for opioid dependence, MAT has limited penetration in drug courts. Political, judicial and administrative opposition appear to affect its use and availability in criminal justice settings. These preliminary data suggest that a substantial, targeted educational initiative is needed to increase awareness of the treatment and criminal justice benefits of MAT in the drug courts.
Financial Support: Reckitt-Benckiser

417

LIVING WITH SUBSTANCE-USING PARENTS AND EARLY MARIJUANA INITIATION IN ILLICIT DRUG USERS.

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Aims: This study aimed to assess the relationship between the substance use history of parents and siblings living at home before age 16 and early onset marijuana use among heavy, illicit drug users.
Methods: The current study used baseline data from NEURO-HIV Epidemiologic Study in Baltimore, MD. The HIV-Risk Behavior Inventory was used to investigate social, behavioral and other risk factors for HIV and hepatitis in injection and non-injection drug users. The present study used a subset (N=589) of the larger study that self-identified as White or African American, and provided information regarding parent and sibling drug use and household composition up to age 16.
Results: Overall, age of marijuana initiation, which was 13.76 for Whites and 15.29 for African Americans, decreased as the number of substance using parents (SUP) increased compared to those with non-using parents (NUP). Age of onset for those with two NUP was 14.30 for Whites and 15.64 for African Americans. Having two SUP not living at home was associated with marijuana use 2.16 years earlier than those with two NUP. Marijuana use was 1.5 and 1.39 years earlier than those with two NUP when one or both SUP lived at home, respectively. Those with only one SUP who did not live at home used marijuana .9 years earlier than those with NUP. Living with siblings did not affect age of marijuana use regardless of their drug use. There was no interaction between race and SUP living situation.
Conclusions: The present study explored the combined effects of absence of parents in the home and family history of substance use as contributors to earlier marijuana use. These findings contribute to the literature outlining a developmental trajectory of substance use that contributes to later illicit drug use.
Financial Support: This study was supported by grants R01DA014498 and T32DA007292 from the National Institute on Drug Abuse.

418

METHAMPHETAMINE USERS AT TREATMENT ADMISSION: HOW IMPAIRED ARE THEY?

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Aims: Methamphetamine continues to be a drug in which females are as likely as males to be users. This paper seeks to determine the differences between genders based on drug use patterns, mental health issues, family and living patterns, physical problems, and abuse and neglect as children and adults.
Methods: This is a study of 222 patients newly admitted to residential treatment in Texas in 2010 and 2011 who participated in a structured survey using computer-assisted interviewing. Inclusion criteria included having used methamphetamine at least six times in the last six months. Statistical methods include t-tests, chi squares and correlations, with significance set at .05.
Results: Females more likely to complete high school, to have more children living with them, and to score 8 on Severity of Dependence Scale vs. 7 for males. Over 89% of all respondents said a family member had drug problem, 94% said a family member had a drinking problem, 90% said family had psychological problem, and 87% had a family member who had been in jail.
Significant findings were that females more likely to inhale meth and males more likely to inject but males had a higher prevalence of use of all drugs queried. Females were more likely to have seen a mental health professional for problems, to have been prescribed meds for such problems, and to have been hospitalized for them. Over half of all clients reported dental and vision problems. Females were more likely to report having felt unloved or been sexually abused as children and to have been sexually and mentally abused as adults. They also lived with partners with drinking, drug, or psychological problems and with partners who had sold drugs or spent time in jail.
Conclusions: These findings show the extent of co-occurring mental health and substance abuse problems among all the respondents. However, females were particularly in need to extensive treatment for co-occurring problems.
Financial Support: Monitoring the Changing Methamphetamine Market in the Austin Area, NIDA, R21 DA025029, Period 8/15/2009-7/31/2012.

419

METHAMPHETAMINE-DEPENDENT ADULTS SHOW ATTENUATED BRAIN RESPONSE TO PLEASANT INTEROCEPTIVE STIMULI.

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Aims: Mechano-receptive C-fiber (MR-CF) stimulation via slow stroking of C-fiber rich skin areas is linked to brain regions involved in reward and interoception and thus may be important aspect of addictive behavior. This study examined whether methamphetamine dependent (MD) individuals show altered brain responses to MR-CF stimulation. MD individuals will show a diminished response to interoceptive stimuli.
Methods: Recently abstinent MD (n=16) and comparison (CO, n=10) subjects completed a continuous performance task during functional magnetic resonance imaging while receiving a pleasant interoceptive stimulus. Anticipatory trials were characterized by either a blue or yellow background signaling a slow brush stroke administered within the next 6 seconds to the left palm or forearm, respectively. Visual analog scales (VAS) indexed interoceptive experience (e.g. pleasantness, warmth). A linear mixed effects model was conducted with group as the between subjects variable, subject as a random factor and condition (anticipation palm and forearm, palm and forearm stroke) as the repeated factor. Correlations between significant brain results, VAS ratings, and behavioral data were computed.
Results: CO exhibited greater insula and thalamus activation than MD across trials. CO also showed greater activation than MD in the inferior frontal gyrus, insula, caudate and anterior cingulate during forearm-specific interoceptive trials. Whereas insula activation in CO correlated with better task accuracy and VAS warmth, insula activation correlated with VAS unpleasantness in MD.
Conclusions: MD exhibit attenuated interoceptive processing and decreased reward responsivity, findings that may relate to a reduced sensitivity to pleasant stimuli. MD may seek stimulant drugs to enhance the experience of afferent interoceptive stimuli.
Financial Support: NIDA 5P20DA027843

420

ENHANCED SUBSTANCE USE DISORDER RECOVERY THROUGH THE USE OF PEER RECOVERY SUPPORT.

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Aims: The 2007 National Survey on Drug Use and Health indicated that over 704,000 people in Virginia suffered from substance use disorders (SUDs), but almost 80% were not receiving needed treatment. The Substance Abuse and Addiction Recovery Alliance of Virginia (SAARA) is a recovery community organization (RCO), based in Richmond, providing addiction recovery support services in central Virginia in an effort to expand the available service options for people seeking recovery from substance use disorders. The SAARA Center serves adults with substance use disorders, offering employment, housing, transportation and psychosocial support services. Over 800 individuals have received some level of service from SAARA over the past four years. The present study investigated the extent to which and in what ways service recipients benefited from their participation. This evaluation also assessed the extent to which perceived support was increased and the extent to which perceived support or the amount and types of support provided were related to outcomes.
Methods: Outcome data was obtained from a locally-designed Entrance Survey, a modified Self-Sufficiency Index, and SAMHSA's Government Performance and Results Act (GPRA) instrument.
Results: Findings across all instruments indicated that participants who completed both the intake and 6-month follow-up evaluation protocols improved significantly across a wide range of functional areas. Significant improvements were reported in substance abuse recovery, emotional well-being, social support, employment, transportation, dealing with legal issues, and overall quality of life. Furthermore, while participants were offered and provided an array of services, those who showed improvement or remained abstinent tended to have received greater dosage of service.
Conclusions: These findings highlight the importance of peer recovery support services and their wide-ranging positive impact in the lives of people with SUDs.
Financial Support: This project is supported by SAMHSA TI-07-002

421

C57BL/6J MICE SELF-ADMINISTER INCREASED DOSES OF OXYCODONE IN EXTENDED SELF ADMINISTRATION SESSIONS.

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Aims: Non-medical use of oxycodone is a rising problem in the United States. There are few animal studies examining long-term oxycodone self administration. The current study was designed to examine chronic oxycodone self administration by mice (14 days), in extended self-administration sessions (4 hours).
Methods: Male C57/BL6 mice were either allowed to self-administer oxycodone (0.25 mg/kg/infusion, FR1) or were used as yoked-saline controls. Mice self administered oxycodone for 4 hours/day for 14 consecutive days. The mice administered oxycodone by nose poking an active hole in the self-administration chamber. Nose poking at an inactive hole was not reinforced. The number of nose pokes in each group was compared over time by 3-way analysis of variance with repeated measures.
Results: The yoked-saline control mice poked the active hole significantly more times than the oxycodone group on the first day of the experiment. However, the oxycodone group poked the active hole significantly more times than the yoked controls by day 14 and over the 14 day period as a whole. The number of nose pokes at the active hole continually rose over the 14 days for the oxycodone group with little responding at the inactive hole.
Conclusions: Consistent with previous studies in rats with other drugs of abuse, C57BL/6J mice self-administered increased doses of oxycodone in extended self administration sessions.
Financial Support: This work was supported by NIH-NIDA 1R01DA029147-01A1 (YZ) and NIH-NIDA DA05130 (MJK)

422

METHAMPHETAMINE FACILITATES REWARD CONDITIONING IN HEALTHY VOLUNTEERS.

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Aims: Studies with laboratory animals indicate that drug-paired stimuli facilitate drug-taking behaviors and that stimulant drugs facilitate the incentive value of drug-paired cues. Previously, we demonstrated that drug conditioning also occurs in humans using a place preference procedure. In the present study, we aimed to see if a stimulant drug would enhance reward-related conditioning of images presented on a computer screen, rewarded with money.
Methods: Healthy volunteers (18-35 years old; N=64) participated in 4 "conditioning" sessions, two with placebo and two with methamphetamine (20mg), followed by one "test" session without drug administration. Subjects were randomly assigned to a Paired Group, who received drug paired with a specific background stimulus present during a computer task or an Unpaired Group who received drug without any relation to the task stimuli. Prior to conditioning, subjects rated their preference for several tasks and backgrounds pictures. During the conditioning sessions, they performed computer tasks of varying reward pay-off, with distinctive backgrounds present during the tasks. In test sessions, preference for backgrounds was again assessed using the same rating task as before. Measures of subjective drug and mood, and physiological effects were taken several times throughout the session, as well.
Results: With approximately half of the subjects completed, methamphetamine induced a preference for the background with which it was paired, without affecting preference in the Unpaired Group.
Conclusions: Consistent with previous work, a stimulant drug can affect preference for a neutral cue paired with a reward, in this case money earned in a task.
Financial Support: This research was supported by NIDA DA02812 and T32 DA07255, and HHMI 5600677.

423

PATTERNS OF NONMEDICAL USE OF PRESCRIPTION OPIOIDS DURING THE TRANSITION TO ADULTHOOD: A MULTI-COHORT NATIONAL LONGITUDINAL STUDY.

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Aims: This study examines the prevalence and patterns of nonmedical use of prescription opioids (NMUPO) in a national sample of U.S. high school seniors as they make the transition from adolescence to adulthood.
Methods: Nationally representative probability samples of high school seniors (wave 1: modal age 18) were followed longitudinally across three follow-up waves (waves 2, 3 and 4: modal ages 19/20, 21/22, and 23/24, respectively). Data were collected via self-administered questionnaires to U.S. high school seniors and young adults as part of the Monitoring the Future study. The longitudinal sample consisted of 32,959 individuals in 30 cohorts (senior years 1976-2005) who participated in all four waves.
Results: Approximately 17% of the sample reported past-year NMUPO in at least one of the four waves of measurement. The mean level of past-year NMUPO held relatively steady over the 4 waves. The majority of high school seniors who reported past-year NMUPO at wave 1 did not engage in this behavior at waves 2, 3 or 4. We identified 16 different patterns associated with past-year NMUPO over time. Among those who reported any past-year NMUPO in any wave (n=5,690), approximately 4% reported past-year NMUPO at all four waves.
Conclusions: The present study provides strong evidence for heterogeneity associated with the patterns of NMUPO based on longitudinal data in a nationally representative sample. These findings have important implications for prevention and intervention efforts aimed towards reducing NMUPO among adolescents and young adults. Additional analyses will examine sociodemographic and individual predictors of these patterns of NMUPO.
Financial Support: Supported by NIDA research grants R01 DA011411, R01 DA016575, R01 DA024678 and R01 DA031160.

424

EFFECT OF HCV INFECTION ON BUPRENORPHINE PHARMACOKINETICS IN OPIOID DEPENDENCE.

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Aims: This study examined the effect of hepatitis C virus (HCV) infection on buprenorphine pharmacokinetics in opioid-dependent, buprenorphine/naloxone-maintained adults.
Methods: A retrospective analysis of buprenorphine pharmacokinetics using baseline sessions (buprenorphine alone) was conducted with data from studies conducted to determine the presence or absence of drug interactions between buprenorphine and antiretroviral drugs or antimicrobial medications for the treatment of tuberculosis. Forty-nine opioid-dependent individuals on a maintenance dose of (16/4 mg) of buprenorphine/naloxone were included in the analysis. Pharmacokinetic data between HCV positive and HCV negative subjects were compared using the independent samples t-test and Mann-Whitney test, for non-normally distributed data.
Results: Twenty subjects were diagnosed with chronic HCV infection. HCV positive subjects had higher buprenorphine exposure as demonstrated by elevated AUC and Cmax buprenorphine concentrations and corresponding elevations in the AUC of buprenorphine glucuronide and norbuprenorphine-3-glucuronide relative to buprenorphine/naloxone maintained individuals without evidence of HCV infection. No increases in adverse events or opioid toxicity was observed in the HCV-infected subjects maintained on buprenorphine/naloxone.
Conclusions: HCV infection was associated with higher buprenorphine plasma concentrations and buprenorphine metabolite concentrations. The results from this study suggest potential for opioid toxicity among HCV-infected patients treated with buprenorphine/naloxone as well as possible hepatotoxic effects related to buprenorphine/naloxone treatment and underscores the importance of monitoring for signs of opioid toxicity as well as ongoing assessment of liver status in these patients.
Financial Support: Supported by: National Institute on Drug Abuse R01 DA13004 (EMK), K24 DA023359 (EMK), and R01 DA10100 (DEM).

425

BUPRENORPHINE AND COSTS OF CARE FOR PATIENTS IN TWO INTEGRATED HEALTH PLANS.

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Aims: Examine the introduction of buprenorphine within two integrated health plans and assess impacts on the utilization and cost of medical care and addiction medicine services.
Methods: A retrospective cohort analysis extracted individuals with two or more diagnoses of opioid dependence per year from electronic health records for the years 2000 through 2008 (System A: N=4,425; System B: N=7,122). Analysis classified patients into four mutually exclusive groups based on the services received: 1) methadone, 2) buprenorphine, 3) addiction counseling, and 4) little or no counseling.
Results: The number of opioid-dependent persons increased over time in both health systems. By 2008, almost one in three opioid dependent patients in System A (34%) and System B (28%) were treated with buprenorphine. In System A, patients receiving buprenorphine had significantly higher costs than those receiving methadone ($Z= -9.22$, $p<.001$), and significantly lower than those with little or no AM counseling ($Z=2.81$, $p=.005$). Costs were equivalent between the buprenorphine and addiction counseling groups. The treatment group by period interaction ($\chi2 = 9.66$, $df=3$, $p=.022$) was significant; costs decreased over time in the buprenorphine group and increased over time in all other groups. At System B, costs were significantly lower for the buprenorphine group than for the group with little or no AM counseling ($Z= -5.14$, $p<.001$) and higher than for the group with AM counseling only ($Z=5.56$, $p=.001$). The treatment group by period interaction was not significant ($\chi2 =1.23$, $df=2$, $p=.540$). Methadone was not available in System B.
Conclusions: Buprenorphine treatment is emerging as a viable alternative to other addiction treatment approaches for persons with opioid dependence. Buprenorphine treatment can be provided at a similar cost to alternative strategies in private integrated health systems.
Financial Support: An award from NIDA supported the investigation (R01 DA016341)

426

UTILIZATION OF COMMUNICATION TECHNOLOGY BY SUBSTANCE ABUSE TREATMENT PATIENTS.

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Aims: Technology-based applications represent a promising method for providing efficacious, widely available interventions to substance abuse patients. However, access to and familiarity with technology could significantly impact the feasibility of these efforts. Therefore, we conducted a survey to characterize access and familiarity with cellular phone and computer-based technologies.
Methods: Participants (N=91) enrolled in outpatient substance abuse treatment completed a survey of access to cellular phones, text messaging, and/or computers. Mean age of the sample was 41 (19-76) yrs old, 76% male and 87% African American. 80% had a yearly household income of less than $30,000.
Results: 78% of participants reported having a cellular phone; however, 58% reported pay-as-you-go contracts, and 63% reported changing phone numbers at least once in the past year. The vast majority of participants with phones were able to send/receive text messages (97%); yet only 48% had ever received a call/text on their phone from a member of the treatment clinic staff. Despite high levels of accessibility to cell phones, only 48% reported at least weekly Internet use.
Conclusions: These data provide an initial examination into technology accessibility for substance abuse treatment patients and will help advance the use of appropriate technology to treatment. The sample utilized cell phones at rates comparable with national adult averages (83%), though frequent changing of phone numbers could be problematic for intervention implementation. In contrast, Internet usage was below national adult averages (78%). Thus, results suggest that web-delivered interventions designed for use outside of the clinic may be limited in their utility due to a low occurrence of Internet access, while cell phone/text applications may be more feasible and accessible, but perhaps only as a supplement to evidence-based treatments.
Financial Support: NIDA grants T32 DA07209 and U10 DA013034.

427

DIVERSIFICATION AND IMPLOSION: THE SURGING HEROIN EPIDEMIC INSIDE COLOMBIA.

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Aims: Colombia, South America, the primary world source nation for cocaine has diversified with concomitant cultivation of both coca plant and opium poppy (amapola). Opium poppy cultivation and heroin production is primarily under control of armed guerilla and paramilitary groups. While most Colombia-produced heroin is exported, significant quantities remain internal to Colombia, supporting the domestic heroin habit.
Methods: Survey data from ongoing heroin use prevalence studies will be presented in tabular and cartographic formats to illustrate the dynamics of Colombia's internal heroin use patterns.
Results: Prelimary results indicate that heroin use is well-established in Colombia's three largest cities (Bogota, Medellin, Cali), capital cities in the coffee-growing region (Armenia, Pereira, Manizales), along the Venezuelan frontier (Cucuta), in resort cities along the Atlantic Coast (Cartegena de Indias), and in areas where amapola is cultivated (e.g. Santander de Quilichao). Salient trends and patterns of heroin use include: 1) initial introduction of high-quality heroin at very low prices (sometimes with inducement of "free" samples); 2) ongoing and accelerating transition from inhalational to injection use of heroin; 3) declining quality of locally-available heroin prompting the transition to injection; 4) availability of needles and syringes at low cost without prescription at local pharmacies; 5) initiation of pre-adolescent and early adolescent youth to heroin use; and 6) rising rates of heroin-related HIV and HCV infection. Considerable geographic variation is apparent regarding: 1) price and quality of heroin, 2) heroin user demographics, 3) routes of administration, 4) transition to injection, and 5) rates of HIV/HCV infection.
Conclusions: While supply reduction strategies remain in force, Colombia is now challenged to invoke demand reduction strategies to respond to the emerging threat of an escalating internal heroin epidemic.
Financial Support: None

428

RISK FACTORS FOR RAPID TIME TO RELAPSE ON COCAINE IN COMMUNITY CORRECTIONS.

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Aims: The time period following release from incarceration carries high risk for drug relapse and associated social, legal, and medical consequences. This study sought to identify risk factors for relapse to cocaine use after release from jail while under community corrections supervision.
Methods: 23,854 inmates released from county jail and enrolled in Treatment Alternatives for Safer Communities (TASC) from 2002-2007 were administered a baseline assessment and provided random urine drug screens for cocaine during their time under community supervision. Logistic regression and Cox Proportional Hazard model analysis was used to examine the factors associated with time to relapse.
Results: While under TASC supervision, 6,676 (28.0%) participants tested positive for cocaine. Both African-Americans and whites with cocaine as the preferred drug of choice relapsed quickest to use of cocaine after release compared to those with other drugs of choice (HR: 1.7; 1.5-1.9 ; HR: 1.5; 1.3-1.6). Predictors of more rapid time to relapse on cocaine included older age, being unemployed, and if Black, having drugs of choice of alcohol, cocaine, marijuana or opioids, and if white participants only with drugs of choice of cocaine or opioids. Protective factors included living in a shelter, a history of being hospitalized for a physical problem, and being arrested for a substance offense
Conclusions: Distinct racial and drug of choice patterns emerged for time to relapse on cocaine after jail while in community corrections. These differences suggest the need for tailored interventions around these specific risk factors.
Financial Support: UAB Department of Psychiatry internal funding

429

JUVENILE EXPOSURE TO METHAMPHETAMINE ATTENUATES BEHAVIORAL AND NEUROCHEMICAL RESPONSES TO METHAMPHETAMINE IN ADULT RATS.

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Aims: Research has shown that children living in methamphetamine (MA) labs are passively exposed to MA. The long-term effects of such early exposure on dopaminergic systems are unknown, but may be important in affecting adult dopamine (DA)-mediated behaviors. Further, clinical studies have indicated significant sex differences exist in MA addiction, which may be due to altered neurochemical responses to MA. The current study tested the hypothesis that juvenile exposure to low doses of MA would lead to altered responsiveness to MA in adulthood, and that sex differences exist in the behavioral and neurochemical response to MA.
Methods: Male and female Sprague Dawley rats (PD20-34) were injected daily (s.c.) with saline or 2 mg/kg MA, or left undisturbed and tested at PD90 (n=57 females and n=60 males). Adult rats were injected with a 2 mg/kg MA challenge and: 1) locomotion was assessed in the open-field; or 2) extracellular DA levels were assessed using in vivo microdialysis.
Results: Adult rats exposed to MA as juveniles had reduced locomotor activity compared to control rats following a subsequent acute injection of MA ($F(3,99)=7.64$, $p<0.01$). Likewise, MA-induced increases in dialysate DA in the dorsal striatum were attenuated in rats exposed to MA as juveniles ($F(8,232)=10.21$, $p<0.01$), although no changes in basal in vivo DA or ex vivo DA content were found. Overall, females displayed a greater locomotor response to MA ($F(3,99)=3.54$, $p<0.05$) and elevated DA dialysate levels 60-120 min after the injection of MA ($F(8,232)=3.18$, $p<0.05$) compared to males. Further studies will investigate if differential trafficking of the vesicular monoamine transporter-2 (VMAT2) contribute to these sex differences.
Conclusions: These findings suggest that exposure of juvenile rats to MA leads to persistent changes in the behavioral and neurochemical responses to stimulants as adults. Further, females had a greater response to MA both behaviorally and neurochemically. These changes may contribute to altered drug abuse liabilities as adults.
Financial Support: None

430

CLINICAL CORRELATES OF THE INSULA IN MARIJUANA-USING ADOLESCENTS.

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Aims: The insula is involved in the pathophysiology of addiction. Our recent study noted reductions in cortical thickness in the bilateral insula in adolescent marijuana (MJ) users and MJ use also has been associated with motor impairment. The aim of this study was to examine whether motor, executive function, and impulsivity measures were correlated with the anterior and posterior insular thickness in adolescent heavy MJ users.
Methods: Thirty-six adolescent heavy MJ users (aged 18.2±1.5) and 36 HCs (17.9±2.2) had MRI scans on a 3T scanner. Morphometric analysis was performed with Freesurfer. Cortical thickness (CT) for right and left insula subregions were extracted and averages for the right and left anterior and posterior insula were computed. Correlations were performed between insula CT and measures of impulsivity utilizing the Barratt Impulsiveness Scale and the Trail Making test (a measure of motor and executive function) for MJ users and for HC.
Results: MJ users showed a significant correlation between left and right posterior insula CT and BIS Motor Impulsivity (left $r=0.52$, $p<0.01$; right $r=0.36$, $p=0.04$). For HC, there was a significant correlation between left posterior insula CT and BIS Motor Impulsivity ($r=0.37$, $p=0.04$) but not right posterior insula CT and BIS Motor Impulsivity. MJ users had a negative correlation between left posterior insula CT and Trail Making B ($r= -0.44$, $p<0.01$). Correlations between both right and left posterior insula CT and Trail Making B were significant for HCs (right posterior insula $r=0.44$, $p<0.01$; left posterior insula $r=0.34$, $p=0.04$).
Conclusions: The association of motor impulsivity with posterior insula thickness bilaterally in MJs and motor and executive function with insula CT bilaterally in HCs is consistent with previous studies of motor abnormalities in MJ users. These results suggest possible developmental delays or neurotoxic effects associated with MJ use during adolescence.
Financial Support: NIH: 1R01 DA020269-01 & NIMH: 1 K23 MH087831-01A1

431

GENDER DIFFERENCES IN CLINICAL CHARACTERISTICS OF PRESCRIPTION-OPIOID-DEPENDENT PATIENTS.

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Aims: Despite evidence for higher rates of heroin abuse among men, rates of prescription opioid abuse appear to be similar (or higher) among women, underscoring the importance of examining gender differences in this population. This study examined baseline data from the multi-site Prescription Opioid Addiction Treatment Study in the NIDA Clinical Trials Network to identify gender differences in characteristics of patients presenting for treatment. Consistent with literature on gender differences in substance dependent patients, we hypothesized that women would (1) exhibit greater medical and social functional impairment, (2) endorse greater psychiatric severity, and (3) exhibit more coping motives for use, relative to men.
Methods: Patients (N = 653, 40% female) completed a battery of measures, and gender differences were tested using t-tests and chi-square tests. In addition, exploratory analyses (correcting for multiple comparisons) were conducted with other variables of interest.
Results: Hypotheses were supported, with the exception of medical functioning, which was similar in men and women. Although men and women endorsed similar levels of pain severity, women were more likely to use opioids to cope with pain and to have received opioids first via a legitimate prescription. Men exhibited greater opioid craving and alcohol use than women and were more likely to report a route of administration other than oral.
Conclusions: These differences between men and women mirror the literature with other substances of abuse, and indicate that women dependent on prescription opioids are more likely to have initiated opioid analgesic use via a legitimate prescription for pain, and to use them via the intended route. Understanding gender differences in prescription opioid dependence is important to better characterizing this significant public health problem.
Financial Support: Support was provided by NIDA grants K24DA022288 and U10DA015831(Dr. Weiss)and K23DA022297 and U10DA020024 (Dr. Potter).

432

PREDICTORS OF EARLY ENGAGEMENT IN SUBSTANCE ABUSE TREATMENT: PRELIMINARY ANALYSES.

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Aims: Client attrition remains a critical barrier to successful substance abuse treatment outcomes. This study examines predictors of early treatment engagement, defined as attending the first several scheduled sessions within a month of treatment admission, among 412 clients participating in an ongoing study of adaptive treatment in primarily two settings: the Philadelphia Veterans Affairs Medical Center's Addiction Recovery Unit and the Presbyterian Hospital's Intensive Outpatient Program.
Methods: Clients were identified by treatment staff as new to treatment and were approached by research staff for recruitment. Participating clients completed a structured interview with a research assistant at baseline which included a number of instruments assessing demographic characteristics, recent alcohol and drug use, self-help participation, abstinence confidence, commitment to abstinence, and treatment motivation. These factors were examined as potential predictors of early treatment engagement in bivariate and multivariate logistic regression models.
Results: Only 64% of the sample met criteria for early engagement in treatment. Among the various demographic, behavioral, and attitudinal predictors significant at the bivariate level, only educational attainment (some college, $OR=0.52$, $p<0.01$), positive drug screen ($OR=0.51$, $p<0.01$), and abstinence confidence ($OR=1.01$, $p<0.01$) significantly predicted engagement in the final multivariate model.
Conclusions: Early identification and intervention with clients more likely to become disengaged could enhance the success of substance abuse treatment. Our preliminary findings suggest that individuals who have some college education, have recently used drugs, and are less confident in their abilities to resist alcohol or drug taking urges are less likely to initially engage in treatment and may benefit from targeted strategies or interventions to foster engagement.
Financial Support: NIAAA 1-P01-AA016821-01A1 and NIDA 2-P60-DA005186-21

433

LINKING DRUG USERS TO HEPATITIS C CARE: UTILIZING INFOGRAPHICS TO DEPICT HETEROGENEOUS OUTCOMES.

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Aims: Hepatitis C virus (HCV) infection remains prevalent among drug users (DUs), yet many are not engaged in HCV care. Strategies to link DUs to HCV care are critical; however HCV evaluation involves several steps with potential barriers. This RCT utilized a motivational-enhanced case management (ME-CM) model to address personal and structural barriers to HCV care.
Methods: DUs were recruited from two methadone programs in New York City and San Francisco and tested for HAV, HBV and HCV. HCV+ DUs were either referred to HCV care (control) or a case manager, who made their appointment and provided 6 months of ME-CM support to facilitate linkages to HCV care (intervention). This study examines data from NYC only.
Results: HCV prevalence in NYC was 45%. Sixty one (53%) HCV+ participants attended an HCV evaluation appointment, with a significant difference by arm [42 in intervention (69%); 19 in control (31%); p= 0.029]. Twenty-seven made it to their first scheduled appointment, while the remainder needed an average of 2.52 appointments. Half of participants (52%) had a viral load test, with 63% having a "detectable" viral load; 35 (30%) participants had a genotype test; 36 (55%) had a sonogram; a CT or MRI was ordered for 8 participants; and 2 biopsies were ordered. Barriers to accessing HCV care included: patient-level barriers such as substance use, mental illness, and health issues; and issues related to insurance coverage. Given the lack of homogeneity, a graphic data display (Tufte, 2001) was created to gain a better understanding of individual barriers to seeking HCV care.
Conclusions: Evaluation for HCV treatment is important in determining clinical eligibility for treatment; however, it is a multi-stepped and variable process, resulting in heterogeneous outcomes which can be richly depicted with multivariable infographics.
Financial Support: National Institutes on Drug Abuse, R01DA020781, R01DA020841, P30DA 011041, P50DA009253, U10DA015815.

434

STRESS-INDUCED INCREASES IN COCAINE-SEEKING AND DEPRESSION-LIKE BEHAVIOR ARE REVERSED BY DISRUPTION OF MEMORIES DURING RECONSOLIDATION.

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Aims: Exposure to traumatic stress may result in maladaptive behavioral responses. Post-traumatic stress disorders (PTSD) of this type are notably resistant to treatment after their establishment. We hypothesized that the disruption of memories during a reconsolidation might reverse established stress-induced increases in depression-like and cocaine-seeking behaviors.
Methods: Male C57BL/6J mice were subjected to repeated social defeat stress (SDS). Cohorts of mice were place conditioned with cocaine (n=48) or untested (n=48), and tested 24 h later for cocaine-conditioned place preference (CPP) or time spent immobile in a subsequent forced swim test (FST). Stress-exposed mice administered vehicle or the protein synthesis inhibitor cycloheximide (CHX) were exposed again to SDS, and tested in CPP or FST assays the next day. Results were analyzed by ANOVA with Tukey's HSD post hoc testing for significance.
Results: Compared to unstressed mice, C57BL/6J mice subjected to repeated social defeat stress (SDS) demonstrated significant increases in time spent in socially-defeated postures across trials, and increases in subsequent time spent immobile in the FST or cocaine-paired chamber. Vehicle-treatment followed by additional SDS-exposure did not alter these effects, but CHX-treatment reversed each of the potentiated responses in a time- and dose-dependent manner.
Conclusions: Overall, these results suggest that the initial exposure to a stressor potentiates the behavioral response to a future stressor (social defeat) as well as increasing depression-like and cocaine-seeking behavior. Moreover, these data support the notion that a pharmacological disruption of stressful memories made labile by re-exposure may have therapeutic value in the treatment of established PTSD-related behaviors.
Financial Support: NIDA grant DA016415, NIMH grant MH085607 and funds from the State of Florida.

435

LONGITUDINAL OPIOID USE IN PATIENTS TREATED WITH BUPRENORPHINE: A 'MISSING NOT AT RANDOM' (MNAR) AND 'MISSING AT RANDOM' (MAR) GROWTH MODEL COMPARISON.

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Aims: This investigation compares 3 different modeling strategies for the handling of missing values (i.e., missing at random (MAR) model versus 2 different missing not at random (MNAR) models), and we hypothesized that the treatment effect size is dependent on the missing data strategy used.
Methods: Data for this investigation came from National Drug Abuse Treatment Clinical Trials Network—0003, a clinical trial (N=516, Ling et al., 2009) of 2 different buprenorphine tapering schedules (7- versus 28-day). This investigation used urine analysis (UA) data collected the baseline visit and 4 subsequent weekly during the treatment period.
Results: The MAR (i.e., direct maximum likelihood) model showed an effect of the 28-day taper (β= -0.45, p<.05) being predictive of the opioid-positive urine (UA+) slope. The Diggle & Kenward (1994) model demonstrated an effect of the 28-day taper group (β= -0.64, p<.05) on the slope as well. While visit-specific UA+ did not predict concurrent or future dropout, the 28-day taper group was predictive of dropout after week 1 (OR= 0.43, p<.05), 2 (OR= 0.40, p<.05), and 3 (OR= 82.01, p<.05). The Wu & Carroll (1988) model demonstrated that the 28-day taper showed a significant effect on the UA+ slope (β= -0.41, p<.05), and the 28-day taper predicted dropout after week 3 (OR= 72.31, p<.05).
Conclusions: The trial arm effect size changes across the MAR and MNAR growth models, indicating that missing data assumptions are critical to understand and explain in clinical trials. Future research should explore similar sensitivity analyses in order to understand the nature of the missing information.
Financial Support: Department of Justice, Life Science Discovery Fund (Roll, PI). Pilot Study Support Program as part of the Center for Advancing Longitudinal Drug Abuse Research (CALDAR, award number P30DA016383) from the National Institute on Drug Abuse (NIDA), Washington State University Spokane Seed Grant Program (McPherson, PI).

436

EFFECT OF OXYTOCIN ON STRESS-INDUCED REACTIVITY IN MARIJUANA-DEPENDENT INDIVIDUALS.

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Aims: Stress is a significant factor in maintenance of chronic marijuana use. Oxytocin is a hypothalamic neuropeptide that has been shown to mediate behavioral responding to stress as well as play a role in neuroadaptations that occur as a consequence of long-term drug use. Given these effects, oxytocin may have a therapeutic role in ameliorating the negative affect commonly observed prior to relapse in marijuana-dependent individuals. The current study evaluated the impact of oxytocin pre-treatment on stress and craving responses following a psychosocial stress task in marijuana-dependent individuals.
Methods: In a laboratory setting, baseline measurements of craving (assessed using the Marijuana Craving Questionnaire; MCQ), salivary cortisol, stress, and anxiety were collected in 16 participants (age 18-65) meeting DSM-IV criteria for marijuana dependence. Participants were then administered either oxytocin 40IU (n=8) or placebo (n=8) nasal spray 40-minutes prior to completion of the Trier Social Stress Task (TSST). Measurements were repeated pre-TSST, immediately post-TSST, and 5-, 35-, and 60-minutes post-TSST. Linear mixed model analysis was used for planned comparisons; model-based estimates were used to construct group level tests.
Results: A significant attenuation in both MCQ total score and cortisol response from baseline to immediate-post TSST was observed with oxytocin treatment as compared to placebo (p=0.013 and p=0.019, respectively). A trend for reduced anxiety response was also observed in the oxytocin versus placebo groups (p=0.067). There were no significant between group differences in subjective stress rating.
Conclusions: Although preliminary, these results suggest that oxytocin may help ameliorate stress-induced reactivity and craving in marijuana-dependent individuals. Further research is needed to replicate these findings and to explore potential therapeutic implications.
Financial Support: Supported by the South Carolina Clinical & Translational Research (SCTR) Institute, NIH/NCRR Grant number UL1 RR029882.

437

DOES DELAY DISCOUNTING MEDIATE THE RELATIONSHIP BETWEEN COCAINE DEPENDENCE AND SEXUAL RISK BEHAVIOR IN HIV-INFECTED PERSONS?

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Aims: Many HIV-infected persons engage in sexual risk behaviors associated with forward transmission of the virus. Prior research has documented that cocaine users are more likely than non drug users to engage in sexual risk behavior and to be more impulsive, preferring smaller immediate rewards over larger delayed rewards. Such impulsivity may help to explain the relationship between cocaine use and sexual risk behavior in HIV-infected persons.
Methods: The sample comprised of 107 HIV-infected adults with current cocaine dependence ("active", n= 51), past cocaine dependence ("recovered", n= 31), and no lifetime substance dependence ("non", n= 25). Assessments included the Monetary Choice Questionnaire, HIV Risk Behavior Survey, and Structured Clinical Interview for DSM-IV.
Results: In the past 3 months, 36% engaged in unprotected intercourse (11% with HIV-negative partners), 36% had multiple partners, and 13% participated in sex trade. Active cocaine users reported greater sexual risk behavior (4.24 vs. 2.45; t= 2.09, p= .039) and had higher discount functions (0.084 vs. 0.030; t= 4.32, p< .001) compared to recovered/non cocaine users. Impulsivity was associated with sexual risk behavior in women (r= .47, p= .006) but not men (r= .10, p= .40). In a multivariate regression, impulsivity remained a predictor of sexual risk behavior in women after accounting for active cocaine use (β= .45, p= .013). Among men, after controlling for sexual orientation, only active cocaine use predicted sexual risk behavior (β= .45, p= .013).
Conclusions: Many HIV-infected cocaine users engage in behaviors associated with HIV transmission to others. Impulsivity may mediate the relationship between cocaine dependence and sexual risk behavior in women but not men. Further research is necessary to clarify why/how gender moderates the relationship between cocaine dependence, delay discounting, and sexual risk behavior among HIV-infected persons. Sexual behavior is multi-determined, and other factors (e.g., social context) may be more influential than impulsivity in certain sub-groups.
Financial Support: NIH K23-DA030086; amfAR 106884-42-RFBR

438

AGE-SPECIFIC RISK OF STARTING TO ENGAGE IN EXTRA-MEDICAL USE OF PRESCRIPTION STIMULANTS: UNITED STATES, 2004-2008.

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Aims: Aims: In a discovery process intended to clarify the age bands of peak risk for onset of extra-medical drug use, we already have reported on tobacco and opioids. We now turn attention to the amphetamines and other internationally regulated stimulant drugs (other than cocaine). Here, using the same methods used to study other compounds, we look into the early 21st century experiences of recent birth cohorts, as each cohort has traversed the adolescent years toward adulthood.
Methods: Methods: In recent nationally representative sample surveys, a total of 138,729 12-21 year olds completed computerized self-assessments for the US National Surveys on Drug Use and Health (NSDUH, 2004-8). A total of 676 were found to be newly incident extra-medical users of prescription stimulants (EMUPS), with calendar year of onset being the same as the year of assessment, and with no prior EMUPS history before that year. Based on these data, we estimated birth cohort-specific incidence rates for each year, tracing the risk experience of each US birth cohort born between 1982 and 1992, as each cohort matured from 12 toward 21 years old, using appropriate sample weighting, variance estimation, and meta-analysis procedures.
Results: Results: Estimates of risk for starting EMUPS show peaks between ages 15-17, with a secondary peak at age 19. By age 20-21 years, the estimated risk of newly incident EMUPS declines to levels seen in early adolescence.
Conclusions: Conclusions: With respect to timing of interventions intended to prevent or disrupt newly incident use of stimulant medicines occurring outside the boundaries of a doctor's prescription, adaptation of prevention policies and programs that have effectively curbed tobacco and alcohol use in childhood and early adolescence may be indicated. Limitations of our epidemiological research approach will be discussed.
Financial Support: Financial Support: National Institute on Drug Abuse awards K05DA015799 (JCA); R01DA016558. EAM is a postdoctoral fellow and JPT is a predoctoral fellow in MSU's NIDA Drug Dependence Epidemiology Training Program (T32DA021129).

439

RAPID TEST FOR HCV IS A NEW AND VERY INTERESTING STRATEGY. A STUDY FOR 194 DRUG USERS IN A FRENCH CENTER: CSAPA 52.

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Aims: In france officialy 50% to 70% of the drug users(DU) are infected by VHC. Near than 20% have a probleme for blood acces. And 33% of those infected patients don't realise a serology. What is the problem? How can we do better? Are the prevention programme adapted for testing?
Methods: During may 194 patients with substitution traitement received a prescription to have a bood ponction to do serology against HIV HBV and HCV(elisa 3 generation). During june all of this patients received a proposition to do a rapid test with blood finger(ora-quick). After this study we compared sensibility specificity and compliance for this tow tests.
Results: in may 147/194 DU(75.8%)realised the blood tests 18(12.2%)were found positiv against HVC(elisa 3 generation) In june all of them 147 DU receveided a proposition for a rapid test.All of them accepted (100%). 17(11.56%) were positiv with this test.This test have a good sensibility and specificity. For 47 DU who don't made the test 44(97%) accepted a rapid test during the physician consultation. 9 DU were positiv(20.4%). But more intersting 21/44(48%)DU developped a major anxiety symptome during the 15 minutes of the waiting test and needed help and medical assistance. our resultes are the same like the princep study: Lee SR et al. J Virol Methods 2011; 172: 27-31
Conclusions: Blood test like OraQuick vhc are a revolution and they are secure. We can use them for easy testing in a larged population of drug user. The DU who refused to do the classic test are more infected 11,5% versus 20.4% and they need our help. In the future we can developpe prevention programme with this test for DU. In all the addiction center the new professionnal and DU need rapid testing for HCV,HBV,and HIV. but all the team need formation and training.
We can do that it is a epidemiologic priority
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440

THE REINFORCING EFFECTS OF NS11808, A NOVEL FUNCTIONALLY SELECTIVE GABAA RECEPTOR MODULATOR.

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Aims: In this study, we investigated the reinforcing effects of a novel compound, NS11808, that has functional selectivity for alpha3 and alpha5 subunit-containing GABAA receptors compared with alpha1 and alpha2 subunit-containing GABAA receptors.
Methods: A progressive-ratio schedule of i.v. midazolam self-administration was used for determining the reinforcing effects of NS11808, in comparison with conventional BZ-type drugs. Adult rhesus monkeys (N=4) were trained to press a lever that resulted in an i.v. midazolam injection via a chronic venous catheter. The response requirement (RR) started at 40 responses per injection (0.056 mg/kg/injection midazolam, 30-min time-out between injections). After four trials the RR doubled. Reinforcing effects of a compound were determined by comparing the average number of injections/session and the average break point (highest RR completed in a session) to results from saline tests. Each dose of test compounds (NS11808, the non-selective BZ alprazolam, and alpha1-selective drug zolpidem) was evaluated twice in counterbalanced order.
Results: At least one dose of all test compounds was self-administered above levels maintained by saline availability. The maximal level of self-administration, measured by injections/session and breakpoint, did not differ across the three test compounds (p>0.05).
Conclusions: These results demonstrated that NS11808 was self-administered to a degree similar to conventional BZ-like drugs. However, given that NS11808 is functionally selective, the relative contributions of alpha1, 2, 3 or 5 subunit-containing receptors is difficult to determine. Previously we have demonstrated that the functionally-selective alpha3-containing GABAA compound, TP003, was self-administered robustly. Therefore, our findings with NS11808 are consistent with the hypothesis that relatively high in-vitro efficacy (i.e., >50% relative to a BZ) at alpha3-containing GABAA receptors is sufficient for self-administration of compounds binding to the BZ site.
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441

GENDER RESPONSIVE AND TRAUMA INFORMED TREATMENT DECREASES PTSD AMONG WOMEN OFFENDERS.

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Aims: Objective: Childhood traumatic experiences among women offenders can impact their psychological well-being and patterns of substance use and offending. However, rigorous research in this area and in treatment for women offenders with a history of trauma are sparse. This study examined the trauma histories and prevalence of post-traumatic stress disorder (PTSD) among women offenders in gender-responsive and trauma-informed substance abuse treatment and assessed their change over time.
Methods: Methods: Women in gender-responsive treatment (GRT; N = 134) were compared to women in non-GRT (N = 143) in their change in PTSD and related symptomatology from baseline to follow-up. This study combined data from two previous studies of women offenders using the same measures. The pooled sample comprised women who were predominantly White (58%) or Hispanic (22%), had never been married (47%), were approximately 36 years old (SD = 8.9), and had 12 years (SD = 1.8) of education. Methamphetamine was their primary drug (71%). Fifty-five percent of the women reported histories of sexual abuse and 37% physical abuse. Thirty-one percent had a PTSD diagnosis.
Results: Results: Using Generalized Estimating Equations, the GRT group had significant reductions in PTSD (OR = .15) and related symptomatology (re-experiencing: OR = .26; avoidance: OR = .23; arousal OR = .32; and functioning: OR = .30) compared with the non-GRT group.
Conclusions: Conclusions: Given the aggregate impact of trauma in the lives of women offenders, the field can benefit from research on how trauma influences their lives and on services that mitigate the negative impact of such histories.
Financial Support: This study was funded by the National Institute on Drug Abuse (NIDA Grant No. R01 DA22149-01), the California Department of Corrections and Rehabilitation (Contract No. C06.441), and the California Endowment (Grant No. 20081206). The findings and conclusions of this paper are those of the authors and do not necessarily represent the official policies of the San Diego County Adult Drug Court Programs or the Los Angeles County Second Chance Women's Re-Entry Court Program.

442

A MACHINE LEARNING APPROACH FOR PATIENT CLASSIFICATION IN COCAINE ADDICTION VIA SPECT IMAGES.

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Aims: The abuse and dependence of stimulants is a major public health problem with significant health, legal, social and occupational associated costs. While biologically oriented studies, particularly those using imaging techniques, have yielded significant advances in the understanding of neural processing during affective and cognitive processes relevant to the development and persistence of addiction, this knowledge has done little to assist in the diagnosis or treatment of these disorders. In particular, identification of cocaine addicted patients requires readings of brain images by the psychiatrists. Intra- and inter-variability is a major drawback in this time consuming process. This study is to develop a computer-aided diagnosis framework to provide automatic consultation to psychiatrists for the identification of cocaine addicted patients.
Methods: We developed a statistical framework to identify cocaine-addicted patients with the support vector machine (SVM), a statistical machine learning algorithm. SPECT images of 69 healthy and 93 cocaine-addicted subjects in a voxel space of 95x79x69 were assessed. A superset of significant voxels was selected by Mann-Whitney test in the mask of the brain regions. This superset was then refined with SVM feature selection and 10-fold cross validation was employed using SVM classifiers.
Results: The resulting 96 densely connected voxels from eight distinct brain regions and demographics (age, gender, race) are used in the assessment of model and prediction accuracy of the framework. We found 100% accuracy model accuracy with d=2 polynomial kernel. A similar but slightly different parameters yielded an accuracy of 86% in a 10-fold cross-validation.
Conclusions: This study is one of the very first computer-aided diagnosis systems aiming classification of cocaine-addicted patients. The new regions will be investigated further to find more neurological foundations of the drug addiction.
Financial Support: This study is partly supported by NIH/NIDA.

443

MARIJUANA'S ACUTE EFFECTS ON ATTENTIONAL BIAS FOR AFFECTIVE CUES.

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Aims: Marijuana has reward enhancement properties including acute increases in positive subjective effects and decreased reactivity to negative affective stimuli (Phan et al. 2008; Somaini et al. 2011). This placebo-controlled study examined attentional interference by appetitive and aversive stimuli on Pleasantness Rating and Emotional Stroop tasks after smoking marijuana.
Methods: Marijuana users (N=89, 34% female) were tested in a 2 (drug: 3.0% THC vs. placebo) X 2 (cues: positive or negative vs. neutral) within-subjects study.
Results: On the Pleasantness Rating task, THC significantly increased response latency (i.e., attentional bias) to all stimuli (pleasant, aversive, and neutral) relative to placebo (p's < .001). 2 X 2 repeated measures ANOVAs showed significant drug X positive and drug X negative images interactions, $F(1, 88)=4.94$ and 4.34, p's< .05, with the relative difference in response times (RT) between affective and neutral pictures reduced after smoking marijuana compared to placebo. To clarify, a significant RT difference was found between positive and neutral pictures in the placebo ($p=.01$) but not in the marijuana condition. The differences between RT to negative and neutral cues were significant in both drug conditions (p's< .01) but smaller in the marijuana condition. On the Emotional Stroop Task, the main effect of negative vs. neutral words was significant $F(1, 88)= 4.92$, $p < .05$, and effect of positive vs. neutral words was at the trend level, $p=.09$, with increased RT to affective stimuli. Drug effect and interaction with drug were not significant.
Conclusions: Findings suggest that marijuana does not acutely change attentional processing of positive emotional stimuli beyond a general slowing of response. It is possible that marijuana users find pleasant experiences more positively reinforcing after marijuana without a specific change in attentional cognitive processing. However, there was some evidence of attentional bias to negative visual stimuli when on THC, possibly suggesting a closer link between marijuana intoxication and negative emotions.
Financial Support: R03DA027484 (Metrik, Knopik)

444

DO YOUNG ADULTS INTERPRET THE DSM DIAGNOSTIC CRITERIA FOR ALCOHOL USE DISORDERS AS INTENDED?

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Aims: To use novel investigative techniques informed by survey methodology to explore potential shortcomings in the alcohol use disorder criteria as applied to young adult drinkers aged 18 to 24.
Methods: All participants were administered a structured diagnostic interview as well as a structured cognitive interview. The cognitive interviews were comprised of a set of pre-determined and standardized probe questions designed to shed light on young adults' understanding of interview questions that tap the AUD diagnostic criteria. Interviews were transcribed and coded according to a quantitative coding scheme designed to explore sub-group differences between those who do and those who do not endorse a given diagnostic criterion.
Results: Results showed that there were substantial inconsistencies in young adults' interpretations of the diagnostic criteria reflecting impaired control over alcohol.
Conclusions: Survey questions designed to tap compulsive patterns of alcohol use require close attention to ensure they reflect the intentions of the DSM diagnostic criteria for alcohol use disorders.
Financial Support: Australian National Health and Medical Research Council Project ID# 630414

445

THE EFFECT OF HOUSING CONDITION ON RESPONSE TO NOVELTY AND AMPHETAMINE SELF-ADMINISTRATION IN LEWIS AND FISCHER RATS: GENE-ENVIRONMENT INTERACTION.

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Aims: Previous research has demonstrated both genetic and environmental influences on substance abuse vulnerability. The current work sought to investigate the interaction of genes and environment on novelty seeking and amphetamine (AMPH) self-administration using inbred Lewis (LEW) and Fischer (F344) rat strains raised in either an enriched condition (EC) or isolated condition (IC). These inbred strains were used because LEW are more responsive to novelty and self-administer more AMPH than F344. In addition, this environmental manipulation was used because outbred IC rats are more responsive to novelty and self-administer more AMPH than outbred EC rats.
Methods: Male LEW (N=12-16 per environment) and F344 (N=12-16 per environment) were housed in either an EC, social condition (SC) or IC environment beginning on postnatal day (PND) 21. Assessment of response to inescapable and free-choice novelty began on PND 56. This was followed by the assessment of acquisition, maintenance, dose effect, extinction, and reinstatement of AMPH self-administration.
Results: Response to inescapable novelty in EC LEW and F344 was decreased compared to IC LEW and F344. When compared to IC rats, EC rats showed reduced acquisition of AMPH self-administration in both LEW and F344 strains. In contrast, when compared to IC rats, SC rats showed reduced acquisition of AMPH self-administration in F344 only. Environment-dependent differences in the dose effect function for AMPH self-administration were also obtained in both strains, with IC rats showing greater sensitivity to dose adjustments than EC rats.
Conclusions: These results demonstrate that genetic determinants of amphetamine self-administration are moderated by social influences during development, thus representing a gene x environment interaction.
Financial Support: Research supported by USPHS grants DA12964 and DA05312.

446

ECSTASY USE AMONG ADULTS RECEIVING AIDS PREVENTION SERVICES IN LOS ANGELES COUNTY.

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Aims: Previous research has focused on ecstasy use in other countries, on the national level, or on the east coast of the US. The purpose of this study was to evaluate ecstasy users in Los Angeles County who were receiving HIV prevention services
Methods: This study of ecstasy use recruited 2,122 participants throughout Los Angeles County as part of a Countywide Risk Assessment Survey in 2004.
Results: Of those recruited, 6.6% (141/2122) reported having ever used ecstasy. Over half, 68.1% (96/141), of the ecstasy users were male and 42.6% (60/141) identified as Hispanic or Latino. The participants ranged from 12 to 69 years old (M = 27.1, SD = 7.5). Ecstasy use was associated with polysubstance use, and ecstasy users were significantly younger, had more sexual partners, and held more negative views on condom use, than non-ecstasy users. Heterosexuals were found to be significantly less likely to use ecstasy. Logistic regression indicated that younger age, past six-month use of alcohol, marijuana, crystal methamphetamine, inhalants, and opiates, as well as accessing mental health or psychosocial support services were associated with ecstasy use.
Conclusions: The associations between ecstasy use and use of multiple substances, as well as risky sexual behaviors, put this population at risk for negative health consequences, and there is an opportunity to place interventions in mental health or psychosocial support services.
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447

INTRANASAL OXYCODONE SELF-ADMINISTRATION IN SPORADIC OPIOID ABUSERS.

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Aims: Oxycodone, a prescription opioid analgesic with known abuse liability, is often misused by the intranasal (IN) route. The objective was to develop a model of IN oxycodone self-administration useful for assessing the relative reinforcing effects of opioids and potential pharmacotherapies for opioid use disorders.
Methods: Healthy, adult, sporadic opioid abusers (n=8) with IN opioid use completed this inpatient 2.5-week, randomized, double blind, placebo-controlled, crossover study. Each IN oxycodone dose (0, 14 & 28 mg) was tested in a separate 3-day block of sessions. The first day of each block was a sample session in which the test dose was given. Self-administration sessions were conducted on the next 2 days using a progressive ratio schedule in which subjects could work (i.e., button presses) during 7 trials for either 1) a portion of the test dose ($1/7^{th}$/trial) or 2) a portion of the test dose or money ($3/trial). Physiological and subjective measures were collected before and after drug administration in all sessions.
Results: IN oxycodone dose-dependently increased VAS ratings (e.g., 'high,' 'like') during sample sessions and decreased pupil diameter ($p<0.05$). The maximum reported street values were $14±5 and $18±5 for the 14 and 28 mg doses, respectively. Subjects never worked to self-administer placebo regardless of whether money was available. In both self-administration sessions, oxycodone self-administration was dose-dependent. Subjects worked less for drug when money was an alternative reinforcer after the 28 mg dose, but only modestly so. Subjective reports of positive drug effects during sample sessions were positively correlated with self-administration behavior (e.g., 'like', $r=0.65$).
Conclusions: These data suggest that this is a useful and sensitive model of IN opioid self-administration that could be employed to compare relative reinforcing efficacy of opioids and assess potential pharmacotherapies for opioid use disorders.
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448

AMERICAN INDIAN/ALASKA NATIVE CULTURE AND ACCEPTABILITY OF A WEB-BASED INTERVENTION FOR SUBSTANCE USE DISORDERS.

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Aims: With high rates of substance abuse and barriers to treatment, American Indian/Alaska Native (AI/AN) clients could benefit from culturally sensitive web-based treatments. This study examined culture and ethnicity in AI/AN clients enrolled in outpatient substance abuse treatment and how culture is related to the acceptability of the Therapeutic Education System (TES), a web-based version of the Community Reinforcement Approach.
Methods: AI/AN clients from two programs (Northern Plains and Pacific Northwest) completed assessments at baseline and 1 week after the 8-week intervention phase. Participants completed the Scale of Ethnic Experience and questions from the ASI-Native American Version. Participants were asked to complete 32 skills-based TES modules on topics such as problem-solving, coping and HIV. Participants rated each module on acceptability and relevance.
Results: Sixty-eight clients were approached to participate in twice weekly TES and assessments; 40 (58.8%) agreed. The sample was about half female (53%), mean age 36. Over 80% participated in AI/AN cultural activities, including AI/AN religious ceremonies (73%), dance activities (76%) and church meetings (32%). About half (49%) were familiar with their native language. 73% ever lived on a reservation. Analyses will include exploratory chi-square (categorical) and t-tests (continuous) to determine if cultural involvement variables are related to TES acceptability.
Conclusions: The majority of AI/AN clients in outpatient treatment who were approached to participate in a web-based substance abuse intervention agreed. Clients are actively involved in AI/AN culture. This study explores how culture and ethnicity relate to the acceptability of a web-based intervention.
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449

ADOLESCENT SUBSTANCE USERS EXHIBIT DIMINISHED INTEROCEPTIVE PROCESSING AND ELEVATED REWARD RESPONSE TO PLEASANT STIMULATION.

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Aims: Interoception, the processing of bodily information, may play an important role in the developmental trajectory of addiction. This study examined whether adolescents with substance use disorders (SUDs) show an altered response to pleasant mechano-receptive C-fiber (MR-CF) stimulation. We hypothesize SUD teens would show hypoactive insular activation to a positively valenced interoceptive stimulus.
Methods: Human adolescents ages 15-17 with SUDs (n = 10) and non-using controls (n = 9) performed a MR-CF task during functional magnetic resonance imaging. Stimulation consisted of slow stroke on the forearm (high MR-CF density) and the palm (low MR-CF density). Interoceptive sensations (e.g., pleasantness, intensity) were rated using visual analog scales (VAS). A linear mixed effects model was performed with group as the between subjects factor, subject as a random factor and condition (anticipation palm and forearm, stroke palm and forearm) as a repeated factor. Correlations were run between significant results and VAS ratings.
Results: Across conditions, SUD teens displayed less insula activation than controls. During stroke conditions, SUD teens exhibited more caudate activation but less inferior frontal gyrus (IFG) activation than controls. Whereas for controls IFG activation was associated with pleasantness, it was linked to unpleasantness for SUD teens.
Conclusions: The interoceptive system of SUD teens is hypo-responsive to pleasant stimulation, perhaps leading users to seek intense pleasure. Conversely, the reward system of users is hyper-responsive to pleasure, which may increase the urge to pursue gratifying sensations. Interoceptive and inhibitory hyposensitivity and reward hypersensitivity may reflect unstable internal homeostasis that contributes to excessive substance use.
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450

COCAINE DEPENDENCE TREATMENT AFFECTS COMORBID DEPRESSION: ABSTINENCE MAKES THE DIFFERENCE.

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Aims: Research suggests effective treatment for one Axis I Anxiety Disorder improves comorbid depression. We examined the impact of abstinence on depression and vice versa during treatment for cocaine dependence.
Methods: Participants (N=203) received Contingency Management with or without behavioral day treatment for 6 months. Depression was measured by the Beck Depression Inventory (BDI) at baseline, 2, 6 and 12 mos. Abstinence was defined as consecutive weeks abstinent (CWA) based on urine toxicology. Toxicologies were completed MWF in treatment/aftercare ending at 6 months, and randomly 1/wk. mos. 7-12. Last observation carried forward was used for missing BDIs. Missing toxicologies allowed excused missing without re-setting a CWA string. Unexcused missing were treated as non-abstinent. Auto-regressive cross-lagged Structural Equation Model evaluated reciprocal relationships between depression and abstinence over time after accounting for stability in each construct.
Results: The model had acceptable fit to the data [$\chi 2(10)=34.15$, $p<.001$, Comparative Fit Index (CFI) = .94, and the Root Mean Square Error of Approximation (RMSEA) = .11]. Longer abstinence predicted decreased depressive symptoms at each time point. Depressive symptoms did not predict changes in abstinence at any time point.
Conclusions: Effective substance abuse treatment reduces comorbid depressive symptoms, but reduced depression does not contribute to improved abstinence. Effects of abstinence on reducing depression persisted even after treatment ended. Results are consistent with recent findings on evidence-based treatments for anxiety reducing comorbid depression.
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451

TRACE AMINE ASSOCIATED RECEPTOR 1 (TAAR1) IS A TARGET FOR THE DEVELOPMENT OF THERAPEUTICS FOR ALCOHOL USE DISORDERS.

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Aims: Along with cognitive, behavioral and spiritual approaches, medications are used to assist in reducing alcohol consumption or craving during abstinence. Three medications are approved in the US for treating alcoholism. Each acts via different mechanisms to reduce alcohol consumption or attenuate alcohol craving during abstinence, but have variable effectiveness and acceptance levels within populations, and are used by a minority of people harboring a medical diagnosis of alcoholism. Accordingly, more and better treatment options for alcoholism and the prevention of alcohol use disorders (AUDs) are a national imperative. This study tests the hypothesis that Trace Amine Associated Receptor 1 (TAAR1), implicated in monoamine regulation, is involved in alcohol consumption and responsiveness.
Methods: We compared the effects of alcohol in wild-type and TAAR1 knockout (KO) mice, in tests of consumption and reinforcement-related effects (two bottle choice, conditioned place preference), alcohol-mediated motor impairment (loss of righting reflex, locomotor activity) and stress (tail suspension).
Results: We found that: 1) KO mice have a significant and more robust preference for alcohol across a range of concentrations; 2) KO mice are substantially more sensitive to the sedative-like effects of alcohol, even though their blood alcohol level and rates of alcohol clearance are highly similar to wild type mice; 3) KO mice show a greater decrease in the locomotor response to alcohol in the open field test and significantly greater immobility in response to alcohol during the tail suspension test, measures which do not differ in the absence of alcohol.
Conclusions: These findings raise fundamental questions on the role of TAAR1 in modulating the behavioral and reinforcement-related effects of alcohol and whether TAAR1 drugs will reduce alcohol consumption in humans. Accordingly, TAAR1 drugs may serve as a new generation of medications that target mechanisms which are distinct from other medications developed to treat AUDs and alcoholism.
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452

ACTIVE IMMUNOPHARMACOTHERAPY FOR METHAMPHETAMINE PROVIDES FUNCTIONAL PROTECTION IN RATS.

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Aims: At present, there are no approved pharmacotherapies for methamphetamine (METH) addiction and existing therapies have limited effect. Recent successes in early clinical trials using immunotherapeutic approaches for cocaine and nicotine addiction have motivated interest in creating similar approaches for METH. The goal of the current study was to investigate whether a candidate vaccine (MH6) has the potential to attenuate responses to METH, in vivo.
Methods: Experiment 1 investigated the effects of MH6 on METH-induced disruptions in thermoregulation and locomotor activity in Sprague Dawley rats (n=16). Groups of rats were pretreated with MH6 (n=8) or a control vaccine (KLH; n=8) during an 8-week dosing regimen. This consisted of a priming dose followed by 3 booster doses at 2, 5, and 9 weeks after the prime. During weeks 11-12 rats were challenged with 1.0 and 5.6 mg/kg METH (s.c.). In Experiment 2, groups of Sprague Dawley rats were inoculated with MH6 (n=18) or a control vaccine (KLH; n=18) according to the dosing schedule described above. After that, the effects of MH6 on METH self-administration were investigated.
Results: In Experiment 1, body temperature and locomotor activity were increased at the 5.6 mg/kg dose in the KLH group but not in the vaccinated (MH6) group. In Experiment 2, vaccinated (MH6) rats self-administered less METH than non-vaccinated (KLH) rats, although different patterns were observed depending on whether the rats were pellet trained prior to initiation of the self-administration procedure.
Conclusions: These data provide evidence that active immunopharmacotherapy can provide functional protection against the physiological and behavioral effects of METH.
Financial Support: NIH/NIDA DA024705

453

PERSONAL SOCIAL NETWORKS OF WOMEN IN RESIDENTIAL AND OUTPATIENT SUBSTANCE ABUSE TREATMENT: CHANGES OVER 12 MONTHS.

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Aims: Establishing positive social networks is a priority but also a challenge for women in substance use disorder (SUD) treatment. Little is known about social network changes in different treatment modalities and into post treatment recovery. We examine longitudinal patterns of women's social networks in both residential (RT) and outpatient treatment (OPT) to identify structural, compositional and social support changes over 12 months.
Methods: Women (N=204) were interviewed in 3 treatment programs at intake (T1) and at follow ups 1 (T2), 6 (T3) and 12 (T4) months later (80% retention). Network software program, Ego Net, elicited 25 network members (alters), social support and network connections. A mixed model repeated measures analysis was used to account for correlated responses within a subject controlling for covariates.
Results: Total sample was 62.7% African American; mean age 37 (SD=10.1). 72.5% dually diagnosed (DD); 49% dependent on alcohol, 64.2% on cocaine. RT women had higher trauma symptoms, higher treatment motivation & lower abstinent self efficacy than OPT women ($p<.05$). By T4, 66% of the women were out of treatment. At intake RT women had more alters they "used with" (7.5 vs. 5.6), more substance users (5.5 vs. 3.8) and fewer reciprocal relationships (15.6 vs. 17.1), and their networks were more centralized than OPT women (31.5 vs. 26.7). These differences disappeared by T3. Abstinence self-efficacy at all time points was related to fewer substance using alters, and more alters providing emotional and sobriety support. DD status was related to fewer reciprocal relationships and lower density.
Conclusions: RT women enter treatment with fewer social network resources than OPT women. Understanding social networks can help providers enhance the recovery process. DD women may need assistance to build and maintain reciprocal networks. Future research should examine social networks and post treatment outcomes.
Financial Support: NIDA R01 DA022994

454

METHADONE MAINTENANCE PATIENTS AND COGNITIVE PERFORMANCE.

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Aims: The aim of this study was to assess cognitive performance in methadone maintenance patients (MMP) as a function of maintenance dose level (range: 40-200 mg) and time relative to daily methadone dosing.
Methods: Across two sessions, MMP (N= 51; minimum methadone maintenance treatment duration: 6 months) completed a performance assessment battery at the expected time of peak methadone effects (2 hr post-dosing; peak session) and trough methadone effects (24 hr post-dosing; trough session). A control group of currently abstinent, former opioid abusers (N=15) also completed the performance assessment battery during two separate sessions (without dosing).
Results: GEE analysis revealed that at peak, MMP showed significantly decreased overall arousal (flicker fusion task) and divided attention accuracy, and slower reaction time (simple reaction time and working memory tasks), relative to trough ($p < .05$). Reaction time (divided attention and working memory tasks) slowed as methadone maintenance dose increased ($p < .05$). An interaction between time and maintenance dose was observed such that MMP on higher doses showed more impairment (slower reaction time on divided attention and psychomotor tracking tasks; decreased working memory accuracy) at peak (versus trough) than MMP on lower doses. An additional GEE analysis that included the control group confirmed the significant impairing effects of peak methadone in MMP on arousal, divided attention, working memory, and simple reaction time after controlling for practice effects, and also replicated previous findings of impaired performance for MMP relative to abstinent opioid abusers on a range of psychomotor and cognitive measures.
Conclusions: These results suggest that attention and working memory may be impaired following daily methadone dosing relative to before dosing in MMP, and that more impairment may occur in MMP on higher maintenance doses. These findings may have implications for daily performance in MMP particularly for individuals engaged in activities requiring precise timing following dosing.
Financial Support: Supported by DA17688, DA07209, and DA023186.

455

THE EFFECTS OF CATECHOL-O-METHYLTRANSFERASE INHIBITION ON IMPULSIVITY: A FUNCTIONAL MRI STUDY IN GENOTYPED SUBJECTS.

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Aims: Impulsivity is a risk factor for substance use disorders, rendering its understanding and remediation a high priority. Delay discounting tasks (DDT), in which subjects are offered the choice between a smaller-sooner and a larger-later reward, quantify impulsivity: more impulsive subjects tend to choose smaller-sooner rewards and this tendency is reflected in higher impulsive choice ratios (ICRs). We recently demonstrated that higher ICRs are associated with a particular polymorphism in the catechol-O-methyltransferase (COMT) gene, whose protein product degrades dopamine in prefrontal cortex (PFC; Boettiger et al, 2007). Specifically, the Val-Val (Val158Met) genotype, linked to greater COMT activity and therefore to lower levels of PFC dopamine, was associated with greater ICR. This finding indicates that a brain-penetrant COMT inhibitor, tolcapone, will reduce impulsive behavior.
Methods: To investigate this prediction we conducted a randomized, double blind, placebo controlled, counterbalanced study of the effect of tolcapone on delay discounting behavior in healthy subjects.
Results: Subjects with greater (more impulsive) scores on the Barratt Impulsivity Scale (BIS) showed greater declines in ICR on tolcapone ($r = -0.45$, $p = 0.03$). Subjects also showed a statistically significant decrease in ICR in the tolcapone condition: $\Delta ICR = -0.05$, $T(22) = -2.16$, $p = 0.04$. Additionally, negative correlations were seen between change in ICR on tolcapone and BOLD activity on tolcapone in the right striatum ($p < .05$) and right anterior insula ($p < .05$). The tolcapone condition was associated with greater resting state connectivity between medial PFC and the same striatal region ($p < .05$).
Conclusions: These findings are consistent with previous theories that PFC modulates impulsive responding promoted by striatal activity. We are now evaluating the influence of COMT genotype on the magnitude of drug-induced changes for ICR and BOLD activity.
Financial Support: Telemedicine and Advanced Technology Research Center (TATRC), ABMRF / The Foundation for Alcohol Research, State of California

456

SMOKING MOTIVATION IN ADULTS WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

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Aims: Smokers with attention-deficit/hyperactivity disorder (ADHD) differ from non-ADHD smokers in many respects, such as higher prevalence rates of smoking, earlier initiation, faster progression to regular smoking, and greater difficulty quitting. It is unclear, however, which motivational factors may account for this comorbidity. The aim of this study was to assess whether specific smoking motivation factors differentiate ADHD smokers from non-ADHD smokers as measured by the Wisconsin Inventory of Smoking Dependence Motives (WISDM-68; Piper et al., 2004). Given previous findings from our lab, we were also interested in the effects of sex on smoking motives in those with and without ADHD.
Methods: Smokers with (n = 93; 38 males, 55 females) and without ADHD (n = 63; 28 males, 35 females) participating in a range of laboratory and clinical studies completed the WISDM-68 and the Fagerstrom Test of Nicotine Dependence.
Results: A series of one-way ANOVA's controlling for nicotine dependence yielded a number of significant group x sex interactions on the following WISDM-68 subscales: affiliative attachment, automaticity, behavioral choice, cognitive enhancement, taste and sensory properties, and weight control subscales ($F's = 5.58\text{-}8.47$, $p's \leq .01$) and the interactions were characterized by higher scores in women with ADHD. Group main effects emerged as well in which the ADHD group scored significantly higher on the following subscales than the non-ADHD group: craving, cue exposure, loss of control, negative reinforcement, and positive reinforcement ($F's = 4.02\text{-}12.36$, $p's < .05$).
Conclusions: These findings suggest certain motivational factors that maintain smoking in an at-risk psychiatric population, particularly among women. Clarifying the role of these motivational factors has implications for smoking prevention and treatment.
Financial Support: None reported

457

IOP VS. OP WITH BUPRENORPHINE: 6-MONTH TREATMENT OUTCOMES.

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Aims: To compare 6-month treatment outcomes for African American buprenorphine patients receiving intensive outpatient treatment (IOP; 9 or more hours of psychosocial services per week) versus standard outpatient treatment (OP; 2-8 hours of psychosocial services per week).
Methods: 300 African Americans newly admitted to buprenorphine treatment at one of two outpatient treatment centers in Baltimore, MD (USA) were randomly assigned to receive IOP or OP level treatment. Participants were assessed at baseline, 3-, and 6-month using a battery of standardized instruments and urine testing for opiates and cocaine. Outcomes included meeting diagnostic criteria for dependence on opioids and cocaine, drug use, and retention in treatment. Analyses were conducted using logistic regression and Generalized Estimating Equations.
Results: On average compared to baseline, participants in both conditions had substantially less drug use and drug-related impairment at each follow-up point. Overall, retention in buprenorphine treatment was 76% and 64% at 3- and 6-months, respectively. There were no significant differences between IOP and OP conditions in retention, opiate use, and meeting diagnostic criteria for opioid or cocaine dependence. However, participants in IOP had significantly greater reductions in cocaine-positive urine samples from baseline to 3 months (OR=0.35; $p<.05$) and 6 months (OR=0.23; $p<.01$) compared to the OP group.
Conclusions: Participants receiving OP level care generally did not have worse outcomes than those in IOP treatment, although IOP may offer some modest advantages for reducing concurrent cocaine use. Buprenorphine treatment is effective in retaining individuals in treatment and reducing drug use and its negative consequences, irrespective of the level of psychosocial services provided.
Financial Support: NIDA 1RC1 DA 028407

458

ARE FEMALES WHO INJECT DRUGS MORE LIKELY TO BECOME INFECTED WITH HIV THAN MALES?

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Aims: There are multiple reasons why females who inject drugs may be more likely to become infected with HIV than males who inject drugs. Where this is the case, special HIV prevention programs for females would be needed.
Methods: Countries with high seroprevalence (>20%) HIV epidemics among persons who inject drugs (PWID) were identified from the Reference Group to the UN on HIV and Injecting Drug Use. Systematic literature reviews collected data on HIV prevalence by gender for these countries. Non-parametric and parametric tests along with meta-analytic techniques examined heterogeneity and differences in log odds ratios (OR) across studies.
Results: Data were abstracted from 117 studies in 14 countries (N=128,745). The mean weighted OR for HIV prevalence among females to males was 1.18 [95% CI 1.10-1.26], with high heterogeneity among studies ($I2 = 70.7\%$). There was a Gaussian distribution of the log ORs across studies, no difference in the summary ORs for low/middle income versus high income countries, but an increase in ORs in studies where the authors noted a high likelihood of sexual transmission.
Conclusions: There was a significantly higher HIV prevalence among females compared to males who inject drugs in high seroprevalence settings, but the effect size is extremely modest. The high level of heterogeneity and Gaussian distribution suggest multiple causes of differences in HIV prevalence between females and males, with specific differences determined by local factors. Female targeted HIV prevention programs should be implemented in areas where sexual transmission is common. Greater understanding of factors that may protect females from HIV infection may provide insights into more effective HIV prevention for females and males who inject drugs.
Financial Support: The funding for this research study was provided by the National Institutes of Health through grant R01AI0832035

459

NALTREXONE REDUCES THE SUBJECTIVE EFFECTS OF ORAL D-AMPHETAMINE BUT NOT SMOKED COCAINE IN HUMANS.

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Aims: Amphetamines modulate several key neurotransmitters in the brain including dopamine, serotonin, and norepinephrine. Despite the prevalent worldwide abuse of amphetamine, there are no medications approved for treatment by the FDA. Recent studies suggest that the opioid antagonist naltrexone (NTX) is effective in reducing the subjective effects of amphetamine in humans. This suggests that the opioid receptor system may modulate the euphoric effects of amphetamine. The purpose of this study was to further evaluate the ability of oral NTX to alter the cardiovascular and subjective effects of d-amphetamine (AMPH) compared to cocaine (COC).
Methods: Non-treatment seeking COC users (N=9) participated in this randomized, within-subject, double-blind inpatient study. Participants received 0, 12.5, or 50 mg of NTX one hour prior to stimulant administration. Oral AMPH (0, 10, and 20 mg) was administered in ascending order using a 60-min interdose interval. Smoked COC (0, 12.5, 25, and 50 mg) was administered in ascending order using a 14-min interdose interval. Subjective and cardiovascular effects were measured before and repeatedly after drug administration.
Results: Both AMPH and COC produced dose-related increases in subjective and cardiovascular effects under placebo NTX conditions. The cardiovascular effects of AMPH and COC were of similar magnitude, but the subjective effects of AMPH were less robust. NTX 12.5 and 50 mg administered in combination with the highest dose of AMPH (20 mg) reduced ratings of "High," "Potent," and "Quality" compared to placebo NTX (all $p<0.01$). NTX did not alter any of the subjective effects of COC, and it did not alter the cardiovascular effects of either drug.
Conclusions: These results demonstrate that NTX attenuates the positive subjective effects of AMPH, but not COC in COC-abusing participants. Future studies should evaluate both oral and sustained-release NTX as potential therapeutic agents for AMPH dependence.
Financial Support: Supported by DA022222 (PI: Comer).

460

TRAMADOL ABUSE AND ITS ASSOCIATION WITH DEPRESSION.

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Aims: Tramadol is a centrally acting synthetic opioid medication mostly used as an analgesic drug for moderate to severe pains. Since its marketing as older opioid drugs there were concerns regarding its abuse and dependency potential. In this study we aimed at finding the characteristics of tramadol abusers and assessing them for depression symptoms.
Methods: This study is a part of larger prescription drug abuse study. We assessed 37 patients admitted to a substance abuse outpatient treatment clinic in Iran for tramadol abuse or dependency over the year 2010. We have used a demographic questionnaire and Beck Depression Inventory (BDI).
Results: Among 37 patients assessed there were 27 (73.0%) males and 10 (27.0%) females. The age range was between 15 and 43 with a mean of 28.4 years. Twelve people including 6 females were unemployed and there were 9 health professionals (24.3%) in the group consisting of 3 physicians, 5 nurses and an emergency paramedic. Four persons had history of war physical and/or mental trauma.
Only 9 (24.3%) patients have been prescribed tramadol at the time of their first use. The used dose was between 50 to 250 mg with a mean of 114.7 mg. The duration of dependency (daily use) was between 2 to 27 months with a mean of 7.3 months. Using BDI with a cutoff point of 19 and above for clinical depression 18 patients (48.6%) including 6 female and 12 males. Among this group 8 patients stated that they have started the drug in order to relieve their depressive symptoms.
Conclusions: Tramadol abuse and dependency is a new emerging prescription drug abuse and although it can be used as a self-medication for depression, its long term use can be associated with depression.
Financial Support: Zanjan University of Medical Sciences and National Institute on Drug Abuse - DA 027633

461

WITHDRAWN

462

PREVALENCE OF CANNABIS IN DRIVERS, AND DRUGS IN PAIRED ORAL FLUID: BOOD SPECIMENS.

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Aims: To address the issue of driving under the influence of drugs, it was necessary to understand the scope of the problem. The aim of the study was to establish the prevalence of drugs and alcohol in biological specimens taken from randomly selected drivers in a National Roadside Survey (NRS).
Methods: In 2007, the NRS included collection of oral fluid (OF) and blood from randomly selected drivers for the first time. Specimens were screened by ELISA, and confirmed using LC/MS-MS or GC/MS. Analyses of samples were conducted to identify the presence of over 75 drugs and alcohol, including illegal, prescription, and over-the-counter drugs.
Results: Overall, 16.3% of nighttime drivers were positive for at least one drug in either OF or blood. Of the paired specimens, 559 pairs had at least one matrix drug positive; 326 pairs were positive in both matrices. 75.7% were exact drug matches in both OF and blood; 21.4% had at least one drug in common. Data from all 559 pairs in which either OF, blood or both were positive for one or more drugs were further scrutinized for the most prevalent drug class, cannabinoids, being detected in 130 pairs. THC, the active constituent of marijuana, was detected in 201 OF specimens (36% of drug positive specimens), with concentrations up to 1183 ng/mL; in blood, 229 specimens (41%) were positive for one or more cannabinoids, with THC, 11-OH-THC, and THCA maximum concentrations of 61, 12 and 233 ng/mL, respectively. The ratio between THC in oral fluid and THC measured in blood in the paired specimens varied greatly (0.68-360.0). THC was found in OF but not blood in 72 cases; however, THCA in blood documented prior cannabis exposure in 43 specimens.
Conclusions: This NRS study provided a much broader perspective on alcohol and drug use in the driving population than previously available. Such data are essential to developing more precise estimates of the presence of drugs in drivers.
Financial Support: The study was supported by NHTSA.

463

PATIENT INPUT ON A WEB-BASED SELF-MANAGEMENT INTERVENTION FOR CHRONIC PAIN AND ABERRANT OPIOID-TAKING BEHAVIOR.

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Aims: To elicit patient input to inform development of an interactive, web-based self-management intervention for opioid-treated, chronic pain patients with aberrant opioid-taking behavior.
Methods: Twenty-three chronic pain patients with aberrant opioid-taking behavior were recruited from a pain management program to participate in 1 of 4 audio taped 90-minute focus groups. Focus group questions probed interest in and relevance of planned content and the structure of the program. Two researchers with expertise in qualitative methods thematically analyzed the transcripts.
Results: Participants stressed the need for additional pain management and the majority felt a web-based tool would be useful and acceptable. Participants emphasized themes consistent with planned program content including: (1) the importance of recognizing physical limitations and to increase functioning by pacing activity; (2) the need for education about opioids; (3) improving stress management; and (4) goal setting inclusive of planning and scheduling. Participants provided input on how to make the program easier to use, appealing, and motivational (e.g. advance at own pace). Lastly, participants offered important insights: (1) ambivalence about opioid-treatment (e.g. necessary to reduce pain yet insufficient); (2) the reciprocal relationships among cognition, mood, attitude and pain; (3) the need to accept the loss of identity associated with chronic pain (e.g. productive member of society to "drug-seeker"); and (4) the desire for a community of peers with whom to address feelings of isolation and to share stories and strategies for managing daily life.
Conclusions: The results suggest the potential value of self-management for chronic pain patients as well as the potential acceptability of web-based delivery of intervention content. The focus group methodology highlights the usefulness of including potential program users in the process of intervention development.
Financial Support: NIDA Grant R01DA026887

464

IMPACT OF MENSTRUAL CYCLE PHASE ON BRAIN ACTIVITY IN COCAINE-DEPENDENT WOMEN DURING A PSYCHOSOCIAL STRESS TASK.

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Aims: Cocaine-dependent women appear to be more vulnerable to relapse in response to stressors than men and exhibit significantly different patterns of brain activity in response to stress tasks. A convergence of data have demonstrated that menstrual cycle phase and ovarian hormones have a significant impact on drug craving. The focus of the present study is to examine the impact of menstrual cycle phase on the neural correlates of stress in cocaine-dependent women.
Methods: Cocaine dependent women (n=3 follicular phase; n=4 luteal phase) were placed in a Siemens Trio 3T scanner and exposed to two runs of the Montreal Imaging Stress Task (MIST). The study utilized a block design of three conditions (rest, control, and stress). Negative feedback was provided during the stress condition and by the investigator after each run. Individual images were thresholded using clusters determined by Z>2.3 and a corrected cluster significance threshold of p=0.05. Subjective ratings of stress and craving were obtained at baseline and at the end of each run.
Results: During the stress condition of MIST1, compared with women in the follicular phase, women in the luteal phase exhibited significantly greater activity in the medial frontal cortex. In contrast, during the stress condition of MIST2, compared with women in the luteal phase, women in the follicular phase exhibited greater activity in the anterior cingulate and paracingulate gyri. No baseline differences in subjective craving were found, however women in the luteal phase reported greater craving after MIST2 than women in the follicular phase. Subjective stress was significantly greater in women in the follicular phase than women in the luteal phase.
Conclusions: These preliminary data support the extant literature and suggest that menstrual cycle phase has a significant impact on brain activity, subjective stress, and drug craving of cocaine-dependent women.
Financial Support: NIH/NICHHD K12HD055885; NIH/NIDA/ORWH P50DA016511; NIH/NCRR; UL1RR029882NCRR

465

SALVINORIN A AND ITS ANALOGUE ATTENUATE COCAINE PRIME-INDUCED DRUG SEEKING IN RATS.

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Aims: Kappa opioid receptor (KOPr) activation attenuates drug seeking behaviours but produces severe adverse effects which prevents its clinical use. Recent studies show that salvinorin A (Sal A), a neoclerodane diterpene derived from the plant Salvia divinorum is a selective and potent KOPr agonist. Although Sal A is structurally different from classical KOPr agonists, it shares similar pharmacology at KOPr. Therefore, we studied the effect of Sal A and its 2-mesylate analogue (DS1) in a rat model of cocaine reinstatement.
Methods: Effect of Sal A and DS1 on cocaine-seeking was tested using cocaine prime induced drug seeking paradigm in rats. We also tested the effect of acute exposure to these compounds on sucrose reinforcement in rats. In addition to their effect on natural reward reinforcements, we measured the motor suppressive effects of these compounds using spontaneous open field test in rats.
Results: Our results indicate that single injection of Sal A (0.3, 1.0 mg/kg) and DS1 (0.3, 1.0 mg/kg) attenuated cocaine prime induced drug seeking in rats ($p<0.05$). Both these compounds at doses which attenuated cocaine-seeking did not suppress sucrose reinforcement or motor function ($p>0.05$).
Conclusions: These findings indicate that Sal A and its structural analogues, just like classical KOPr agonists attenuates cocaine-seeking in rats. Unlike classical KOPr agonists, Sal A and DS1 produced attenuation of cocaine-seeking was selective and without suppression of motor function. This result warrants future work to determine the underlying mechanism by which these compounds produce their anti-cocaine effects.
Financial Support: This study was supported by Neurological Foundation of New Zealand and Health Research Council.

466

PRESCRIPTION OPIOID MISUSE AMONG PATIENTS WITH A HISTORY OF SUBSTANCE USE DISORDER.

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Aims: Research indicates that history of substance use disorder (SUD) is associated with elevated risk for opioid medication misuse, but little data are available regarding predictors of opioid misuse specifically among patients with a SUD history.
Methods: Participants with chronic pain, history of SUD, and current opioid prescription for chronic pain were included (n=81). Participants completed measures of opioid misuse, pain severity, pain-related function, pain catastrophizing, attitudes about managing pain, emotional functioning, and current substance abuse.
Results: Participants were subdivided into groups based on likelihood of misusing opioids, as assessed by the Pain Medication Questionnaire. There were no differences between the groups in opioid dose or demographic characteristics based on likelihood of misuse. However, participants in the High-Risk group reported greater pain severity, pain interference, pain catastrophizing, depressive symptoms, and lower self-efficacy for managing pain than participants in the Low-Risk group (all p-values <0.05). Participants in the High-Risk group also had higher rates of an active SUD (28% versus 10%, p=0.02). A hierarchical linear regression evaluated factors associated with risk of opioid misuse. The final model accounted for 41% of the variance in opioid misuse. The only variables significant in the final model were male gender and greater pain catastrophizing.
Conclusions: Among patients with SUD histories, those at high-risk of opioid misuse reported more pain, poorer pain-related function, more depressive symptoms, and were more likely to meet criteria for an active SUD, relative to low-risk patients. In adjusted analyses, male gender and pain catastrophizing were significantly associated with opioid misuse. Active SUD status was not a significant predictor in the regression model. These results identify factors associated with opioid misuse within a sample of chronic pain patients with a history SUD.
Financial Support: Grant 023467 from NIDA.

467

BEHAVIORAL AND PHARMACOLOGICAL EFFECTS OF TWO NOVEL SEROTONIN 5-HT2 MODULATORS.

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Aims: The desired serotonin 5-HT2 receptor pharmacology for treatment of endogenous and drug-induced neuropsychiatric and behavioral disorders is antagonism at 5-HT2A receptors and activation of 5-HT2C receptors. All effective antipsychotic compounds attenuate the robust head-twitch response (HTR) in mice elicited by the 5HT2A/2C agonist (-)DOI (a hallucinogenic compound). We tested the hypothesis that a novel aminotetralin compound demonstrated to be an agonist at 5-HT2C receptors but an antagonist at 5-HT2A/2B receptors would attenuate the HTR.
Methods: The (+)- and (-)-trans-enantiomers of the novel aminotetralin compound p-Cl-PAT (trans 4-[p-chloro]-phenyl-2-dimethylaminotetralin) were synthesized and converted to the hydrochloride salt for in vitro and in vivo pharmacological assessment. Compound affinity was determined in radioligand competitive displacement binding assays using HEK membrane preparations. Function was measured as activation of phospholipase-C (PLC) and formation of inositol phosphates (IP) in HEK cells preincubated with [3H]-myo-inositol. C57Bl/6J male mice were injected with p-Cl-PAT or saline (20 min pretreat), various doses of (-)DOI or saline (10 min pretreat), followed by a 10-min test session in which HTRs were counted by a trained observer.
Results: Both isomers of p-Cl-PAT were agonists at 5-HT2C receptors and antagonists at 5-HT2A receptors, with the (+) isomer being approximately 6- and 3-fold more potent at 5HT2A and 2C receptors, respectively. DOI produced dose-dependent increases in HTRs (45 responses in a 10-min session following 1.0 mg/kg). Both the (+) and (-) isomers of p-Cl-PAT dose-dependently blocked the DOI-elicited HTR, when administered by injection (i.p.) or gavage (oral, p.o.). The (+) isomer was approximately 2-fold more potent relative to the (-) isomer.
Conclusions: Here we report the pharmacological and initial behavioral characterization of two isomers of an orally active, novel 5-HT2A antagonist/5-HT2C agonist that may have therapeutic efficacy as an antipsychotic medication.
Financial Support: NIH NIDA DA030989

468

LOW-DOSE PRENATAL IV NICOTINE EXPOSURE INCREASES HYPOTHALAMIC OREXIN CELL BODIES AND APPOSITIONS ONTO DOPAMINE NEURONS IN THE VTA.

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Aims: Gestational nicotine alters development of the mesocorticolimbic dopamine system, which is integral in motivated behavior. Orexin originates in the lateral hypothalamus (LH) and projects to regions involved in motivation. This study examined if intravenous prenatal nicotine exposure alters orexin in the LH, and orexin projections to the ventral tegmental area (VTA). To confirm that nicotine doesn't cause global neuronal change in the LH, melanin concentrating hormone (MCH) was also examined. MCH originates in the LH and is involved in similar homeostatic processes as orexin.
Methods: During gestational days 8-21, dams were injected 3x/day via IV catheters with nicotine (0.05 mg/kg). Serial sections through the LH and VTA were processed for immunohistochemistry for orexin A (OxA), tyrosine hydroxylase (TH), or MCH from adult male offspring. Orexin and MCH cell counts were from the LH and OxA appositions on TH-positive neurons were processed in the VTA.
Results: A significant main effect of gestational nicotine was found for LH OxA [$F(2, 40) = 8.58$, $p< .05$], as well as a significant difference between medial and lateral expression for nicotine condition [$F(1, 26) = 5.79$, $p<.05$]. In the VTA, a significant main effect of gestational nicotine [$F(1, 10) = 11.54$, $p< .05$], was observed for VTA OxA appositions onto DA neurons. Finally, no difference [$F(1, 26) = .067$, $p=.798$] between groups for MCH LH was found.
Conclusions: Low-dose IV prenatal nicotine exposure significantly increased the number of orexin neurons in the LH, particularly its medial division. No difference was seen in MCH neurons. Nicotine subjects also show increased OxA appositions onto DA-producing cells in the VTA. These data contribute to a growing body of literature suggesting that orexin-dopamine interactions play a crucial role in behavioral and cognitive correlates of chronic psychostimulant exposure.
Financial Support: NIH T32 grant 5T32GM091740, NIDA grant DA 021287, and NIA grant AG030646

469

REVIEW OF AND RECOMMENDATIONS FOR YOUTH-ORIENTED MENTAL HEALTH AND SUBSTANCE-USE DISORDER SCREENING TOOLS.

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Aims: The need for more evidence-based screening and assessment of co-occurring mental health and substance use-related issues is well documented. There is considerable research and development underway regarding dual-diagnosis screening among adults presenting to both generic (e.g., primary care) and specialized mental health and addiction treatment facilities. However, a synthesis of the research and recommendations for well validated screening and assessment tools is still needed for youth.
Methods: Approximately 3500 abstracts and several hundred screening and assessment tools and protocols were distilled to a subset of 20 tools and 33 studies for detailed review and rating using the Standards for Reporting of Diagnostic Accuracy (STARD) criteria. This process included an overview of validity and reliability data across different populations, settings, and cultural contexts. A stakeholder group reviewed the recommendations based on the research synthesis and rated issues such as usability, practicality, and cost.
Results: A small number of tools emerged that fulfill a "dual function" by serving both mental health and addiction programs, including those specifically focused on youth with co-occurring disorders. While some tools fit well as first-stage screeners (i.e., pointing to the presence of any disorder), such as the GAIN-Short Screener; other tools were better suited as second-stage, targeted screeners (i.e., pointing to specific disorders), such as the DISC Predictive Scales.
Conclusions: From a systems lens, there are many doorways into mental health and addiction treatment, and it is critical to proactively screen for co-occurring symptoms. The results of this review point to the use of several high performing tools based on multiple criteria. Stakeholders expressed high value in using the same tool across a range of services and saw this as facilitating local coordination between services. Information on tool reliability and validity plus administration time outweighed concerns about application costs.
Financial Support: CAMH

470

MITIGATING THE RISKS OF ADDICTION, ABUSE, AND DIVERSION: UNDERGRADUATE PAIN MANAGEMENT CURRICULA.

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Aims: Identify needed changes in undergraduate pain management curricula to mitigate the risks of drug addiction, abuse, and diversion
Methods: Many primary care physicians report inadequate training in assessing patient risk, relative risk of analgesic choices, drug monitoring, and responding to aberrant drug behavior. Research indicates most US and Canadian medical schools relegate pain education to a subtopic of a general requisite course and few have mandatory pain training. Clinical pharmacology and substance abuse are underemphasized in curricula and licensing exams. Effective mentoring in pain management is complicated by the inadequate pain management skills of many practicing physicians who act as mentors.
Results: Key elements of pain management curricula include nonpharmacologic therapy; clinical pharmacology of analgesics; appropriate selection, dose, and duration of therapy; predictors of medication abuse (eg, patient/family history of alcohol/substance abuse, depression/mental illness); factors influencing the attractiveness of a drug for abuse (eg, subjective effects, availability, cost, formulation characteristics); how to use key clinical tools (eg, risk assessment, patient contracts, abuse-deterrent formulations, urine monitoring); responding to aberrant drug behavior (eg, greater monitoring, supervised dispensing, tapered reduction, referral); and mentoring in these skills. Motivating medical schools to effect change may involve government; regulatory bodies; professional, academic, and alumni associations; and patient and public interest groups.
Conclusions: Undergraduate pain management curricula must teach appropriate prescribing of opioid and nonopioid analgesics incorporating evidence-based guidelines. A focus on factors that mitigate risks of addiction, abuse, and diversion will increase the ability of physicians to identify and care for patients at risk.
Financial Support: Endo Pharmaceuticals Inc., Chadds Ford, PA

471

CRACK AND COCAINE USERS SHOW MORE SEXUAL RISK BEHAVIOR AND FAMILY PROBLEMS THAN ALCOHOL AND OTHER DRUG USERS.

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Aims: To compare family problems and sexual risk behavior among different groups of drug users in Brazil.
Methods: A Brazilian cross-sectional multi-center study selected 285 current adult substance abusers from outpatient and inpatient specialized clinics in four state capitals. Subjects were evaluated with the sixth version of the ASI, and 293 crack users were compared to 126 cocaine snorters and 316 alcohol and other drug users, mostly marijuana users.
Results: Cocaine users showed more family problems when compared to other drug users, with no significant difference between smoking or inhaling. These problems included arguing (crack 66.5%, powder cocaine 63.3%, other drugs 50.3%, p=0.004) and having trouble getting along with partner (61.5% x 64.6% x 48.7%, p=0.013), and need for additional childcare services in order to attend treatment (13.3% x 10.3% x 5.1%, p=0.002). The majority of crack/cocaine users had spent time with relatives in the last month (84.6% x 86.5% x 76.6%, p=0.011). Crack users had significantly more sexual partners (1-4 x 1-3 x 0-2, p<0.001) and more prostitution (6.5% x 4% x 0.6% p<0.001).
Conclusions: Treatment programs for crack and cocaine users should enhance family treatment strategies, once they are poorly developed in most services in Brazil. Childcare services need to be included, since its absence may be a barrier to treatment attendance. Interventions addressing sexual risk behavior for crack users are also crucial for this population.
Financial Support: National Secretariat of Drug Policies (SENAD 005/2005)

472

WORKING MEMORY TRAINING DECREASES DELAY DISCOUNTING RATES IN ALCOHOL ABUSERS.

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Aims: Excessive discounting is known to be a behavioral marker of drug addiction. Working memory training has been shown to decrease delay-discounting rates in stimulant abusers. This research studies the generalization of this effect to alcohol abusers.
Methods: Before and after a course of working memory training, 10 alcohol abusers completed 4 kinds of discounting assessments – for future gains of (1) $100 and (2) $1000, past gains of (3) $1000, and (4) gains shared by persons of varied social distances; all gains were monetary and hypothetical. The results were analyzed using generalized estimating equations with delay, assessment time, and the interaction entered into the model as within-subjects factors.
Results: Results showed that for the $1000 future gains discounting assessment there was a significant interaction between pre- to post-treatment change and reward delay in the dependent measure, indifference points, Wald χ 2 (df=1) = 4.919, p =.027. This indicates that for choices between outcomes involving $1000 monetary future rewards, working memory training reduced discounting of delayed rewards, and did so more at the more distant delays.
Conclusions: These results support extending to the alcohol-abusing population the method of training working memory as a means to modify excessive discounting. As excessive rates of discounting have been strongly associated with substance abuse in general, these results add to the support for working memory training as a general therapy method for combatting substance abuse.
Financial Support: This work was funded by NIDA grant # 5 R01 DA012997-11

473

THE INFLUENCE OF AGE AND SOCIOMETRIC NETWORK POSITION ON INJECTION DRUG USE AMONG RURAL APPALACHIAN PRESCRIPTION DRUG USERS.

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Aims: High risk drug use among rural Americans is not well characterized. Age is one attribute that may have a direct influence on both the formation of social networks, as well as the likelihood of engaging in high risk injection drug use. The current study tested the direct effects of age and centrality on injection drug use and examined the potential mediating role of network centrality.
Methods: The study included sociometric data from the drug network of 503 rural drug users recruited via respondent driven sampling. Data were also collected on demographics, drug use and injection drug use. Structural equation modeling was employed using AMOS 19 to determine the association of age and a latent construct consisting of four centrality measures (i.e. eigenvector, degree, betweenness, and closeness) on engagement in injection drug use.
Results: Individuals more central in the rural drug network were more likely to engage in injection drug use ($\beta = .12$, $p \leq .05$), as were younger participants ($\beta = -.95$, $p \leq .05$). However, age was not associated with network centrality ($\beta = -.08$, $p = .09$). Monte Carlo bootstrapping was employed to examine the indirect effect of age on injection drug use and the result was not significant (90% confidence interval -.003-.000) and fit indices suggested that the model was a very good fit for the data, X^2 (df = 8, $N = 503$) = 7.272, $p = .508$; $X^2/df = .909$; *RMSEA* = .000 with 90% CI .000-.049; *NFI* = .989; *CFI* = 1.00, *SRMR* = .0207.
Conclusions: Network centrality did not appear to mediate the relationship between age and injection drug use. However, both age and centrality were independently associated with an increased likelihood of engaging in injection drug use. Given the relationship of both individual- and network-level factors with injection drug use found in this analysis, these results may inform interventions aimed at reducing HIV and other disease transmission via injection drug use.
Financial Support: This research is supported by NIH R01DA024598

474

COTININE LEVELS IN NON-CIGARETTE-SMOKING MARIJUANA BLUNT VS. JOINT USERS.

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Aims: It has been assumed that the tobacco leaves and paper that blunts and joint are made with do not contain significant amounts of nicotine. To our knowledge, cotinine levels in marijuana blunt smokers and joint smokers have not been systematically compared. We hypothesize that non cigarette smoking blunt smokers will have higher urine cotinine levels than non cigarette smoking joint smokers.
Methods: 51 participants seeking treatment for current cannabis dependence were screened at the Substance Abuse Research and Treatment Service (STARS). Demographic variables, pattern of substance use and baseline cotinine levels were obtained. Non-cigarette smoking blunt users (BU) or joint users (JU) were compared. Cigarette smokers or combined blunt and joint users were excluded from the analysis.
Results: 51 non cigarette smoking participants were included in the analysis; 74% were male, 36% were Caucasian, 20% were African American, 32% Hispanic, 6% Asian and 6% self identified as Other. The average age was 36.7 +/- 11.6 years. BU (n=17) had significantly higher levels of urine cotinine compared to JU (n=34); Median 13.6 ng/ml vs 0 ng/ml or mean 21.45 ng/ml vs 9.87 ng/ml [Mann-Whitney U= 138.00, p= 0.001].
Conclusions: This study found that non-cigarette using blunt smokers had significantly higher urine cotinine levels than joint smokers. This may indicate that blunts possibly contain more nicotine than joints do. This has important clinical implications in that blunt smokers may experience more withdrawal symptoms when ceasing use and their withdrawal symptoms may be from both cannabis and nicotine making treatments that focus on cessation particularly difficult in this subpopulation of marijuana smokers. Currently, it is thought that blunt smokers are more difficult to retain in treatment because they use greater amounts of marijuana than joint users. However, it may be the added nicotine complicates treatment efficacy as well.
Financial Support: NIDA Grant DA007294-19

475

A LATENT CLASS ANALYSIS OF SAFE AND DRUG-FREE SCHOOLS.

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Aims: To classify schools into subgroups on the basis of crime and safety indicators.
Methods: The national School Survey on Crime and Safety was used in this analysis; the SSOCS is a nationally representative survey of public schools. The SSOCS collects school-level data on crime and safety.
Ten indicators from the SSOCS were selected for the analysis. Latent class analysis was used to classify the sample into sub-classes. ANOVA was used to test if there was a significant difference in the mean number of violent and substance abuse related incidences between the latent classes.
Results: Fit statistics (BIC = 26853.9) indicated that a 3 class model provided the best fit. The prevalence of the 1st latent class was 33%; this latent class was classified by high probabilities (> 0.90) of having a prevention curriculum and programs to promote a sense of community integration for students. The mean number of violent incidents was 13.28 and 0.62 for substance abuse related incidents. The prevalence of the 2nd latent class was 43%. The 2nd latent class was characterized by high probabilities (> 0.90) of having a prevention curriculum, programs to promote a sense of community integration for students, having security personnel on campus, and student verbal abuse of teachers. The mean number of violent incidents was 33.64 and the mean number of substance abuse related incidents was 6.1. The prevalence of the 3rd latent class was 24%. The 3rd latent class was classified by very low probabilities (<0.05) of programs that involve parents. Schools in the 3rd latent class were also less likely to have a prevention curriculum. The mean number of violent incidents was 17.34 and 3.17 for substance abuse related incidents.
Conclusions: This analysis suggests that schools with the can be distinguished by the presence or absence of prevention programs and programs that involve parents. Further research is needed contextual variables that predict latent class membership.Safe and drug free schools indicators should be refined to make the latent class membership more distinct.
Financial Support: The researcher is supported by a NIDA T32 training grant (T32DA007292).

476

NONMEDICAL PRESCRIPTION DRUG USE AMONG SCHOOL ADOLESCENTS IN ISRAEL.

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Aims: Nonmedical prescription drug use (NPDU) has become alarmingly prevalent among young adults in North America and elsewhere. Little is known about the patterns of NPDU in Israel. This study describes the prevalence of past-month NPDU among Israeli school-attending adolescents.
Methods: The study population comprised a nationally representative sample of Jewish and Arab students in grades 7-12. Data was collected in 2009 via an anonymous, self-administered questionnaire. Analyses were performed on 6,950 students aged 13-18. NPDU refers to past-month nonmedical use of prescription-type sedatives, stimulants, tranquilizers, and cold medicine.
Results: Overall, 5.6% of respondents reported NPDU. Arab boys were considerably more likely to report past-month NPDU than Arab girls – 9.0% and 3.0% respectively, (OR=3.3, 95%CI=2.1-5.1); no sex difference was noted among Jewish respondents – 5.9% and 5.3% of boys and girls (OR homogeneity p<.001). In logistic regression, NPDU was significantly associated with gender (Adjusted OR=1.4, 95%CI= 1.2-1.7), but not with Arab-Jew (AOR=1.1, 95%CI=0.8-1.4). Nearly 50% of Arabs and 25% of Jews who reported NPDU also used illicit drugs in the past month compared with about 2% of non-NPDU respondents, and were 2-5 times more likely to use inhalants, binge drink and smoke. NPDU youth were also nearly 3 times more likely to be truant for 7 or more days in the past month.
Conclusions: Among Israeli youth, nonmedical prescription drug use is more prevalent than illicit drug use, and is associated with other risky behaviors and with school truancy, as reported in other countries. The relative availability of these drugs (also via e-pharmacies), their legal status, and the perception that they are less dangerous than other drugs, makes NPDU prevention and control particularly challenging. Research and prevention efforts are warranted, including enhancing the knowledge and awareness of youth, parents, teachers and health care providers.
Financial Support: Anti-Drug Authority of Israel

477

THE ACE INHIBITOR PERINDOPRIL MAY ATTENUATE PSYCHOSTIMULANT EFFECTS PRODUCED BY METHAMPHETAMINE IN NON-TREATMENT-SEEKING, METHAMPHETAMINE-DEPENDENT VOLUNTEERS.

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Aims: Most treatment development research for drug abuse and dependence has focused directly or indirectly on manipulating dopaminergic systems. Emerging evidence implicates noradrenergic mechanisms in mediating effects of stimulants, including methamphetamine (MA). Angiotensin converting enzyme (ACE) inhibitors, such as perindopril, attenuate noradrenergic neurotransmission, and may be helpful as treatments for MA dependence.
Methods: To test this hypothesis, we administered MA to non-treatment-seeking MA-dependent volunteers during brief treatment (4-6 days) with perindopril or placebo. Participants were assessed during treatment with perindopril (4, 8, and 16 mg) and placebo. MA doses (15 and 30 mg) were administered IV on different days. Effects of MA were collected using visual-analogue scales probing for ratings of "High", "Crave Methamphetamine", "Stimulated", as well as "Good Effects", "Bad Effects", and "Like".
Results: 48 participants have completed the study to date. Participants were ~35 years of age, used MA for ~13 years, and had used the drug on ~18 of the past 30 days. Most were cigarette smokers (87%) but none met criteria for dependence on other drugs of abuse. Participants showed reductions in ratings of "Stimulated" following administration of MA (15 and 30 mg, IV) during treatment with 8 mg perindopril, but not during treatment with the other doses. Perindopril treatment was well tolerated.
Conclusions: Perindopril should be further evaluated as a treatment for MA dependence. These results are consistent with earlier research showing that other medications that reduce noradrenergic signaling reduce the effects of cocaine. The non-dose-dependent effects of perindopril may be due to inhibition of the metabolism of other peptides, such as substance P. Substance P facilitates the effects of stimulants, and treatment with higher doses of perindopril may inhibit its metabolism, enhancing its effects.
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478

RELATIONSHIP BETWEEN SUBSTANCE ABUSE TREATMENT OUTCOME AND SEXUAL RISK BEHAVIORS.

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Aims: Many substance users enrolled in drug treatment programs continue to engage in high-risk sexual behaviors despite the threat of sexually transmitted infections (STIs). Little is known about the impact of drug abuse treatment on these behaviors. We examined the association of substance abuse treatment with sexual risk behaviors among participants in a multi-site trial of the NIDA Clinical Trials Network. We hypothesized that decreased drug/alcohol problem severity would coincide with decreases in sex risk behaviors.
Methods: We assessed 356 men who participated in an HIV/STI prevention project. Measures included the Addiction Severity Index (ASI) and Sexual Behavior Interview (SBI). Changes in ASI composite scores and risk behaviors were compared with repeated measures linear regression.
Results: Interactions were found between drug/alcohol use severity and condom use with regular partners. Decreased severity of drug problems ($F=5.20$, $p=0.024$) and decreased severity of alcohol problems ($F=5.08$, $p=0.025$) were associated with increased condom use with regular sex partners, when controlling for number of treatment sessions attended. There were interactions between decreased number of sex partners and decreased severity of drug ($F=5.49$, $p=0.020$) and alcohol ($F=5.65$, $p=0.018$) problems, and between decreased sex under the influence and decreased severity of drug ($F=6.75$, $p=0.010$) and alcohol ($F=5.83$, $p=0.016$) problems, but these interactions disappeared when including treatment sessions attended. Condom use with casual sex partners and having at least one high risk partner did not interact with decreased drug/alcohol use severity.
Conclusions: Some sexual risk behaviors decreased in those whose drug/alcohol use severity also decreased independent of specialized treatment-based intervention sessions. Enrollment in drug treatment may serve as an effective method for reducing HIV risk behaviors among drug users. Further research is needed to pinpoint the effect of drug treatment independent of other factors.
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479

RECEPTOR MECHANISMS OF CARISOPRODOL ANTAGONISM USING DRUG DISCRIMINATION.

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Aims: Carisoprodol, a commonly prescribed muscle relaxant, has been increasingly recognized as a drug of abuse. Previous studies have suggested an addiction potential similar to that of long-acting benzodiazepine or barbiturate compounds. The purpose of the current study was to determine possible GABA-A receptor mechanisms of the discriminative stimulus effects of carisoprodol using various GABA-A receptor antagonists.
Methods: Male Sprague-Dawley rats were trained to discriminate carisoprodol (100 mg/kg, ip) from methylcellulose vehicle. Attenuation of discriminative stimulus effects of carisoprodol was determined using administration of (i) bemegride (2.5, 5, 10 mg/kg), a barbiturate antagonist, (ii) flumazenil (2.5, 5, 10 mg/kg), a benzodiazepine antagonist, and (iii) bicuculline (0.5,1,2.5 mg/kg), a GABA-A antagonist.
Results: Bemegride produced rightward and downward shifts in the carisoprodol dose effect curve. Flumazenil failed to produce dose-dependent attenuation of the discriminative stimulus effects of carisoprodol, but consistently produced partial antagonism at intermediate doses (2.5 - 5 mg/kg). Bicuculline decreased drug-appropriate lever responding when administered with lower doses of carisoprodol (25, 50 mg/kg); however, it failed to block the carisoprodol effects at the 100 mg/kg training dose.
Conclusions: GABA-A antagonists, selective for different sites, affected carisoprodol discriminative stimulus effects differently. The failure of bicuculline to block the effects of the training dose of carisoprodol may indicate that an allosteric mechanism could play a role in carisoprodol discriminative stimulus effects, especially since the barbiturate site antagonist, bemegride, antagonized carisoprodol's stimulus effects. The successful blockade of carisoprodol effects by bemegride, but not by flumazenil, indicates that the barbiturate site may be more important than the benzodiazepine site in the behavioral effects of carisoprodol.
Financial Support: NIH R01DA022370

480

BRIEF INTERVENTIONS WITH ENVIRONMENTAL ENRICHMENT FOR COCAINE-CUE EXTINCTION AND RELAPSE PREVENTION: EVALUATION OF CONCEPT IN RATS.

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Aims: In an animal model of cue exposure therapy, glycine-based cognitive enhancing drugs have been shown to facilitate cocaine-cue extinction (CCE) learning, which deters subsequent reacquisition of cocaine seeking in both rats and monkeys. Based on the established benefits of environmental enrichment (EE) for improving learning and memory in animals and humans, we hypothesized that EE scheduled in conjunction with extinction training would augment CCE learning and deter reacquisition of cocaine seeking.
Methods: Rats were trained to self-administer cocaine under a second-order schedule of i.v. cocaine injection (0.3 mg/kg/injection) and were maintained under these conditions for at least 4 weeks before undergoing CCE. During CCE training, drug seeking was extinguished by substituting saline for cocaine while maintaining response-contingent cue presentations. For the EE group (n=8), rats were housed together in groups of 4 in a large chamber for two 4hr periods, beginning 24hr before and immediately after each of three weekly 1hr CCE sessions. The EE chamber allowed opportunity for social interaction, and contained various structures for cognitive stimulation and physical exercise. A control group (n=8) received weekly CCE training, but without EE (No-EE). Testing for reacquisition of cocaine self-administration (conditions as above) began 1wk after the last CCE session.
Results: EE facilitated CCE learning, as responses by the EE group were significantly lower during the first two CCE sessions compared to No-EE controls ($p<0.01$). EE combined with CCE also significantly deterred reacquisition of cocaine seeking, as responses by the EE group were significantly lower during the first 5 reacquisition sessions compared to No-EE controls ($p<0.03$).
Conclusions: These findings support the concept that brief interventions with EE might augment exposure therapy for relapse prevention in cocaine addicts. Changes in plasticity of AMPA receptor transmission may underlie these effects of EE.
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481

IDENTIFICATION OF GENETIC VARIANTS OF THE HLA LOCUS ASSOCIATED WITH RESPONSE TO A COCAINE VACCINE.

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Aims: To identify genetic markers modulating the immunogenic response to the cocaine vaccine in cocaine dependent subjects.
Methods: Cocaine and opioid dependent subjects were vaccinated with 360 mg of cocaine vaccine (SNC-rCTB) or placebo at weeks 0, 2, 4, 8, and 12. Urines were collected thrice weekly over 20 weeks and tested for cocaine metabolites. From weeks 8 to 20, blood was drawn and tested for antibodies reactive to the cocaine. DNA from 34 subjects who were treated with the vaccine was genotyped with the Illumina Golden Gate MHC mapping panel assay. A subset of 1244 markers from candidate genes were considered of these 1227 markers (16 markers were monoallelic and one marker had all missing alleles). Markers used had a call rate of > 0.90 and a minor allele frequency > 0.05 leaving a total of 960 markers. The maximum IgG anti-cocaine antibody level was evaluated versus these variants. Due to the small sample size (N = 34), the rare homozygote was combined with the heterozygote to estimate a recessive effect.
Results: The most significant association was with the variant rs2582 (P = 9.2 x10-05). This variant is located in the HLA-DOA gene. HLA-DOA is a HLA class II alpha chain paralogue, and forms a heterodimer with HLA-DOB to form the heterodimer HLA-DO. This heterodimer is found in lysosomes in B cells and regulates HLA-DM-mediated peptide loading on MHC class II molecules.
Conclusions: This study indicates that a patient's genetic make-up may be used to identify patients who respond to the cocaine vaccine. Furthermore, the identification of genes that modulate response to the cocaine vaccine may reveal new treatment regimes.
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482

BUPRENORPHINE INDUCTION FOR PRESCRIPTION OPIOID USERS: FINDINGS FROM THE PRESCRIPTION OPIATE ADDICTION TREATMENT STUDY (POATS).

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Aims: The increasing prevalence of prescription opioid (PO) dependence has created a need for treatment research. The Prescription Opiate Addiction Treatment Study (POATS) examined buprenorphine treatment for PO dependence. The aims of this secondary analysis were: (1) to compare induction experiences between participants using of 4 prescription opioids, and (2) to examine factors associated with difficult buprenorphine induction.
Methods: The POAT Study was a multi-site, randomized clinical trial, using a two-phase adaptive research design. This analysis examines buprenorphine induction in Phase 1 of this study. Comparisons were between participants who self-reported primary use of Short Acting (SA) oxycodone, Long Acting (LA) oxycodone, methadone, or hydrocodone. Additionally, analyses examined characteristics associated difficult induction, defined as increased withdrawal symptoms (measured by the Clinical Opiate Withdrawal Scale (COWS)) after first buprenorphine dose.
Results: Induction experiences did not differ based on primary PO. An association between primary PO and maximum buprenorphine dose was found [$F(3, 528) = 3.093$, $p = 0.027$]. Maximum buprenorphine dose for hydrocodone users was lower than that for LA oxycodone users (17.04 mg vs. 19.00 mg). Those who experienced an increase in withdrawal symptoms (determined by COWS score) after their first dose had lower pre-dose COWS (10.09 vs. 12.77, $t(624) = -13.56$, $p < .001$). Differences in demographic characteristics, depression or pain did not predict increase in post-dose COWS.
Conclusions: Primary PO was not associated with difficult buprenorphine inductions. Lower pre-dose COWS scores were associated with an increase in opioid withdrawal symptoms after initial buprenorphine dose. Recommendations regarding a minimum pre-dose COWS score prior may be considered in light of this finding.
Financial Support: NIDA Grants 2U10DA015831, U10DA020024, U10DA013045, K24 DA022288, K23 DA022297.

483

SOCIAL STRESS-INDUCED SENSITIZATION TO AMPHETAMINE: ESSENTIAL ROLE OF BDNF SIGNALING IN THE MESOCORTICOLIMBIC CIRCUITS.

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Aims: Brain-derived neurotrophic factor (BDNF) mediates neuroadaptation to drugs of abuse and stress. BDNF from the ventral tegmental area (VTA) and the prefrontal cortex (PFC) is released in the nucleus accumbens (NAc), where TrkB receptor stimulation determines the level of BDNF signaling. We have shown that repeated social defeat stress increases BDNF in the VTA, and ΔFosB in mesocorticolimbic terminals, accompanied by cross-sensitization to amphetamine. We hypothesized that BDNF-TrkB signaling in the NAc is required for the development of social stress-induced drug cross-sensitization.
Methods: Adeno-associated viral constructs of shRNA targeted against TrkB (shTrkB) or control AAV-GFP were infused bilaterally into the NAc of Sprague-Dawley rats. Intermittent social defeat stress consisted of four brief confrontations between the experimental rat and an aggressive rat over the course of 10 days. Amphetamine (1.0 mg/kg, ip) challenge was performed ten days after the last stress or handling control procedure. Western blot analyses for BDNF, TrkB, and ΔFosB were performed in the NAc, VTA, and PFC.
Results: Repeated social defeat stress induced cross-sensitization to amphetamine in rats that received AAV-GFP infusions, but not in shTrkB rats. After repeated social defeat stress, ΔFosB expression increased significantly in the NAc and PFC of AAV-GFP rats, but was unchanged in shTrkB rats. TrkB knockdown in the NAc prevented social defeat stress-induced elevation of BDNF in the VTA and reduced BDNF in the PFC. Also, BDNF level in the NAc was significantly lower in AAV-shTrkB rats, which is consistent with a reduction of BDNF afferent supply originating in the VTA and PFC.
Conclusions: Reduction of BDNF signaling in the NAc prevented social defeat stress-induced cross-sensitization to psychostimulants. TrkB knockdown in the NAc inhibited accumulation of ΔFosB that could trigger cross-sensitization after social defeat stress.
Financial Support: USPHS awards DA026451 and MH066954.

484

LOWER SENSITIVITY TO METHAMPHETAMINE IN ACCUMBAL DOPAMINE D2 RECEPTOR KNOCKDOWN MICE BY USING AAV VECTOR.

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Aims: Addictive drugs lead to their rewarding effects by targeting the mesolimbic dopaminergic neuronal system, which originates in the ventral tegmental area and projects mainly to the nucleus accumbens (NAc). Almost all neurons in the NAc are medium spiny neurons divided into two major subtypes expressing dopamine D1 receptor (D1r) versus D2r. In the present study, we investigated the role of accumbal D2r-mediated neurotransmission in behavioral responses induced by methamphetamine (METH), using specific knockdown mice generated by the infection of the adenoassociated virus vector containing the iRNA sequence for D2r (AAV-iD2r vector).
Methods: We bilaterally injected AAV-iD2r or AAV-Mock vector into the NAc of male C57BL/6J mice. The mRNA expression levels of D2r in AAV-iD2r vector-injected mice were assessed at about 50% reduction in the NAc, but at no change in the dorsal striatum, compared with that in AAV-Mock vector-injected mice.
Results: There were no differences in the mRNA expression levels of D1r in the NAc between both groups. Acute treatment with METH induced hyperlocomotion in the D2r knockdown mice was significantly decreased compared with that in the control mice. Furthermore, the development of locomotor sensitization induced by repeated treatment with METH exhibited a significantly less extension in the D2r knockdown mice. In the place conditioning paradigm, METH (induced place preference in both groups. However, the preferred effects of METH were significantly weaker in the D2r knockdown mice than the control mice.
Conclusions: These findings suggest that accumbal D2r knockdown suppresses behavioral sensitivity to METH. Thus, the D2r-mediated neurotransmission in medium spiny neurons of the NAc plays an important role in the development of drug dependence.
Financial Support: The study was sipported in part by the Funding Program for Next Generation World-Leading Researchers(NEXT Program)

485

EFFECTS OF NEONATAL VISCERAL PAIN ON DISCRIMINATIVE STIMULUS AND REINFORCING EFFECTS OF MORPHINE IN RATS.

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Aims: Describe the roles of neonatal visceral pain on discriminative stimulus and reinforcing effects of morphine in rats.
Methods: In these pilot studies, we were interested in examining the effects of neonatal visceral pain on the discriminative stimulus and reinforcing effects of opioids. We studied four groups of adult male rats: two of the groups received a colorectal distension procedure on PND's 4, 6, and 8 to induce NPS, while the other two groups were controls. In the drug discrimination study, rats were shaped to lever-press under a terminal FR20 reinforced by food presentation, then trained to discriminate morphine (1.5 mg/kg, SC) from saline. Dose effect functions for morphine were acquired in NPS and control rats, and repeated in the presence of the non-selective opioid antagonist naltrexone (0.1 mg/kg, SC). In the self-administration study, rats were trained to respond for food pellets under an FR20 prior to catheter implantation. After recovery from surgery, intravenous morphine (0.3 mg/kg/inj) was available for self-administration under an FR20, an FR10, and a continuous reinforcement schedule.
Results: NPS rats discriminated lower doses of morphine than controls, and the antagonist effects of naltrexone against the interoceptive effects of morphine were less pronounced in NPS rats. Morphine did not maintain responding under the FR20 or FR10 schedules, but maintained dose-dependent responding in all animals under conditions of continuous reinforcement.
Conclusions: In summary, these findings demonstrate that neonatal visceral pain has persistent pharmacological consequences into adulthood, and may suggest that NPS increases sensitivity to abuse-related effects of opioids across development.
Financial Support: The project described was supported by RR029884 and RR029884 from the National Center for Research Resources.

486

EXPLICATING THE ROLE OF POSITIVE AND NEGATIVE AFFECT IN ALCOHOL CRAVING IN INDIVIDUALS WITH POSTTRAUMATIC STRESS DISORDER AND ALCOHOL DEPENDENCE.

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Aims: Posttraumatic stress disorder (PTSD) commonly co-occurs with substance use disorders (SUD) and negatively impacts SUD treatment outcomes. PTSD-related negative affect has been shown to enhance drug and alcohol craving in laboratory cue reactivity studies of individuals with SUD, but the role of positive affect in craving has not been established using this paradigm. As an extension of the ambivalence model of cravings, we hypothesized that exposure to alcohol cues would increase both positive and negative affect and that positive affect would explain significant variance in cue-elicited craving, over and above negative affect.
Methods: In the current study, 108 SUD treatment-seeking adults with current PTSD and alcohol dependence were presented with 4 counter-balanced trials consisting of an audio script presentation (personalized trauma or neutral script) followed by a beverage cue presentation (alcohol or water).
Results: Findings were generally consistent with hypotheses: exposure to alcohol cues increased both positive and negative affect, and positive affective responses explained significant incremental variance in both self-reported craving and salivation, but only when cues were accompanied by neutral not trauma imagery.
Conclusions: Findings highlight the importance of independently assessing both positive and negative affective responses to cues in understanding the complexity of cravings in individuals with comorbid PTSD and alcohol dependence.
Financial Support: This research was supported, in part, by National Institute on Alcohol Abuse and Alcoholism grant R01AA016816 (PI: Coffey).

487

INTIMATE PARTNER VIOLENCE AND SUBSTANCE MISUSE: A SURVEY OF WOMEN USING SPECIALIZED POLICE STATIONS IN SAO PAULO, BRAZIL.

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Aims: To investigate the association between substance use by perpetrators and the severity of Intimate Partner Violence among women attending police stations specialized in violence against women (Women's Police stations – WPS) in Sao Paulo, Brazil.
Methods: We interviewed 794 women who filed a domestic violence complaint at one of the nine existing WPS in São Paulo city. Questions regarding violence were based on the multi-center study tool of the WHO, and were categorized as psychological, physical and sexual violence. To identify the severity of the violence episode we summed all positive items for each type of violence and secondly we classified as mild, moderate and severe. Victims also informed about the use of substance by the perpetrator. The association was estimated by Ordered Logistic Regression.
Results: Most participants reported more than one type of violence (79.1%). Nearly all women (98.7%) reported at least one positive item for psychological violence, 79.2% for physical and 12.0% for sexual violence. In nearly half of all violence episodes women reported that the perpetrator were under the effect of a substance. Alcohol use by perpetrator was reported in 34.4% and illicit drug in 15.4%. The severity was higher for illicit drugs for all types of violence compared to those who had not used any substance (psychological: OR: 2.17, 95%CI: 1.41-3.36; physical: OR: 2.03, 95%CI: 1.37-3.00; and sexual: OR: 2.58, 95%CI: 1.40-4.76). Under the effect of alcohol, associations were statistically significant for psychological (OR=1.50, 95%CI: 1.10-2.06) and physical (OR: 1.57, 95%CI: 1.17-2.10), but not with sexual violence (OR=0.70; 95%CI 0.41-1.22).
Conclusions: These findings suggest that the nature of the substance used by aggressors is associated to the severity and type of violence attended at WPS. WPS and Health Services should work together to promote preventive programs for both public health issues: Intimate Partner Violence and substance abuse.
Financial Support: Grant FAPESP 07/59906-8 and financial support of AFIP (Associação Fundo de Incentivo à Pesquisa)

488

THE (MIS) ESTIMATION OF NEIGHBORHOOD EFFECTS IN SUBSTANCE USE EPIDEMIOLOGY.

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Aims: There has been a longstanding interest in the role of neighborhood effects on positive youth development. This work considers the specification and estimation of neighborhood effects, particularly decomposition of variation (e.g., neurological, familial, neighborhood) within neighborhoods, and Bayesian spatial regression and geospatial information system (GIS) approaches to model the effect of neighborhood effects that consider the geographical proximity of neighborhood types to one another.
Methods: Using data drawn from the Project on Human Development in Chicago Neighborhoods, we present a statistical model that defines two types of neighborhood effects: One for parents choosing neighborhoods to raise their children and another for state and federal agencies to evaluate neighborhood interventions (e.g., retail tobacco and alcohol outlet restrictions, local prevention programming). The data are drawn from 4 cohorts of youth (ages 9, 12, 15, and 18) surveyed over 3 years, and their primary care givers. Extensive neighborhood level data were collected from a systematic social observation rating of all neighborhoods, and a neighborhood survey all a sample of all neighborhood residents. The final sample included residents of 80 neighborhoods in Chicago (n=2213).
Results: In the first model, we illustrate the direct effect of neighborhood inequality, tobacco/alcohol outlet availability, and access to prevention resources (e.g., youth centers), and how these effects erode in subsequent models when including meditational mechanisms related to family functioning (e.g,. parental monitoring, parent substance use), and individual differences in mental status (e.g., neurological functioning—impulsivity/sensation seeking, mood/anxiety disorders). Finally, we re-estimate these models using a Baysian approach to incorporate the spatial dependencies among neighborhoods and their adjacent areas as well.
Conclusions: We discuss the role of neighborhood evaluations in a broader agenda of research in support of neighborhood improvements.
Financial Support: R01DA023377 (kral, PI) and R01DA030427 (Novak, PI)

489

ARIPIPRAZOLE EFFECTS ON CIGARETTE SMOKING AMONG COCAINE USERS.

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Aims: Aripiprazole (AZ) is an atypical antipsychotic with partial D2 agonist activity. Studies among schizophrenic smokers have suggested that atypical antipsychotics may reduce cigarette (CIG) smoking. The study aims were to: 1) validate a model of nicotine withdrawal in an inpatient research setting, and 2) evaluate the efficacy of AZ to reduce smoking, nicotine withdrawal and craving. These were secondary aims from a trial that evaluated the effects of AZ on cocaine use.
Methods: Healthy adults currently using cocaine and CIGs completed a randomized, placebo-controlled inpatient study. After a single blind placebo lead-in (~9 days), subjects were randomly assigned to double blind oral AZ (0, 2, or 10 mg daily, N=7/group) for ~18 days. Two smoking topography sessions were completed in both the placebo lead-in and the AZ dose phase, one after 40 hours of CIG abstinence and one in satiety. Session outcomes included number of CIGs smoked and smoking topography measures (e.g., puff duration) of the first CIG. Also, at baseline and after each smoked CIG, expired breath CO levels, CIG drug effects and craving, and nicotine withdrawal were assessed. Daily CIG use was measured by subject and nurse report and collection of smoked CIGs.
Results: During both phases, subjects had lower baseline CO levels, higher baseline nicotine withdrawal and craving scores, and smoked more in sessions under abstinent versus sated conditions ($p<0.05$). However, abstinence had no effects on topography outcomes. AZ dose dependently increased nicotine withdrawal scores during abstinence ($p<0.05$). Surprisingly, ratings of 'any effects' from the first smoked CIG in both abstinent and sated sessions were highest in the 2mg AZ group and lowest in the 10mg AZ group ($p<0.05$). Daily CIG use did not differ by AZ dose.
Conclusions: These data suggest that 40 hours of supervised abstinence is viable in an inpatient setting, yielding a reliable and valid model of nicotine withdrawal. These data do not support AZ as a treatment for smoking cessation.
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490

LONGITUDINAL ANALYSIS OF THE UNEMPLOYMENT RATES OF VETERANS ENTERING MISSION.

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Aims: From 2005-2008, homeless veterans with co-occurring mental health and substance use disorders were offered placement in a low intensity treatment engagement intervention, Maintaining Independence and Sobriety through Systems Integration, Outreach, and Networking (MISSION) program, to assist with transitioning from residential care to the community.
Methods: Homeless veterans with co-occurring mental health and substance use disorders (n=354) participated in three assessment interviews at baseline, 6, and 12 months. Employment data were collected and compared across grant years.
Results: Results show that at 12 months post treatment, there was an increase in unemployment from FY 2005 to FY 2008. Specifically, yearly rates were 2005 (26.8%), 2006 (46.2%), 2007 (45.8%), and 2008 (64.7%). Moreover, this increase in unemployment rates across grant years was independent of treatment assignment. Additional comparisons to matched local and national samples will be presented.
Conclusions: The current research addresses the employment status and needs of homeless veterans within a changing economy. While VA services reduced unemployment rates during study participation, this economic downturn drastically undercut the effectiveness of employment services offered by the VA, as demonstrated by the increase in unemployment from 2005-2008. Results provide evidence to support President Obama and Secretary Shinseki's Employment Expansion Initiative and partnerships with other government agencies.
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491

HIV RISK BEHAVIORS BY AGE GROUP AMONG PRESCRIPTION OPIOD ABUSERS IN SOUTH FLORIDA.

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Aims: Recent research has indicated elevated levels of risk taking among young treatment-based prescription opioid abusers. However, very few studies have systematically examined the effects of age on patterns of HIV and hepatitis risk among large, diverse samples of prescription opioid abusers. This paper examines HIV-related risk factors that differ by age group as reported by participants in a South Florida study targeting opioid abusers.
Methods: Eligible respondents were 18 years of age or older and reported misuse of a prescription drug 5 or more times in the previous 90 days. Those who reported misuse of a prescription opioid (N=791) were included in the current analysis. Trained interviewers administered standardized health and social risk assessments, including detailed drug use histories, routes of drug administration, and sexual risk behaviors. Descriptive analyses compare patterns of risk stratified by age. 42% of participants were18-29 years old (n=330) and 58% of participants were 30 years old and above (n=461).
Results: Our findings indicate significantly elevated HIV risk behaviors among the younger age group compared with the older participants. This includes needle risk behaviors such as recent intravenous prescription opioid use ($p<.001$), reusing unsterile needles ($p=.04$), letting someone else use a needle after them ($p=0.048$) and allowing someone else to inject them ($p < 0.001$). Participants ages 18-29 were also significantly more likely than older participants to report sexual risk behaviors, including sex with an injection drug user ($p=0.002$), and recent unprotected sex ($p < 0.001$).
Conclusions: Our findings demonstrate that younger opioid abusers are more likely to inject their prescription opioids, are more likely to endorse unsafe needle use behaviors, and to participate in risky sexual behaviors, which present an elevated risk for exposure to HIV and hepatitis C. Given this, age-targeted disease prevention measures appear warranted.
Financial Support: This work was supported by NIH Grant R01 DA021330.

492

EMOTIONAL RISK FACTORS FOR SUBSTANCE ABUSE IN A CHRONIC PAIN POPULATION.

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Aims: The aim of the present study was to evaluate risk factors for prescription opioid misuse, abuse, and dependence in chronic pain patients, and examine whether adding emotional factors to the traditionally considered risk factors improves prediction of prescription and substance misuse.
Methods: Participants were 100 patients with chronic pain (lasting > 3 months) who were receiving a self-administered opioid medication through a local pain management clinic. The sample averaged 47.57 years old (SD = 11.57), was 53% female, and primarily African-American (81.0%). Researchers assessed personal and family history of substance use, pain, personality, emotion regulation factors, and symptoms of prescription opioid use disorders and use of alcohol and illicit substances.
Results: Regarding presence of diagnoses: 26% reported a current opioid use disorder, 24% alcohol use disorder, and 25% other substance use disorder; 38% of participants had a score indicative of problematic use on the Prescription Drug Use Questionnaire (PDUQ). A regression predicting prescription misuse was significant, ($p < .01$), and the addition of ambivalence over emotional expression to the model explained a significant increase in variance (change in $R2 = .03$, $p < .05$); greater ambivalence predicted greater prescription misuse ($\beta = .22$, $p < .05$). In a regression predicting prescription opioid abuse and dependence symptoms, higher ambivalence over emotional expression was marginally predictive ($\beta = .18$, $p = .08$). Surprisingly, trauma symptoms did not predict prescription misuse ($p = .66$) or symptoms of opioid abuse or dependence ($p = .75$).
Conclusions: In addition to replicating the role of personal and family history of substance use problems, this study indicates that ambivalence over emotional expression is an additional risk factor for prescription opioid misuse and use disorders. These findings suggest that suppressing emotions is problematic.
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493

EVALUATION OF THE BUPROPION-INDUCED SENSITIZATION TO THE LOCOMOTOR ACTIVITY.

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Aims: Methamphetamine is one of the strongest addictive psychostimulants that dramatically affects central nerves system functions. Accumulating evidence suggests that repeated administration of psychostimulants induces long-lasting neuronal changes, so called neuroplasticity. Neuroplasticity in dopaminergic neurotransmission provides neuronal framework change for altered behavioral changes (like sensitization), which underlies the development of psychological dependence on drugs of abuse. Bupropion is an atypical antidepressant and smoking cessation aid, and pharmacological effects of bupropion are depend on the inhibition of the uptake of dopamine and norepinephrine. Thus, pharmacological profiles of bupropion are similar to those of cocaine, however little information is available whether bupropion itself may induce the abuse potential or not. Therefore, to imply the abuse potential of bupropion, we examined the bupropion-induced sensitization to the locomotor activity in mice.
Methods: Male ddY mice (20-25g) were used to measure the locomotor activity. Bupropion (30 mg/kg, s.c.) or methamphetamine (2 mg/kg, s.c.) was administered repeatedly for 5 times.
Results: Acute administration of bupropion -induced significant locomotor activity, like those induced by methamphetamine. Furthermore, repeated administration of bupropion and methamphetamine induced a significant sensitization to the locomotor activity. Furthermore, cross-sensitization was observed between bupropion- and methamphetamine-induced sensitization to the locomotor activity.
Conclusions: These results suggest that bupropion could induce sensitization to locomotor activity which is mediated by activation of mesolimbic system. Therefore, further examination is required to demonstrate that these psychostimulants-like effects of bupropion may link to their reinforcing effects.
Financial Support: The Supported Project for Creating a Strategic Research Infrastructure in Private Universities of the Ministry of Education, Culture, Sports, Science and Technology of Japan.
Project: Pharmaceutical Studies on Change in Higher Cerebral Function by Diabetes and pain.

494

RELATIONSHIP BETWEEN POST TRAUMATIC STRESS DISORDER (PTSD) AND SUBSTANCE USE AMONG NIGERIAN ADOLESCENTS?

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Aims: This study aimed to examine the relationship between PTSD and substance use among adolescents.
Methods: A cross-sectional survey of 120 Nigeria students who following informed consent completed instruments including WHO Students' Drug Use Survey and MINI to elicit information on socio-demographics, psychoactive substances and PTSD.
Results: Majority were males (77.5%), from monogamous homes (77.5%) and lived with parents (81.7%). Current, and lifetime use of alcohol/other drugs was 30% and 45% respectively; 12 month prevalence of PTSD was 6.7%. Students with substance use and PTSD did not differ significantly from those with substance use but without PTSD on sociodemographic variables. However, adolescents with substance use disorder were more likely to report a history of trauma/abuse than adolescents without substance use. And adolescent males had higher rates of co-morbid PTSD and substance use (76.5%) than females. PTSD was significantly associated with alcohol use compared with other drugs (40% vs. 28.4%).
Conclusions: The diagnosis of PTSD was significantly associated with high risk of adolescents' alcohol abuse and adolescents with PTSD should be diagnosed early so that prompt intervention be instituted to prevent the onset of complications such as substance abuse.
Financial Support: Self-funded

495

CLINICAL EFFICACY OF DISULFIRAM AT HIGHER DOSES IN COCAINE-DEPENDENT PATIENTS.

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Aims: Previously we showed that disulfiram (62.5, 125 mg/day) increased COC use relative to placebo and DSF (250 mg/day) in COC dependent methadone patients. These results suggested that higher doses of DSF may be necessary to be efficacious. This 14-wk, double blind, placebo-controlled clinical trial examined the efficacy of DSF at higher doses.
Methods: COC dependent participants (N=82) with opioid dependence (OD; N=48) were inducted onto methadone while those without opioid dependence (NOD; N=34) underwent a two-week baseline period (wks 1-2) and then both groups were randomized to receive DSF at 0, 250, 375 or 500 mg/day during weeks 3-14. In addition, all participants received weekly 1-hour cognitive behavior therapy (CBT). Thrice-weekly urine samples were tested for the presence of COC metabolites.
Results: Med groups generally did not differ on subject characteristics or retention, although OD participants were retained significantly longer than NOD participants (10.56+/-4.03 vs.7.64+/-4.34 weeks, p=0.002). COC-positive urines decreased over time in the 375 mg DSF group, but not 250 or 500 mg DSF groups, relative to the placebo group (p<0.02). This 375 DSF effect was also significant in the OD group (p<0.02), but not the NOD group (p=0.48), although COC use did show a similar pattern of effect in the NOD group. The most commonly reported adverse event was nausea/vomiting/stomach discomfort, with severity of symptoms being positively related to dose. Five participants were discharged due to AEs that were at least possibly related to DSF. Two participants left the study because they did not like/want to take DSF.
Conclusions: These preliminary results suggest that the therapeutic dose range for disulfiram may be higher than 250 mg/day and that disulfiram at doses as high as 500 mg/day was relatively well tolerated.
Financial Support: Supported by NIDA grants DA13441, 5T32DA022981 and CTSA grant 1UL1RR029884.

496

PREDICTING DRUG USE AT 6 MONTHS USING CHANGES IN SELF-REPORT OF MOTIVATION, INTENTION, AND EFFICACY DURING A COMPUTER-DELIVERED BRIEF INTERVENTION SESSION.

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Aims: Participant ratings of state variables such as motivation or intention to quit have been shown to change significantly during single-session computer-delivered brief interventions for substance use, and to predict later drug use. These ratings may have an important role, for example as a proxy outcome for fast, inexpensive developmental trials of various brief intervention configurations. These trials could optimize brief interventions before submitting them to a traditional clinical trial. This study was designed to replicate, in a new sample, the ability of in-session ratings to predict later drug use.
Methods: This analysis used data from a computer-delivered brief intervention trial with drug-using post-partum women. A total of 41 participants in that trial were assigned to the computer-delivered brief intervention for drug use and completed 6-month follow-up, including provision of urine samples, and so were included in this analysis. All participants provided pre- and post-session ratings for five motivation-related state variables (intention to change, confidence, etc.). Changes in those ratings from pre- to post-intervention session were combined and used to predict 6-month drug use (confirmed self-report).
Results: The final dynamic change scale consisted of the mean change score (post-pre) for five state ratings. This scale, which was normally distributed and ranged from -4.6 to 7.2, showed an area under the curve (AUC) of .73 in predicting 6-month drug use (p = .039).
Conclusions: This analysis provides further evidence that dynamic, during-session changes in state variables are consistently related to drug use months later. Although preliminary, these findings suggest that in-session ratings may support developmental trials using proxy outcomes, and perhaps other important new methodologies. Further research should examine a wide range of potential dynamic indicators and scoring approaches.
Financial Support: R01DA021329

497

THE ASSOCIATION BETWEEN STRESS SENSITIVITY AND ATTENTION/EXECUTIVE FUNCTION IN MALE COCAINE-DEPENDENT TREATMENT-SEEKERS.

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Aims: Recent models on cocaine abuse have proposed stress effects on cognitive function is associated with decreased time to relapse and difficulty achieving abstinence. The purpose of this study was to investigate the role of stress reactivity on attention/executive function in cocaine users.
Methods: Eleven cocaine-dependent men were administered the Cold Pressor Test (CPT; physical stressor), a stress-inducing audio imagery (psychological stressor) and a neutral audio imagery. Stress sensitivity was measured by heart rate (HR), systolic blood pressure (sBP), and diastolic blood pressure (dBP) before and after introduction of stressors. On a separate day, participants completed a battery of assessments including the Wisconsin Card Sorting test (WCST), the Drug Stroop (DS), and the Trailmaking Test.
Results: Both the CPT and the audio imagery increased sBP from baseline, and the physical stressor increased dBP ($p<0.05$; Wilcoxon Signed-ranks test). The sBP effect of audio imagery (stress –neutral) was positively correlated with Trails B completion time (Spearman's $\rho=0.79$, $p<0.05$). The dBP effect of audio imagery was positively correlated, at the trend level, with WCST standard errors ($\rho=0.73$, $p=0.06$). There were no relationships between CPT and performance on cognitive measures.
Conclusions: Psychological stress sensitivity was associated with decreased performance on attentional/executive cognitive tasks while in non-stressful conditions. Physical stress sensitivity was not associated with cognitive performance. Attention is relevant to the ability to attach salience to alternate reinforcers that may displace cocaine as the preferred object. Future studies should look at how stress affects attention and how it determines success in achieving or remaining cocaine abstinent.
Financial Support: NIDA grant: K23DA027044-01 and K24022412

498

AFRICAN-AMERICAN WOMEN'S TOBACCO AND MARIJUANA USE: THE EFFECTS OF FAMILY HISTORY AND DRUG USE RISK PERCEPTIONS.

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Aims: Tobacco and marijuana are often considered gateway drugs and positive family relationships may be protective for substance use initiation and continued use among African Americans. Moreover, perceptions about the risk of tobacco and marijuana may be shaped by one's family, particularly among African Americans. Thus, this study will examine the effects of a family history of substance abuse and drug use risk perceptions on both tobacco and marijuana use in the past 6 months among a sample of African American women.
Methods: This study uses data from 386 African American women collected as part of the Black Women in the Study of Epidemics protocol. Family history and perception of risk variables that are significantly associated with either tobacco or marijuana use are included in multivariate logistic regressions.
Results: In the past 6 months, 36% of participants used marijuana and 55% used tobacco. Younger participants (OR=.97), those who perceived minimal harm from regular marijuana use (OR=.65) and those who have a family member with substance abuse problems (OR=4.30) were significantly more likely to use tobacco. Likewise, younger participants (OR=.96), those who perceived minimal harm from regular marijuana use (OR=.41) and those who have a family member with substance abuse problems (OR=4.63) were also significantly more likely to use marijuana. Women recruited from prison or probation (OR=.40), compared to the community, were less likely to use marijuana.
Conclusions: Perceptions of harms associated with regular marijuana use influence both tobacco and marijuana use, suggesting the need for early prevention interventions to accurately portray risks and reduce initiation. While some of the family history variables considered were not associated with adult tobacco or marijuana use, the most robust correlate in both models was having a family member who had substance abuse problems, providing support for both the genetic and learned components of addiction.
Financial Support: This research is funded by NIDA (R01-DA022967, PI: Oser).

499

POLICY AND PROGRAM BARRIERS FOR DRUG-USING WOMEN TO ACCESS TREATMENT SERVICES IN THE REPUBLIC OF GEORGIA.

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Aims: Drug-using women represent a seriously understudied and underserved segment of the drug-using population in the Republic of Georgia. Women constitute less than 1% of patients in Georgian drug treatment centers. Understanding barriers and strengths regarding policy, program, social, psychological and other factors impacting women's access to drug-related treatment services represents an important public health objective.
Methods: In-depth qualitative interviews with 55 drug-using women and 34 health-service providers were conducted and analyzed.
Results: nVivo analyses indentified the following factors as impacting drug-using women's access to and demand for drug services: An overall tendency on the part of all Georgian women not to seek adequate medical care; a perceived lack of resources for long-term treatment for drug use; a lack of a supportive and tolerant treatment service environment coupled with judgmental attitudes toward drug-using women on the part of service providers; and, harsh drug legislation that compromises the ability to provide drug treatment and harm reduction services by social service agencies and drug treatement providers, and that drives drug-using women from seeking and/or engaging in any services.
Conclusions: Strictly confidential comprehensive women-specific drug treatment services need to be developed with a focus on long-term sustainability. Significant efforts should be directed towards educating staff of the women-specific programs in order to ensure a non-judgmental and supportive environment that would attract drug-using women to and retain them in treatment. Policy reform to eliminate legal barriers for drug-using women to seek assistance should be implemented.
Financial Support: Supported by NIDA grant R01DA029880

500

SUBSTANCE USE OUTCOMES AMONG PREGNANT AND POSTPARTUM WOMEN IN METHADONE MAINTENANCE.

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Aims: Pregnancy may lead opioid dependent women to seek treatment, but the postpartum period may increase relapse risk. This study aimed to determine whether pregnancy status (non-pregnant, pregnant, or postpartum) is associated with opiate abstinence among women in a methadone maintenance treatment program (MMTP).
Methods: Using the medical record of an urban MMTP, we conducted a retrospective study of 315 women who enrolled from 2006-2010. We examined the first 18 months of enrollment for each woman. The primary independent variable was pregnancy status, a three-category (non-pregnant; pregnant; postpartum), time-dependent variable. The primary outcome was opiate abstinence, defined as giving an opiate-negative urine test. To account for multiple tests from each woman, generalized estimating equations logistic regression models were used to evaluate the association between pregnancy status and giving an opiate-negative test.
Results: Compared to non-pregnant women (n=91), pregnant women (n=224) were younger and more likely to be white and new to MMTP. Pregnancy status was significantly associated with giving an opiate-negative test ($p<0.001$) when adjusting for age, race, living situation, HIV status, prior MMTP, transferring from another MMTP, smoking status, and time from enrollment to each test. Pregnant (AOR 3.26, 95% CI 2.17, 4.90) and postpartum women (AOR 1.99, 95%CI 1.21, 3.30) had significantly higher odds of giving an opiate-negative test compared to non-pregnant women; pregnant women also had higher odds of giving an opiate-negative test than when postpartum (AOR 1.64, 95%CI 1.05, 2.55).
Conclusions: Both pregnant and postpartum women had higher odds of being abstinent from opiates than women who enrolled in MMT while non-pregnant. In addition, women had higher odds of being abstinent when pregnant than when postpartum. A better understanding of the needs of postpartum women with opioid dependence may identify ways to help them maintain their recovery.
Financial Support: National Institutes of Health R25DA13582 and T32 AI052074-06A2.

501

THE BIDIRECTIONAL ASSOCIATION BETWEEN ALCOHOL, MARIJUANA, AND CO-OCCURRING ALCOHOL AND MARIJUANA USE DISORDERS WITH MAJOR DEPRESSION.

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Aims: To describe the association between 1) prevalent alcohol use disorders (AUD), marijuana use disorders (MUD), and co-occurring alcohol and marijuana use disorders (AUD+MUD) at baseline with incident depression at follow-up; as well as, 2) prevalent depression at baseline with incident AUD, MUD, and AUD+MUD at follow-up.
Methods: Data for these analyses came from the NESARC (Wave 1 N=43,093; Wave 2 N=34,653), a nationally representative longitudinal survey of non-institutionalized residents of the United States. The sample for the first aim was restricted to individuals who had a lifetime alcohol and/or marijuana use disorder (abuse and/or dependence) and no history of depression at baseline, and were successfully re-interviewed at Wave 2 (n=13,872). The sample for the second aim was restricted to individuals with no lifetime alcohol or marijuana use disorder who had prevalent depression at baseline, and were followed up at Wave 2 (n=3,320). Descriptive statistics and logistic regression analyses were used to describe the associations between substance use disorders and depression.
Results: Preliminary findings indicate that relative to individuals without AUD or MUD, having an AUD (adjusted odds ratio (aOR)=1.35, CI=1.15-1.60), MUD (aOR=1.78, CI=1.17-2.71), and AUD+MUD (aOR=1.54, CI=1.20-1.98) increased the probability of developing incident depression at follow-up. Furthermore, individuals with baseline depression were more likely to develop incident MUD at follow-up (aOR=2.28, CI=1.28-4.05).
Conclusions: Although positive associations were found bidirectionally, the strength of the associations for alcohol and/or marijuana with depression differed by specific substance, with a tendency for stronger associations found with marijuana use disorders. The findings have implications for preventive as well as treatment programs and initiatives.
Financial Support: This work was supported by: T32DA007292 (Furr-Holden), DA023434 (Martins), and AA016346 (Crum).

502

MODELING LONGITUDINAL POST-TREATMENT CLIENT OUTCOMES FROM OPEN-ENROLLMENT THERAPY GROUPS.

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Aims: In studies of group therapy interventions delivered in alcohol and other drug (AOD) treatment settings, primary client-level outcomes such as AOD use are frequently measured following group therapy. Our analytic approach accounts for the complex correlation structure of client post-treatment outcomes induced by open enrollment.
Methods: We employ multiple membership (MM) modeling to link the effect of each session attended by a client to his/her outcomes. Under standard MM, post-treatment outcomes are modeled using conditionally independent random session effects. We combine MM with conditional autoregression (CAR) to relax this assumption, allowing the analytic model to better reflect the overlap in client attendance session-to-session. We also employ longitudinal growth modeling, under which the posterior distribution of growth parameters is estimated using a non-parametric approach that overcomes parameter identification limitations of standard parametric growth models. We demonstrate these methods in the context of an intervention to deliver group cognitive behavioral therapy to clients with depressive symptoms who are enrolled in residential alcohol and other drug treatment.
Results: MM modeling, with or without correlated session effects, improves upon models that ignore client session attendance with respect to model fit statistics. MM-CAR produces a modest improvement in model fit but provides sharper visualization of session effects. Nonparametric modeling of growth parameters results in improved model fit and greater flexibility to capture the scope of change over time in client outcomes.
Conclusions: Our approach provides a way to account for correlation of client post-treatment outcomes due to open-enrollment into group therapy and to address researchers' concerns about the robustness of the statistical significance of treatment effect estimates given the correlation of outcomes among clients attending open-enrollment therapy groups. To promote the dissemination of our methodology, we are developing a freely available R software package.
Financial Support: NIH/NIAAA Grant R01AA019663

503

EFFECT OF KETAMINE ON LOWER URINARY TRACT SIGNS AND SYMPTOMS.

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Aims: Ketamine is an NMDA-antagonist anesthetic that is also used non-medically. Recent reports have described ulcerative cystitis and other lower urinary tract signs and symptoms (LUTSS) after non-medical ketamine use. The prevalence of this syndrome in ketamine users is unknown. We therefore sought to determine whether individuals using ketamine are more likely to report LUTSS compared to other substance users.
Methods: Participants were recruited through an online survey on erowid.org, a drug information website. The survey collected basic demographic information, psychoactive drug use history, and information regarding symptoms of LUTSS (history of increased urinary frequency, urgency, incontinence, hematuria, and dysuria).
Results: 18,848 individuals responded. Lifetime and past 6-month use of ketamine were 3,514 (18.6%) and 1,085 (5.8%), respectively. On bivariate analysis, any lifetime use of ketamine was significantly associated with frequency, urgency, and incontinence (OR = 1.30, 95% CI: 1.17-1.44; OR = 1.21, 1.09-1.33 and OR = 1.29, 1.08-1.53, respectively). Ketamine use in the last 6 months was significantly associated with frequency and urgency (OR = 1.51, 95% CI: 1.27-1.77; OR = 1.26, 95% CI: 1.07-1.48 respectively). These associations remained significant after Benjamini-Hochberg corrections for multiple comparisons.
Conclusions: Both lifetime and past-6-month use of ketamine are associated with increased odds of developing LUTSS compared to other psychoactive drug use. Internet-based surveys are an efficient and effective alternative to conventional methods of surveying hard to reach populations.
Financial Support: None

504

PROSPECTIVE EFFECTS OF ADOLESCENT ADHD, CONDUCT DISORDER, NOVELTY SEEKING, AND SUBSTANCE USE ON YOUNG ADULT DRUG DEPENDENCE.

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Aims: The purpose of this study was to examine the association between adolescent measures of Attention Deficit Hyperactivity Disorder (ADHD) and conduct disorder (CD) on young adult alcohol, tobacco, and cannabis dependence while controlling for adolescent substance use and novelty seeking (NS).
Methods: Participants were 390 male and female twins from the Center for Antisocial Drug Dependence who participated at the first (mean age = 17.6, SD =.49) and second (mean age = 22.6, SD =.97) waves of assessment. Structured interviews were used to obtain symptom levels for the inattention and hyperactivity subscales of ADHD, CD, NS, number of substances used, and DSM-IV drug dependence symptoms. Robust linear regression models were used to examine the effects of adolescent ADHD, CD, and NS on young adult drug dependence symptom levels.
Results: Adolescent substance use and NS were generally predictive of young adult drug dependence, whereas the predictive effects of ADHD and CD varied by substance. After controlling for NS and substance use, ADHD Hyperactivity/Impulsivity symptoms independently predicted alcohol (t = 2.53, B = 0.16, p =.01) and illicit drug dependence symptom levels (t = 2.17, B = 0.20, p =.03), as well as dependence vulnerability (t = 2.05, B = 0.13, p =.04). CD symptoms predicted only alcohol dependence symptoms (t = 2.39, B = 0.13, p =.02).
Conclusions: These findings suggest that adolescent substance use and novelty seeking tendencies are robust indicators of future drug problems. On the other hand, the effect of ADHD and CD symptoms varies by substance. These findings build upon the existing literature by showing that components of ADHD and CD are important risk factors for future drug problems.
Financial Support: This work was supported by T32MH019927 (Palmer), MH063207, HD010333, DA011015, and DA021913.

505

DETERMINATION OF BETA-CARBOLINES IN SMOKE CONDENSATES FROM COMMERCIAL TOBACCO CIGARETTE BRANDS.

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Aims: Harmane and norharmane are beta-carbolines found in varying quantities in cooked foods and tobacco smoke. These compounds have been shown to be monoamine oxidase inhibitors. Monoamine oxidase inhibition not only affects levels of neurotransmitters such as dopamine, but is heavily involved in drug interactions. While analyzing smoke condensates for related nicotine and tobacco research, consideration was given as to whether a GC method used to quantify menthol, nicotine and minor alkaloids such as myosmine, anabasine, and nornicotine could also be used to quantify harmane and norharmane. A GC-MS/MS method based on the Coresta method was developed to incorporate analysis of harmane and norharmane while simultaneously quantitating nicotine, menthol, and the minor alkaloids myosmine, anabasine, and nornicotine.
Methods: Cigarette smoke condensates from three commercial tobacco cigarette brands were collected by smoking cigarettes on a Borgwaldt KC smoking machine. The condensates were extracted and analyzed by injection into an Agilent GC/MS/MS equipped with a DB-5MS capillary GC column. The separated peaks were analyzed using a multiple-reaction monitoring (MRM) method to identify and quantitate the analytes present.
Results: Harmane and norharmane were detected in low µg quantities in the smoke condensate of commercial cigarette brands tested. Concentrations of nicotine and menthol were found to be similar to those determined by a previously developed GC-FID method.
Conclusions: Quantitation of harmane and norharmane can be accomplished concurrently with nicotine, menthol, myosmine, anabasine and nornicotine using a GC/MS/MS (MRM) method.
Financial Support: Funding for this work was provided by RTI International in the form of an independent research and development grant.

506

SEX DIFFERENCES IN NEUROPSYCHIATRIC AND COCAINE SEEKING BEHAVIORS AMONG MICE EXPRESSING HIV-1 TAT PROTEIN.

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Aims: Substance abuse is comorbid with HIV infection, and neuropsychiatric effects of HIV may be greater among men compared to women (a reversal of the typical sex difference). The neurotoxic HIV-1 accessory protein, Tat, is known to impair memory and interacts with psychostimulant drugs to produce synergistic neurodegenerative effects. These data suggest that Tat may potentially serve as a biological mediator of HIV-1-induced behavioral dysfunction. Given that sex steroids influence affective/hedonic behavior and neurodegeneration, we hypothesized that anxiety-like and cocaine-seeking behavior would be enhanced among mice exposed to Tat protein, but that the female hormonal cycle would offer potentially "protective" effects.
Methods: Experiments used GT-tg bigenic mice (n=15-20/group), which express Tat protein under doxycycline (Dox) treatment. One week following Dox or saline treatment, proestrous or diestrous female mice were yoked to male counterparts and (1) were assessed for performance in the marble burying task or (2) underwent cocaine (10 mg/kg/d, s.c.) conditioned place preference (CPP) with assessments occurring on days of proestrus or diestrus.
Results: Among males, induction of Tat protein increased the number of marbles buried in the marble-burying task as compared to saline-treated controls. All males demonstrated significant cocaine-CPP; but Tat-induction potentiated this effect 5-fold. Sex differences are described as cycle-dependent differences among females expressing Tat-induced modulation of neuropsychiatric and drug-seeking behavior.
Conclusions: HIV-1-associated Tat protein may mediate neuropsychiatric and drug-seeking sequelae that are associated with viral infection. Fluctuations in endogenous hormones may modulate HIV-related pathology, underlying sex differences in behavioral dysfunction.
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507

INDIVIDUAL DIFFERENCES IN SUBSTANCE USE AS A FUNCTION OF DRD2 ALLELE STATUS.

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Aims: A growing scientific literature suggests that vulnerability for drug abuse is influenced by genetics. Polymorphisms of the D2 dopamine receptor gene (DRD2) in particular are believed to be associated with vulnerability for addictive behaviors. Prevalence of the A1 allele, for example, is more frequent among drug abusers compared to controls. The likely mechanism is a reduced number of DA receptor binding sites in DRD2 A1 carriers, with these individuals showing greater sensitivity to the reinforcing effects of drugs.
Methods: We are currently conducting a NIDA-funded trial examining whether prospectively-identified DRD2 A1 carriers and noncarriers differ in their response to d-amphetamine. Participants are adults without history of alcohol or drug dependence. While the primary aim is to examine the role of genotype in d-amphetamine reinforcement, the study also provides an opportunity to examine a range of other characteristics in the total sample. We hypothesize that A1 carriers will report greater drug use and impulsivity at study intake compared to noncarriers.
Results: Thus far, we have screened 144 adults(48 A1+,96 A1-). Participants are 24 yrs old, 41% female and have 14.5 yrs of education. Preliminary analyses show several significant differences, with A1 carriers reporting more episodes of binge drinking, alcohol and drug related blackouts and illicit benzodiazepine use, greater lifetime history of cigarette smoking, and higher scores on the Barratt Impulsivity Scale ($p<.05$). There is also a nonsignificant trend toward carriers reporting more illicit stimulant use ($p=.07$) and higher Sensation Seeking ($p=.06$) than noncarriers.
Conclusions: These preliminary results suggest that, even among a healthy sample, those with the DRD2 A1 allele appear to have characteristics suggestive of elevated drug use and impulsivity relative to noncarriers. Full analyses of these and other psychosocial measures will be available from the completed study by June 2012. This study will represent the first thorough investigation of psychosocial and drug use characteristics as a function of DRD2 A1 allele status.
Financial Support: Support: R03DA027480 & T32DA007242

508

EFFECTS OF METHADONE ADMINISTRATION DURING PREGNANCY ON HUMAN PLACENTAL EFFLUX TRANSPORTER P-GP.

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Aims: Methadone maintenance programs improve maternal and neonatal outcomes. However, the lack of correlation between neonatal abstinence syndrome (NAS) with the dose of methadone administered to the patient continue to be poorly understood. Data reported from our laboratory revealed that trophoblast efflux transporter P-gp in vitro regulates the extent of methadone transfer from maternal to fetal circuits. The aim of this investigation was to determine the effect of methadone administration during pregnancy on the expression and activity of placental P-gp.
Methods: Placentas were obtained from methadone treated patients at delivery. The activity of placental P-gp was determined using preparations of inside-out vesicles (IOV) derived from the apical membranes of trophoblast tissue. The proportion of IOV vesicles in the preparation was determined by the activity of alkaline phosphatase. The activity of P-gp was determined by the rates of 3H-paclitaxel, the prototypic substrate of P-gp, uptake by the IOV. The expression of P-gp protein was determined, semi quantitatively, by Western blots.
Results: The uptake of paclitaxel by IOV prepared from methadone exposed placentas (n=11) was 5.4 +/- 1.2 pmol/mg protein*min which is significantly lower than that revealed 9.8 +/- 1.3 pmol/mg protein*min for placentas (n=10) obtained from healthy pregnancies. However, the amounts of P-gp protein expressed as determined by Western blots appear to be greater for the methadone exposed placentas (0.06 +/- 0.007 µg P-gp / µg total protein) than for the non-exposed (0.03 +/- 0.004; $p = 0.006$).
Conclusions: Placentas from patients exposed to methadone appear to have higher protein expression and lower activity of the efflux transporter P-gp than that for placentas obtained from non-treated patients. Data also revealed no correlation between P-gp expression and its activity. Currently, we are investigating the relation of P-gp activity with methadone dose and the incidence and intensity of neonatal withdrawal (NAS by the Finnegan score).
Financial Support: This work was supported by NIDA DA13431

509

INVESTIGATING THE D3 DOPAMINE RECEPTOR ACROSS ADDICTED COHORTS WITH [11C](+)PHNO PET.

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Aims: In contrast to consistent findings of low D2-type dopamine receptor levels in addiction, levels of the D3 receptor, a member of the D2 family expressed primarily in limbic regions and associated with drug seeking in animals, may be elevated. The study aimed to assess D3 levels in humans, and to determine whether high levels are characteristic across 3 cohorts: methamphetamine-dependent (MA), cocaine-dependent (COC), and pathological gamblers (PG; as of DSM-5 classified as behavioural addiction).
Methods: Subjects included 16 MA (12 male, 27.9 ±5.7yrs) and 16 age- and gender-matched drug-free healthy controls (HC) (14 male, 28.4 ±5.0yrs); 12 COC (11 male, 41.4 ±7.3yrs) and 16 HC (14 male, 35.1 ±9.5yrs); 13 PG (13 male, 32.7 ±2.9yrs) and 12 HC (12 male, 33.8 ±2.9yrs). MA/COC/PG met DSM-IV dependence criteria, and were medication-free and otherwise healthy. Subjects completed a PET scan with [11C](+)PHNO, which binds to D2-type receptors but has higher affinity for D3 than D2, and measures of impulsivity (Eysenck), subjective states (visual analogue scales), gambling severity (SOGS), and risk-taking (Game of Dice).
Results: PHNO binding in the substantia nigra (SN), where 100% of the signal is attributable to D3, was higher in both MA (46%, p=.02) and COC (25%, p=.1) than their HC counterparts. D3-to-D2 ratio (a measure of relative D3 binding in mixed D2/D3 regions) was also higher in both MA (55%, p=.004) and COC (27%, p=.04) than HC. SN binding correlated with self-reported drug-wanting in MA (r=.8, p= .001), and risk-taking in COC (r=.6; p=.03). In PG, binding did not differ from HC (p=.74), but correlated positively with risk-taking (r=.48, p=.096), impulsivity (r=.65, p=.031), gambling (r=.57, p=.042), and alcoholic drinks/wk (r=.49, p=.087).
Conclusions: The study suggests that D3 may be implicated across addictions, and is the first to show elevated D3 receptor binding in human stimulant (but not behavioural) addiction, supporting therapeutic strategies targeting D3-antagonism.
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510

DEPRESSIVE SYMPTOMS IN HEAVY CIGARETTE SMOKERS: THE INFLUENCE OF RACE AND GENDER.

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Aims: Considerable research has documented that tobacco smokers report higher levels of depressive symptoms and greater frequency of depressive disorders than non-smokers. This study examined the possible roles of gender and race in the expression of depressive symptoms.
Methods: Subjects were drawn from two large genetic studies of nicotine dependence. For the entire sample (N=4758), 46% were male, 68.2% African-American (AA) with the remainder European-American (EA), and mean age=42.8, 68.3% were employed, most were high school educated or higher, and 46% were married. Average CES-D score was 6.5. Amongst smokers, mean cigarettes per day was 27.4, and FTND score was 7.4. Smokers presented with higher CES-D scores than non-smokers (8.7 vs. 4.9, p<0.001).
Results: When examined based on categorical score ranges, fewer smokers scored 0 (38.7% vs. 46.5%), while more smokers scored 16 or above, indicative of possible clinical depression (16.1% vs. 6.3%, p<0.001). Logistic regression controlling for standard demographic variables (chi-square=61.8, p<0.001; OR=2.32, 95% CI: 1.88-2.85), as well as demographics plus social context smoking variables (chi-square=6.8, p<0.01; OR=1.37, 95% CI: 1.08-1.72) supported these findings. Separate logistic models for Race x Gender subgroups including all covariates revealed borderline effects for both AA men and women, but strong effects for EA men (chi-square=7.7, p<0.01; OR=2.46, 95% CI: 1.31-4.65) and women (chi-square=7.4, p<0.01; OR=2.14. 95% CI: 1.24-3.69). Finally, post hoc comparisons based on the entire sample revealed significant differences for EA men and women when comparing smokers to non-smokers, but not AA men or women.
Conclusions: We conclude that heavy smokers do report higher levels of depressive symptoms than non-smokers. Importantly, EA heavy smokers appear to be at elevated risk, which may require greater attention during the course of treatment.
Financial Support: Supported by NIH grant DA-012844.

511

SONOMA COUNTY DEPENDENCY DRUG COURT EVALUATION OUTCOMES AND COST STUDY.

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Aims: 1) To increase the understanding of how the dependency drug court model impacts substance abuse treatment outcomes for women and child welfare service outcomes for children of families affected by substance use.
2) To demonstrate the cost effectiveness of the dependency drug court model in terms of child welfare and substance abuse treatment savings.
Methods: The Sonoma County Dependency Drug Court (DDC) is a 12-month court-supervised treatment program for families whose children have been removed or are at risk of removal as a result of child abuse or neglect associated with a mother's substance abuse. This study employs a quasi-experimental design utilizing a comparison group of families. Program outcomes out to 18 months are assessed in two primary areas: substance abuse treatment services and child welfare service outcomes. A cost analysis calculated daily rates or average costs per client for typical services which were then applied to each group to establish average costs per family and average costs per child.
Results: DDC parents were more likely to enter substance abuse treatment than comparison parents. DDC children were more likely to be in foster care than the comparison children at six months; whereas comparison children were more likely to be on track for adoptions. At 18 months, DDC children were significantly more likely to be reunified and signficantly less likely to be in foster care. Preliminary cost analysis findings indicate savings based on long term outcomes of DDC expansion mothers and children.
Conclusions: Judicial supervision, intensive case management, treatment and court compliance monitoring, and family support offered by the Sonoma County DDC program have been found to have a positive impact on treatment and child welfare outcomes of substance abusing families involved in the child welfare system.
Financial Support: This work is supported through a contract with the County of Sonoma.

512

RACIAL DIFFERENCES OF STIMULANT ABUSERS' PRIOR EXPERIENCES, EXPECTATIONS, AND READINESS TO ENGAGE IN 12-STEP PROGRAMS.

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Aims: Important differences may exist between African American and Caucasian substance abusers regarding involvement in and acceptance of 12-step programs. We examined baseline differences between 171 African American and 224 Caucasian stimulant abusers enrolled in the CTN 12-Step Facilitation clinical trial (STAGE-12) in terms of experiences in and expectations of 12-step groups, understanding of addiction, and spiritual involvement and beliefs.
Methods: Measures included: 12-Step Experiences and Expectations, Survey of Readiness for Alcoholics Anonymous Participation, Your Understanding of Alcoholism and Drug Addiction, and Spiritual Involvement and Beliefs Scale-Revised (SIBS–R).
Results: Caucasian participants indicated a greater likelihood to get involved in self-help groups (Z=3.49, p=.0005) than African American participants, while African Americans scored higher on a scale measuring the perceived benefits of 12-step groups (Z=2.35, p=.019). Caucasian participants reported higher scores on the eclectic subscale reflecting participants' beliefs about the treatment and etiology of addiction (F1,338 = 11.21, p = .0009). African American participants had higher scores than Caucasian participants on the Core Spirituality subscale (F1,329 = 18.71, p < .0001), the Personal Application/Humility subscale (F1,374 = 10.88, p = .0011) and Total SIBS-R measure of spirituality (F1,317 = 14.45, p = .0002).
Conclusions: Although Caucasian participants reported a higher likelihood of attending 12-step groups, African Americans report more perceived benefit from meeting attendance than Caucasians. Such results indicate encouragement to attend 12-step groups may be appropriate for substance abuse clients of both races. Results also indicate that African Americans may be more open to the spiritual aspects of the 12-step philosophy than Caucasians.
Financial Support: NIDA CTN, U10 DA13714 (Dennis Donovan, PI)

513

SUBSTANCE USE, DEPRESSION, AND PUNISHMENT BELIEFS AMONG LOST-TO-CARE AND ENGAGED HIV PATIENTS IN ST. PETERSBURG, RUSSIAN FEDERATION.

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Aims: Suboptimal medication adherence increases the risk of resistant viral strains, treatment failure, and progression to AIDS. Thus, factors leading to drop out and re-engagement are important. This study was conducted to explore patient-identified factors associated with dropping out and returning to treatment. We hypothesized that patients would describe substance use, emotional/psychiatric symptoms and disorders, and unstable housing as leading to dropout, and that resolving them would be associated with returning to treatment.
Methods: Case managers recruited 41 patients who had not attended an appointment or taken HIV medications for > 4 months. Patients were individually interviewed within two weeks of returning to care. Questions included, "What are the factors that lead to your dropping out of treatment?" and "What are the factors that led to your returning to treatment?" Responses were transcribed verbatim and content analyzed.
Results: Themes associated with dropping out: drugs/alcohol(90%); unstable housing/homelessness(40%); emotional/mental health concerns(32%); incarceration(32%); problems with HIV medications(27%); denial(20%); relocation(20%); stigma(17%); and problems with clinic/staff(15%). Themes associated with returning to treatment: concerns about health/death(66%); cutting back/quitting and recovery(54%); positive feelings about the clinic(17%); spirituality/conscience/helping others(17%); stable housing(15%); relocation back to the area(12%); acceptance of the HIV diagnosis/breaking through denial(10%); incarceration/release(7%), and support from family/friends(5%).
Conclusions: Drug/alcohol use impacted multiple life domains and was the most frequently cited cause for dropping out, while health concerns, reducing use, and getting into substance abuse treatment were important for returning to treatment. Interventions addressing substance use will likely be important.
Financial Support: U10-DA-013043 (Woody, PI)

514

BARRIERS FOR TREATMENT LEADING TO RELAPSE AFTER DISCHARGE: A QUALITATIVE STUDY WITH MALE AND FEMALE INPATIENT CRACK USERS.

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Aims: There are few studies that evaluate the search for treatment among crack users, describing attempts for hospitalization and models of hospital care provided to this specific type of high-risk population. This study mapped the treatment trajectories of a sample of male and female crack users, through their narratives about the course of treatment seeking and their attempts to access health care services in Brazil.
Methods: we conducted a qualitative study with structured interviews of a purposive sample by criteria, consisting of 9 men and 5 women urban, inner-city crack users hospitalized in a public psychiatric hospital in Brazil. The interviews were transcribed and data exploration was carried out using Content Analysis.
Results: Respondents reported difficulties with regard to access to hospitalization, and relapse after discharge or abandonment of treatment. There seems to be a model of behaviour peculiar to women and men in order to deal with craving for crack: while most women got involved with prostitution and consequently became infected with HIV, all men of the sample reported crime involvement. Our sample showed that crack users who have overcame their difficulty to obtain treatment and were successfully hospitalized described other difficulties after discharge - especially related to craving.
Conclusions: The relationship between relapse and social environment conducive to consumption, linked to the belief or disbelief in spiritual support, prostitution and the legal complications arising from the use of crack are relevant issues to the development of preventive actions focused on this specific population.
Financial Support: National Secretary for Drug and Alcohol Policies (SENAD).

515

DEVELOPMENT AND VALIDATION OF THE RELAPSE OF CRACK USERS SCALE.

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Aims: To present the development and validation of the Relapse of Crack Users Scale (RCUS) in hospitalized subjects.
Methods: A pilot study with 30 male crack users was conducted to generate 35 sentences related to the construct in focus. Content and semantic validation were later obtained via a focus group of 8 male crack users, as well as an expert panel with 10 drug dependence specialists. A Likert scale of 5 points, with 25 items and initially 9 theoretical factors was formatted and applied in a cross-sectional study with a sample of 250 male hospitalized crack users.
Results: The Cronbach's alpha obtained in the total scale was $\alpha = 0.845$. The Kaiser-Meyer-Olkin Test (KMO = 0.747) was used to evaluate the adequacy of the data and the Bartlett Test (p-value = 0.000) rejected the sphericity, indicating that there are significant correlations between the items of the RCUS. These results fulfilled the premises for the factor analysis, which used Varimax rotation, keeping the 25 items and reducing the primary 9 theoretical factors into 7 definitive factors, which explained 66.28% of the total variance. All 25 items were included, with factor loading > 0.30 and communality > 0.50. Dimensionality: Factor 1. Emotions ($\alpha = 0.851$), Factor 2. Coping ($\alpha = 0.795$), Factor 3. Health, sex and treatment ($\alpha = 0.800$), Factor 4. Legal and social aspects ($\alpha = 0.748$) Factor 5. Positive expectations ($\alpha = 0.726$), Factor 6. Craving ($\alpha = 0.615$) Factor 7. Familiar and affective aspects ($\alpha = 0,702$).
Conclusions: The seven-factor model resulting from the factor analysis of the RCUS reflects the several dimensions of the construct "relapse of crack user", designating satisfactory values and good psychometric properties, including validity and reliability.
Financial Support: National Secretary for Drug and Alcohol Policies (SENAD).

516

RISK FACTORS FOR TRAUMATIC EVENT REEXPOSURE IN COMMUNITY SYRINGE EXCHANGE PARTICIPANTS.

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Aims: Over 25% of syringe exchange participants are reexposed to a new traumatic event each month, with women twice as likely as men to report reexposure (Peirce et al., 2011). Risk factors for traumatic event reexposure in injecting drug users (IDUs) are unknown, although results from general population studies suggest several factors common in IDUs: minority status, drug use, past traumatic events, psychiatric problems, illegal activity, and homelessness. We investigated the relative contribution of baseline demographic, drug use, and psychiatric variables, as well as drug use and drug-related behaviors measured monthly, on risk for traumatic event reexposure in 162 syringe exchange participants (31% women) in a 16-month longitudinal study.
Methods: Generalized Estimating Equations tested univariate and multivariate models. Participants averaged 42 (SD=8) years of age, 74% were minority, and 60% had a high school education. Participants reported an average of 17 past traumatic events.
Results: Three baseline factors conveyed significant risk in both univariate and full models: gender [AOR(95% CI) = 1.64 (1.01-2.68)], psychiatric treatment history [1.89 (1.18-3.02)], and number of past traumatic events [1.03 (1.01-1.04)]. With regard to monthly variables, univariate models demonstrated that days of cocaine use [OR 1.02 (1.00-1.03)] and days of illegal activity [1.01 (1.00-1.03)] were associated with increased risk for traumatic event reexposure measured in the same month. In the full model, only days of cocaine use remained marginally significant [AOR 1.02 (1.00-1.03); p = .054].
Conclusions: Similar to findings in population-based samples, a psychiatric treatment history increased the risk of traumatic event reexposure in IDUs by 89%, and every past traumatic event increased the risk of reexposure by 3%. Ongoing cocaine use also increased IDUs' risk for new traumatic events. In addition to the influence of static risk factors, IDUs can lower their risk for reexposure to new traumatic events by changing daily behaviors, such as reducing their cocaine use.
Financial Support: Supported by R01DA021347 & K23DA15739.

517

SEXUAL ABUSE HISTORY ASSOCIATES WITH DISSOCIATION AND COMPLEX PTSD BUT AMONG METHADONE MAINTENANCE TREATMENT WOMEN IT ASSOCIATES WITH OCD.

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Aims: To evaluate whether the association between a history of sexual abuse and obsessive compulsive disorder (OCD), found to characterize methadone maintained opiate addicted women, also characterizes women with a history of sexual abuse but without opiate addiction.
Methods: Forty-eight patient women from a sexual abuse treatment center (SATC) and 76 from the Adelson methadone maintenance treatment (MMT) clinic were studied using the Yale-Brown Obsessive Compulsive Scale (OCD), Life event inventory for trauma history, Dissociative Experiences Scale (DES), Complex PTSD, CAPS (Clinician-Administered PTSD Scale), and addiction history (modified ASI).
Results: Age of treatment onset did not differ between MMT and SATC clinics (35.0±8.1y vs. 34.7±9.4y respectively) but treatment duration was longer in MMT clinic (7.8y±4.5 vs. 1.2y±0.8, $p<0.0005$). SATC patients were more educated and more of them were Israeli born. Of the MMT patients, 66 (86.8%) experienced sexual abuse during childhood and additional 2(2.6%) as adults. Clinical OCD was more prevalent among MMT vs. SACT patients (63.2% vs. 30.4%, $p<0.0005$) while complex PTSD and dissociation (DES≥30) were less prevalent (10.5% vs. 57.1%, $p<0.0005$ and 18.4% vs. 46.9%, $p=0.001$ respectively).
Conclusions: In this study, most MMT women patients experienced sexual abuse, however unlike the non opiate addicts sexually abused women, they developed less complex PTSD and more OCD. Further study is needed in order to understand whether these comorbidity differences relate to the group characterization differences, or to the addiction and methadone maintenance patterns.
Financial Support: Israeli Ministry of Health

518

DOSE ADJUSTMENT DURING INDUCTION PHASE AND FIRST-MONTH RETENTION AMONG PATIENTS RECEIVING METHADONE MAINTENANCE TREATMENT IN KUNMING, YUNNAN.

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Aims: In order to address the increasing prevalence of HIV and HCV among heroin users, the Chinese government has recently implemented methadone maintenance treatment (MMT) programs nationwide. However, high rates of dropout and relapse continue to be a problem. The aim of this study is to examine if the trend of dose adjustment in induction phase is related to the first 4 weeks retention among MMT patients under a randomized contingency management (motivational incentives) intervention.
Methods: We collected data from 160 newly admitted MMT patients in 2009-2010, in Kunming, Yunnan Province. Patients were randomly assigned to usual care with (n = 80) or without (n = 80) incentives trial. The trend of dose adjustments was computed using methadone dose data from the first week in treatment. We tested the main effects of incentive condition, trend of dose adjustment (increasing vs. decreasing) and their interaction.
Results: There are significant main effects of intervention and trend of dose adjustment as well as their interaction effect. On average, patients in the incentive group who receive increasing dose adjustment stay in the treatment for 27.7 days in the first 4 weeks, longer than the 24.2 days of the patients in the same group but receiving decreasing dose adjustment. In contrast, patients in the control group stay 18.8 days in treatment if receiving increasing dose adjustment, compared to 22.4 days if receiving decreasing dose adjustment during the induction phase.
Conclusions: Contingency management improves treatment retention, while the effect of dose adjustment strategies during induction phase varies by the incentive condition. Further analysis is needed to explore these complicated results.
Financial Support: Supported by NIDA R21 DA025252, P30DA016383, & K05DA017648 (PI: Hser)

519

PHARMACOLOGICAL MANIPULATION OF ADENOSINE RECEPTORS ALTERS CHOICE PATTERNS IN AN INHIBITORY CONTROL TASK.

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Aims: Adenosine 2A receptors (A2ARs) are located almost exclusively in the striatum, where they form heteromers with dopamine D2 receptors (D2Rs), with activation of A2ARs antagonizing D2R activation. Variation in striatal D2R density and function has been linked to performance on tasks measuring inhibitory control, a phenotype thought to be relevant to the compulsive aspects of drug addiction. Thus, drugs that target adenosine receptors might serve to modulate the ability to inhibit pre-potent responses. The present study tested this hypothesis by assessing the effects of various compounds targeting A2ARs on performance of a reversal learning task by rats.
Methods: Using touch-screen based operant chambers, rats (N=22) were trained to discriminate between visual stimuli to earn food rewards. After training, the acquisition of each 3-stimulus set was followed by a reversal stage. The nonselective antagonist caffeine (3 & 15mg/kg), the selective antagonist MSX-3 (3 mg/kg) and the selective agonist CGS-21680 (.05 mg/kg) were administered i.p. prior to reversal sessions.
Results: None of the drugs studied had a significant effect on either accuracy during reversal or on the propensity to respond to the previously rewarded cue. However, caffeine decreased responding to the stimulus rewarded neither during acquisition nor reversal, while MSX increased responding to this never-rewarded stimulus. Additionally, both adenosine antagonists increased, whereas the agonist decreased, measures of response vigor.
Conclusions: The fact that none of the drugs altered accuracy or perseverative responses during reversal argues against them being able to directly modulate inhibitory control. However, the observation that both caffeine and MSX altered responding to the never-rewarded stimulus may point to differences in distinct learning processes (e.g. learned irrelevance), or alternatively, to alterations in exploratory responding. Differences in response vigor are consistent with prior research on dopamine's and adenosine's role in instrumental motivation.
Financial Support: Supported by PHS grants RL1-MH083270 and PL1-NS062410 to JDJ

520

STIMULATION OF SEROTONIN-1B RECEPTORS ATTENUATES COCAINE-ABUSE-RELATED BEHAVIORS FOLLOWING PROTRACTED WITHDRAWAL.

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Aims: The role of serotonin-1B receptors (5-HT1BRs) in modulating cocaine abuse-related behaviors has been controversial due to discrepancies between pharmacological and gene knockout approaches, and opposite influences on cocaine self-administration versus cocaine-seeking behavior. Recently we demonstrated that 5-HT1BR-modulation of these behaviors varies depending on the stage of the addiction cycle, with a facilitative influence during periods of active drug use (i.e. maintenance/intoxication) in striking contrast to an inhibitory influence during protracted withdrawal. To further examine the potential therapeutic effects of 5-HT1BRs on cocaine-abuse related behaviors, we examined the effects of increased 5-HT1BR tone via agonist treatment following either acute (1-5 days) or protracted (21 days) withdrawal.
Methods: Rats trained to self-administer cocaine over 21, 2-h daily sessions were tested for the effects of the 5-HT1BR agonist CP94253 (5.6 mg/kg, s.c.) on cocaine intake on both fixed (FR) and progressive (PR) ratio schedules of reinforcement following 21 days of forced abstinence (i.e. protracted withdrawal).
Results:). In contrast to enhanced cocaine intake reported during periods of active drug use (i.e. maintenance/intoxication stage), following protracted withdrawal CP94253 blunted cocaine self-administration on both FR and PR schedules of reinforcement. In separate cohorts of rats trained to self-administer cocaine for 21 days, CP94253 attenuated both cue- and cocaine-primed drug-seeking behavior following 5, but not 1 day of withdrawal.
Conclusions: These patterns of effects suggest that stimulation of 5-HT1BRs decreases cocaine taking and attenuates the incentive motivational effects of cocaine-priming injections and cocaine-associated cues during protracted withdrawal. These findings suggest that targeting 5-HT1BRs may lead to a novel treatment for cocaine dependence that reduces motivation for cocaine during abstinence, while at the same time reduces cocaine intake if relapse occurs.
Financial Support: DA11064 (JLN)
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521

SOCIAL NOVELTY AND DISCRIMINATION ARE DISRUPTED FOLLOWING ACUTE ADMINISTRATION OF MDMA IN RATS.

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Aims: In humans and rodents alike, acute administration of MDMA increases social interactions; however, the acute effects of MDMA on social learning and novelty-seeking are not known. We used the social discrimination procedure to investigate recognition abilities and short-term social memory processes in rats.
Methods: In this study, rats were administered MDMA (0, 1 or 5 mg/kg, IP) and tested 20 minutes afterwards in a three chamber apparatus with the two end chambers containing a small cage that was either empty or contained an age- and gender-matched conspecific rat. The procedure was divided into three phases: acclimation to the apparatus, recognition of a conspecific, and discrimination between the familiar and a novel conspecific. Rats spent 10 minutes in each phase with 3 minutes between acclimation and recognition and 25 minutes between recognition and discrimination phases.
Results: MDMA did not affect normal sociability (i.e., exploring a conspecific more than an empty cage) during the recognition phase; however, MDMA impaired preference for social novelty (i.e., rats administered MDMA spent equal or more time with the familiar rather than the novel conspecific) during discrimination.
Conclusions: These results suggest MDMA induces behavioral inflexibility and attenuates social novelty-seeking because MDMA-treated rats failed to adapt their behavior to a changing social context.
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522

EVALUATION OF ABUSE POTENTIAL OF CRUSHED AND INTRANASALLY ADMINISTERED OXYCODONE TABLETS.

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Aims: Reformulated OxyContin® (oxycodone HCl controlled-release) tablets (ORF) use a polyethylene oxide controlled-release formulation that imparts resistance to physical and chemical manipulations. Original OxyContin® tablets (OC) provided no tamper resistance. The pharmacodynamics (PD) and pharmacokinetics of crushed ORF, crushed OC, oxycodone powder (OxyAPI), and placebo following intranasal (IN) administration were compared.
Methods: Randomized, double-blind, placebo-controlled crossover study in adult healthy non-physically dependent recreational opioid users. Active treatments contained 30mg oxycodone. PD measures included visual analog scales (VAS) for 'Drug Liking', 'Take Drug Again', and 'High', as well as Subjective Drug Value (SDV), pupillometry and endoscopic IN irritation assessments.
Results: IN coarse- and fine-crushed ORF yielded PD responses greater than placebo, but statistically-significantly smaller than OC and OxyAPI. IN ORF yielded reduced and delayed oxycodone Cmax vs OC and Oxy API, resulting in smaller and more variable maximum PD responses. Peak effects for subjective measures and pupillometry occurred later for ORF vs OC and OxyAPI (1-2h vs 0.5h post-dose). 'High' VAS Emax values were greatest for OxyAPI and crushed OC and lower for coarse- and fine-crushed ORF and placebo. SDV ratings were greatest for OxyAPI and crushed OC and lower for coarse- and fine-crushed ORF and placebo. Highest abuse quotients (AQ = Cmax/Tmax) were observed for OxyAPI and crushed OC (102 and 94ng/mL/h, respectively). Coarse and fine-crushed ORF AQs were 83% lower than OxyAPI. Crushed ORF AQs were statistically significantly lower ($p<0.0001$) than crushed OC and OxyAPI. ORF produced higher IN irritation Emax values than OC and Oxy API.
Conclusions: ORF showed improved resistance to tested physical manipulations. ORF produced smaller and delayed PD effects vs OC and Oxy API. ORF is more likely to be associated with IN irritation vs OC and OxyAPI, suggesting that ORF may have less potential for IN abuse.
Financial Support: Purdue Pharma LP

523

SEX DIFFERENCES IN CART PEPTIDE'S EFFECTS ON DOPAMINE-INDUCED LOCOMOTOR ACTIVITY IN RATS: A HYPOTHESIS AS TO WHY FEMALES ARE MORE SENSITIVE TO COCAINE THAN MALES.

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Aims: Cocaine affects males and females differently. Human and animal studies have shown that females are more sensitive to cocaine and are more motivated to obtain the drug compared to males. Cocaine-amphetamine regulated transcript (CART) peptide decreases psychostimulant-induced locomotion when injected into the nucleus accumbens (NAc) in male rats. However, this phenomenon has not yet been studied in females.
Methods: First, we sought to test for sex differences in locomotor activity (LMA) after the intra-accumbal administration of CART peptide alone. Total distance traveled was recorded for 60 minutes after bilateral injection of either CART1-27 (inactive control) or CART55-102 in male and female Sprague-Dawley rats at a dose of 2.5 μg/0.5μl/side.
Results: Compared to the inactive control, CART 55-102 alone produced no significant difference in LMA in males or females. Next, we tested the effect of dopamine (DA) at two different concentrations (7.5μg and 15μg/0.5μl/side) with concurrently injected CART1-27 (control) or CART55-102. Compared to the control, CART 55-102 produced no significant difference in LMA in females at either dose of DA. In contrast, in males, the higher dose of DA with CART 55-102 significantly decreased LMA compared to controls, as previously shown (Ctl: 1735 cm, CART55-102: 874.3cm; $p<0.05$; N=8).
Conclusions: In conclusion, a significant effect was found with the co-injection of CART 55-102 and DA, but only in males. The lack of an effect in females suggests an additional mechanism influencing the females' response to DA and cocaine, which perhaps requires the presence of estrogen. Because CART peptide in the NAc is thought to be a homeostatic regulator of DA that suppresses the effects of high levels of DA (for example, after cocaine injection) (Nature Rev Neurosci, 9:747, 2008), the lack of a suppressing effect of CART 55-102 in females is postulated to be a reason why females are more sensitive to cocaine than males.
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524

DELAY DISCOUNTING IN TWO CLINICAL SAMPLES OF MARIJUANA USERS.

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Aims: Most studies on delay discounting (DD) have reported that individuals with substance use disorders discount delayed rewards more than controls. However, the only study of DD in marijuana-using individuals found no significant difference in discounting between marijuana users and controls. This study examines the association of DD and marijuana use in 2 independent clinical samples of marijuana users.
Methods: One sample consisted of 94 young adults (average age = 26; used marijuana on 57% of days) in a clinical trial of behavioral therapies for marijuana dependence. The other sample consisted of 69 U.S. veterans (average age = 51; used marijuana on 93% of days) who engaged in a marijuana self-quit attempt. All individuals completed a DD task and provided data on demographics, psychiatric symptoms, and marijuana use characteristics at baseline, as well as marijuana use outcomes over 12 weeks. Bivariate correlations examined the association between baseline DD (i.e., area under the curve or k values) and other baseline characteristics. Linear regression tested whether baseline DD predicted percent days of marijuana abstinence over 12 weeks.
Results: Baseline DD was not significantly related to any demographic, psychiatric, or marijuana use characteristic in either sample (e.g., r of DD and Barratt Impulsivity Scale Nonplanning score in young adult sample = .08, p = .44). Baseline DD did not significantly predict marijuana use outcome in either sample (e.g., $F(1,54) = 0.04$, $p = .84$ in veteran sample).
Conclusions: The lack of association between DD and marijuana use was consistent across both clinical samples. The lack of association is also consistent with the only other study of DD in marijuana users yet contrasts with studies in other substance-using individuals. The association of DD with marijuana may be smaller than with other drugs of abuse.
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525

SEX DIFFERENCES IN THE EFFECTS OF EXERCISE ON SUBSEQUENT COCAINE CRAVING IN RATS.

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Aims: Currently there are no approved pharmacotherapies for treating cocaine addiction. Recent studies using animal models demonstrate that concurrent access to a running wheel can decrease the reinforcing effects of cocaine. Consistent with this idea, our lab has shown in males that 2-hrs/day of exercise during abstinence prevents a subsequent increase in cocaine-seeking. The purpose of this study was to extend the results to females and determine the most efficacious dose of exercise in both sexes.
Methods: Intact adult male (N=33) and female (N=39) rats were trained to self-administer (SA) cocaine (1.5 mg/kg/infusion) under a fixed ratio 1 schedule of reinforcement with a maximum of 20 infusions per session. Once rats acquired cocaine SA, they were given 24/hr extended access (ExA) to cocaine (1.5 mg/kg/infusion) under a discrete trial procedure (4 infusions/hr) for a total of 10 days. Following extended access rats began a 14 day abstinence period in which they were randomly assigned to either 1, 2, or 6 hrs/day access to a locked (sedentary control) or unlocked (exercise condition) running wheel. Cocaine-seeking, assessed under a cued-induced reinstatement paradigm, was examined after the 14th day of abstinence.
Results: Females took more cocaine than males under extended access conditions. Exercising and sedentary rats did not differ on cocaine intake under ExA conditions prior to reinstatement. Two hours per day of exercise significantly decreased subsequent cocaine-seeking in males and tended to decrease subsequent cocaine seeking in females as compared to sedentary controls. In males, exercise dose-dependently decreased subsequent cocaine-seeking. In contrast, in females, less exercise was more effective than higher doses of exercise in this preliminary analysis.
Conclusions: Taken together, these data support the hypothesis that exercise may be an effective intervention for reducing cocaine-seeking in males and females, but that the dose conditions differ by sex.
Financial Support: This work was supported by NIDA grant R01DA024716 (Wendy J. Lynch).

526

METHADONE DOSE-RELATED INCREASE IN QTC WITHOUT SIGNIFICANT PROLONGATION OR ARRHYTHMIA.

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Aims: To prospectively determine the impact of methadone dose on QTc prolongation.
Methods: Methadone-maintained outpatients had electrocardiograms (ECGs) in triplicate at baseline prior to first dose and at 4-6 week intervals for 30 weeks (7 time points). QTc intervals were averaged for each triplicate. We defined QTc prolongation as >450ms for males and >470ms for females. Participants who provided ECGs at baseline and at least one other time point were included in this analysis.
Results: The 93 participants provided 1683 ECGs (561 triplicates). Mean age 38.4 (SD 8.2) years; 55% were African American, and 74% male. Baseline positive urines were 98% heroin, 82% cocaine, and 4% benzodiazepines. Baseline ECG findings and self-report suggested low prevalence of structural heart disease, hypertension, and hyperlipidemia. Use of QTc-affecting medications and electrolyte abnormalities were infrequent. At baseline, mean QTc was 410.2 (SD 16.6) ms, only 1 participant met criteria for QTc prolongation. During the study, 33 (7.5%) of the 561 ECG triplicates met criteria for QTc prolongation. Controlling for age and sex, mean QTc was higher at each time point than at baseline ($p<0.001$), but no mean increase occurred after week 6. Controlling for study week, age, and sex, only mean methadone dose (range 70-190mg) in the 5 days prior to ECG was associated with QTc prolongation ($F(1,338)=19.58$, $p<0.001$). In all 561 ECG triplicates, 7 had an increase in QTc interval of >60ms or >15% from baseline or >500ms. Multiple logistic regressions showed no significant effect of dose on these outcomes. There were no adverse clinical outcomes associated with QTc prolongation in this sample.
Conclusions: Our findings, and the lack of evidence that QTc monitoring is an effective risk stratification tool for sudden cardiac death, suggest that it is premature to recommend QTc risk evaluation in this population.
Financial Support: This research was suported by the National Institute on Drug Abuse, Intramural Reaserch Program, National Institutes of Health.

527

SEXUAL LOCUS OF CONTROL AND ENGAGEMENT IN SEXUAL RISK BEHAVIOR AMONG COCAINE USERS.

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Aims: Crack cocaine use and engagement in sexual risk behavior represent important risk factors for contracting and transmitting HIV. Women crack cocaine users represent a particularly vulnerable group for HIV infection due to higher rates of sexual risk behavior justifying the need to understand gender-specific vulnerability to such practices. Individuals' self-concept in general and the beliefs about one's personal control may play an important role in individuals' vulnerability to risk behavior. Specifically, an individual's perception of control over his or her sexual behavior, may predict sexual riskiness. The present research attempts to examine this hypothesis.
Methods: Crack cocaine-using participants in treatment reported on the number of sexual partners in the past year prior to treatment. Subsequently, they completed a sexual locus of control questionnaire, assessing the extent to which individuals believed the sexual aspects of their life were due to chance/luck, powerful others, or their own personal control.
Results: Gender interacted with participants beliefs about sexual self-control. Specifically, for women, lower personal control over one' sexual behavior was associated with a higher number of sexual partners, thus increased sexual risk behavior. By contrast, men's perception of personal control was not related to the number of sexual partners.
Conclusions: The results of this study indicate that sexual locus of control is significantly related to engagement in sexual risk behavior among crack cocaine users, with important gender differences. Although preliminary, this finding suggests the need to differentially address the role of the sexual self-concept in prevention efforts aimed towards individuals at an elevated risk for contracting HIV.
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528

YEARS OF STIMULANT USE AS A BIOBEHAVIORAL MARKER FOR METHAMPHETAMINE DEPENDENCE.

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Aims: Recent evidence suggests that years and/or amount of drug use affects treatment outcomes. A retrospective analysis was conducted to determine the impact of years of stimulant use on the subject-rated and physiological effects of intranasal methamphetamine. We hypothesized that years of stimulant use would differentially impact sensitivity to the subject-rated drug-effects of methamphetamine.
Methods: Data included in the analysis were from four studies that employed similar methamphetamine dosing procedures, as well as subject-rated drug-effect measures and physiological indices. Participants were dichotomized based on their self-reported years of stimulant use as shorter-term (n=8) and longer-term (n=7) users. During experimental sessions, participants sampled a dose of intranasal methamphetamine (0, 5, 10 or 20 mg) and completed subject-rated drug-effect questionnaires at regular intervals after dosing. Physiological measures were also recorded. A mixed model ANOVA and planned comparisons were used with group and dose as the factors.
Results: Methamphetamine produced dose-related increases in subject-rated effects (e.g., like drug) only in the longer-term stimulant users (mean years of use = 21), which were greater than those observed in shorter-term stimulant users (mean years of use = 11). Significant differences were most often observed for the 20 mg dose. Methamphetamine produced dose-related increases in physiological measures. The differences between groups were mixed on the physiological measures.
Conclusions: These data suggest that longer-term stimulant use may increase sensitivity to the subject-rated effects of methamphetamine, which could be due to additional years of behavioral conditioning and/or pharmacological sensitization. Future research should determine if years of stimulant use might be a biobehavioral marker for predicting outcomes of pharmacotherapies for managing stimulant dependence.
Financial Support: R01 DA 025032 and R01 DA 025591 (CRR)

529

TREATMENT COMPLIANCE AND CHALLENGES AT STATE SUBSTITUTION PROGRAMS IN THE REPUBLIC OF GEORGIA.

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Aims: Background: The Republic of Georgia launched MMT programs in 2008 and Suboxone maintenance programs in 2010. At present, 808 patients (800 men, 8 women) are being treated in these programs; needs assessments and treatment compliance evaluations have not been done.
Aims: Conduct needs assessments and treatment compliance evaluations in MMT and Suboxone Substitution State Programs.
Methods: Methods: Evaluations were done using a structured self-administered questionnaire created that covers demographics, drug use history, general drug use trends, psychotherapeutic sessions' acceptance and open label question regarding treatment challenges and satisfaction.
Results: Results: 506 patients (2 females) were surveyed (92 % on Methadone, 8% on Suboxone) from 6 Tbilisi and 4 regional State Programs. Mean age was 40 (22-65) years; 254 (51.4%) were in treatment for 1-3 years; 305 (60.3%) attended individual and 57 (11.3%) group psychotherapy sessions with 41.21 % attending only once/month. The main reason given for therapy non-attendance was that they did not need for it (29.48%). The main drugs before admission were heroin (80.04%) and buprenorphine (53.49%); additional drugs used during treatment were street methadone (5.38%), sedatives (4.3%) and alcohol (3.58%). More recently, opioid use patterns have changed such that desomorphine ("crocodile") is reported at treatment intake by 53.82%. Commonly used drugs while in maintenance treatment are: 13.62%- alcohol, 10.39%- marihuana, 8.17%- pregabalin (Lyrica), 6.23%- home-made stimulants and 5.45%- sedatives. 55.4% are extremely satisfied with treatment and 82.4%- with program staff. Patients' main wishes are that treatment be free of charge programs (46.4%) and provide take-home doses (22.07%).
Conclusions: Conclusions: Methadone and Suboxone maintenance treatments are being well accepted in the Republic of Georgia and appear to be reducing opioid use, as expected.
Key Words: Substitution treatment, treatment compliance.
Financial Support: GRIA- Georgian Research Institute on Addiction

530

GENE-EARLY ENVIRONMENT INTERACTIONS DETERMINE COCAINE-SEEKING BEHAVIOR IN MICE: A DOSE-RESPONSE ANALYSIS.

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Aims: There is support that genetic background and stressful experience during the prenatal or early postnatal periods contributes to individual differences in the psychostimulant and rewarding properties of cocaine and enhanced responsiveness to cocaine. To investigate the interaction between genetic background and early environmental insults on cocaine-seeking behavior, we determined the effect of prenatal stress (PNS) in two genetically-distinct, inbred strains of mice (C57BL/6J and DBA/2J) on the dose-response curve for conditioned place preference (CPP).
Methods: Pregnant dams were subjected to repeated restraint stress (1h, 3x day) from E14 until birth (PNS) or left undisturbed (control). Cocaine-induced CPP was assessed in the offspring during adulthood. CPP was induced by repeated pairings of cocaine exposure (4x 3, 10, or 30 mg/kg, i.p.) with one of two distinctive chambers of the test apparatus and repeated pairings of vehicle (saline) exposure (4x 10 ml/kg, i.p.) with the other compartment. Then, each mouse was allowed to move freely between the two chambers and the amount of time spent in the cocaine-paired chamber versus the saline-paired chamber indexed CPP.
Results: PNS significantly increased the magnitude of the CPP in B6 mice across doses tested. Conversely, D2, relative to B6, mice exhibited increased psychostimulant response following each cocaine injection, greater sensitization in the psychostimulant response, and increased conditioned locomotion (during the test for place conditioning), however, these measures were not significantly impacted by PNS.
Conclusions: The results of the present study indicate that genetic background interacts with PNS to determine cocaine-seeking behavior in adult mice, thus, PNS and mouse strains offers a viable avenue to elucidate the details of the impact of gene-early environment interactions on adult drug-seeking.
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531

MEASURING THE EFFECT OF HIGH SCHOOL MATH AND SCIENCE EDUCATION POLICY ON TOBACCO USE IN A NATIONAL SAMPLE.

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Aims: Math and science education may be linked to improved understanding of health information, leading to improved health decision making. State-by-state increases in graduation requirements in the mid '80s and early '90s offer an opportunity to explore this potential effect; if it exists it should be linked to measureable outcomes, such as smoking prevalence. To this end, we used a national sample to examine the effects of higher math and science coursework requirements on ever smoking 100 cigarettes, a common measure of smoking initiation.
Methods: Four waves (1999, 2001, 2003 and 2006) of the Tobacco Use Supplement of the Current Population Survey (TUS-CPS) were paired with state mandated high school graduation requirement data; 234,997 TUS-CPS respondents graduated during the period for which we had policy data (1980 to 1999) and were included in the sample. Logistic regression was used to model the effect of the math and science requirement for the year of each respondent's graduation on ever smoking 100 cigarettes. A quasi-experimental approach was taken in which state and graduation year fixed effects were incorporated to account for unobserved correlates.
Results: Higher math and science coursework requirements were associated with lower rates of smoking in the full population, where moving from the lowest to the highest requirements resulted in 12% lower odds of ever having smoked 100 cigarettes (p=0.01). When stratified by race and gender, the largest effect was seen for white women, who were at 17% lower odds to have smoked 100 cigarettes for the same comparison (p<0.001).
Conclusions: Our findings support a modest but significant effect of increasing math and science education on smoking behavior, especially for women of any race and white women, who benefited to a greater degree relative to the general population.
Financial Support: This work was partially supported by NIDA T32DA007313, Training Grant in Drug Abuse Epidemiology, Services and Prevention Research.

532

A PRELIMINARY STUDY OF GAMBLING BEHAVIORS OF ASIAN-AMERICAN ADOLESCENTS IN CONNECTICUT.

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Aims: Gambling behaviors may be problematic among Asian American adolescents, but there is limited evidence on prevalence of pathological gambling and gambling behaviors among Asian American adolescents. Therefore, we examined types of gambling (strategic, nonstrategic, machine gambling), gambling locations (Internet, casino, school ground), urges to gamble, and onset and duration of gambling behaviors among Asian American adolescents.
Methods: We conducted chi-square and t-tests to examine data from a cross-sectional high risk behavior survey conducted in 10 high schools in Connecticut. A total of 4354 students (53% girls; 4% [n=175] Asian Americans) answered questions on gambling.
Results: Compared to non-Asian American adolescents, Asian Americans were more likely to engage in all types of gambling behaviors (strategic: place a bet with a bookie, 17% vs. 7%, p<.001; nonstrategic: buy lottery tickets, 15% vs. 8%, p=.001; gamble on a machine: 32% vs. 24%, p=.021); gamble in various locations (casino: 14% vs. 6%, p < .001; Internet: 17% vs. 11%, p=.038; school grounds: 17% vs. 7%, p<.001); and have gambling urges (pressure to gamble: 10% vs. 5%, p=.015; tension relieved by gambling 15% vs. 5%, p<.001). Of those who reported gambling in the past year, Asian American adolescents were more likely to gamble at a younger age (t=2.38, p=.02) and spend more time during the week gambling (2 hours or more: 23% vs. 15%, p = .039) than non-Asian Americans.
Conclusions: Preliminary examination of wide range of gambling behaviors among Asian American adolescents highlights the need to further examine gambling behaviors in this sample and develop gambling prevention and intervention strategies.
Financial Support: Supported by funds from T32 DA07238, P50AA15632, P50 DA09241, CT Department of Mental Health and Addiction Services, National Center of Excellence in Gambling Research

533

A BIVALENT OPIATE VACCINE REDUCES THE DISTRIBUTION OF 6-ACETYLMORPHINE, MORPHINE AND OXYCODONE TO BRAIN IN RATS.

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Aims: Opioid conjugate vaccines have shown promise in attenuating the behavioral effects of heroin or morphine in animals. Since opioid users can switch or transition between heroin and prescription opioids, we sought to validate a bivalent immunization strategy that would treat abuse of both heroin and oxycodone within the same subject.
Methods: Morphine (MOR) and oxycodone (OXY) haptens were generated by adding tetraglycine linkers at their C6 position. Haptens were conjugated to the carrier protein keyhole limpet hemocyanin (KLH) and administered to rats to screen for immunogenicity and effect of immunization on the distribution of 6-acetylmorphine (6-MAM), MOR and OXY to serum and brain.
Results: Rats immunized with the bivalent MOR/OXY vaccine developed high titers of antibodies that recognized 6-MAM, MOR and OXY. The immunogenicity of the individual immunogens was not compromised by administering them together. In rats given an intravenous dose of both 6-MAM and OXY, prior immunization with the bivalent MOR/OXY vaccine increased 6-MAM, MOR and OXY retention in serum and decreased their respective distribution to brain by 75%. Vaccine efficacy correlated with serum antibody titers for both vaccines, given alone or in combination.
Conclusions: Immunization with the bivalent MOR/OXY vaccine demonstrated the feasibility of generating antibodies against several opioid drug targets in the same subject. These data support the use of a multicomponent opioid vaccine as a potential means of extending vaccine coverage to include both illicit and prescription opioids.
Financial Support: NIH NIDA R01DA026300

534

USING INCENTIVES TO IMPROVE PAROLEE ENROLLMENT AND ATTENDANCE IN COMMUNITY TREATMENT: PRELIMINARY RESULTS.

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Aims: This study is a randomized test of the use of incentives to improve treatment utilization among parolees in community treatment. Aims:(1)Determine whether offering an incentive (voucher) increases admission to community treatment by parolees. (2)For parolees who enter community treatment, determine whether providing incentives for attendance results in greater treatment retention.
Methods: In Admission Phase, consenting clients at prison are randomized to Admission Incentive or Information groups. Upon release to parole, those in the Admission Incentive group who enroll in the treatment program receive a voucher. In Attendance Phase (5months) parolees who enroll in treatment are invited to participate, consented and randomized to Attendance Incentive or Information groups. The Attendance Incentive group receives vouchers for attendance using an escalation/reset schedule.
Currently, 39 of 100 subjects have been recruited into the Admission Phase, and 133 of 200 subjects into the Attendance Phase. Of these, 57.1% are African American, 22.6% are Latino, 13.5% are White, 6.8% are other ethnicities. Kaplan-Meier survival analysis (SPSS 19) was performed to analyze the length of time to treatment exit.
Results: Admission Phase. 70% of Incentive and 63% of Information group clients showed up for community treatment admission. This difference is not statistically significant.
Attendance Phase. At 5 months, 20.3% of the Incentive group was still in treatment compared to 12.5% of the Information group. Mean days in treatment: Incentive group 111 (SE 11.0), Information group 90 (SE 10.1, $\chi 2$ Breslow 2.15, p=.14).
Conclusions: In this preliminary analysis, a greater percentage of the Admission Incentive (vs Information) clients reported for community treatment, but the difference was not significant. The Attendance Incentive group showed a trend toward longer time in community treatment (vs Information). If this trend is borne out once all subjects have been enrolled, then the use of incentives may be an effective way to improve treatment retention and long-term outcomes for parolees with a history of substance abuse.
Financial Support: NIDA R01DA025627-01A1

535

IN VIVO DETECTION OF REDUCED GABA LEVELS IN ADOLESCENT CHRONIC MARIJUANA SMOKERS.

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Aims: Recent proton (1H) magnetic resonance spectroscopy (MRS) studies have demonstrated reduced anterior cingulate cortex (ACC) glutamate (Glu) levels detected in adolescent chronic marijuana smokers compared to non-using controls. Exogenous cannabinoids are known to exert similar effects on presynaptic glutamate and γ-amino butyric acid (GABA) release, and we hypothesized that lower ACC Glu levels detected in adolescent chronic marijuana smokers will be paralleled by reductions in ACC GABA levels. The present study applied metabolite-editing 1H MRS techniques to measure ACC GABA levels in adolescent marijuana users compared and non-using controls.
Methods: Adolescent marijuana (MJ) users (N = 13; average age 18 ±1 years) and similarly aged healthy control (HC) subjects (N = 16; average age 16 ±2 years) were scanned using a Siemens 3T Trio MRI system. Clinical variables recorded from MJ subjects included age of first use and regular use, and total marijuana use. Conventional and GABA-edited 1H MRS methods were used to acquire MRS data from a 22.5 mL voxel positioned bilaterally within the ACC. MEGAPRESS spectra were fitted using automated MATLAB routines, and GABA levels were normalized to the CSF-corrected unsuppressed water PRESS signal integral. Group mean metabolite levels were statistically evaluated using two-tailed t-tests.
Results: GABA levels were significantly lower in the MJ cohort (MJ 0.63 ±0.12; HC 0.81 ±0.25, $p = 0.03$) and the MJ subjects showed significantly lower ACC Glu (MJ 4.84 ±0.52; HC 5.61 ±0.88, $p = 0.01$) levels. Statistical significance remained for both GABA and Glu after co-varying for subject age. Correlation analysis showed a trend towards a significant negative relationship between GABA levels and total MJ use ($r = -0.54$, $p = 0.06$).
Conclusions: These findings infer that altered glutamatergic and GABAergic status is associated with chronic marijuana exposure during adolescence, adding to the neuroimaging data documenting altered cingulate function in individuals with marijuana-abuse.
Financial Support: This study was supported by NIH 1R01 DA020269 (DYT) and NIH K24DA015116 (PFR).

536

REAL-TIME SELF-REPORTS OF MOOD, CRAVING, AND EXPOSURE TO RELAPSE TRIGGERS BEFORE, DURING, AND AFTER COGNITIVE-BEHAVIORAL THERAPY (CBT).

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Aims: We used Ecological Momentary Assessment (EMA) to investigate the effects of CBT on response to drug-use triggers.
Methods: Methadone-maintained cocaine/heroin users received up to 12 weekly manualized CBT sessions for cocaine addiction during weeks 7-18 of a 25-week study. Participants carried personal digital assistants (PDA) during weeks 4-25 to provide EMA data on moods, craving, and exposure to putative triggers in 3 daily randomly prompted entries. Ratings of happiness, stress, and drug craving in the presence and absence of 4 types of triggers (positive- and negative-affect, drug cues, and temptations) before, during, and after CBT were analyzed in an ABA design with SAS Proc Mixed.
Results: In the presence of negative-affect triggers, stress ratings increased over the 3 phases (before, during, and after CBT), but cocaine and heroin craving decreased (p<.0001). In the presence of drug-cue triggers, happiness increased over the 3 phases, and cocaine and heroin craving decreased (p<.0001); stress was significantly higher during the CBT phase. In the presence of temptation triggers, stress increased over the 3 phases (p=.0190), and heroin craving was lower during CBT (p<.0001); happiness and cocaine craving were unchanged over phases. In the presence of a "good mood" trigger, happiness was higher after CBT. In the absence of triggers, the general pattern was for happiness to increase and cocaine and heroin craving to decrease over phases, while stress increased during CBT and then decreased.
Conclusions: Thus, we found complex interactions among subjective states, exposure to triggers, and phase of treatment. In the absence of triggers, ratings of happiness increased and stress and cocaine and heroin craving decreased with CBT. Response to triggers after CBT was mixed: craving for cocaine decreased while stress increased. Additional EMA studies that include a comparison condition for CBT may increase our understanding of CBT's effects.
Financial Support: Supported by NIH National Institute on Drug Abuse Intramural Research Program.

537

TRAUMA SPECTRUM DISORDER: IMPLICATIONS FOR SUBSTANCE ABUSE RESEARCH ON TRAUMATIZED POPULATIONS.

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Aims: Psychological injuries in response to traumatic exposure, best known as post-traumatic stress disorder (PTSD), often induce or exacerbate psychoactive substance abuse. In the military and veteran populations, manifestations of trauma response share common psychophysiological and recovery processes. Trauma spectrum disorder (TSD), pathological expressions of such processes, include symptoms of depression, anxiety disorders including PTSD, alcohol and drug abuse, mild traumatic brain injury (mTBI) symptoms, cognitive impairments, and somatic dysfunctions. The aim of this study is to examine the construct validity and common predictors of TSD dimensions.
Methods: Data are derived from an on-going longitudinal study of National Guard service members who returned from Iraq and Afghanistan, and their family members, sampled from the roster of the entire Guard deployment returning units in a Midwest state starting in April 2011. Metric screening measures consist of 6 of the typical TSD components and are available from a telephone followup conducted between 2-4 months after returning home (to date 2 units in study, n=246; telephone n=107).
Results: Preliminary analysis based on service members only (n=60 to date) show 3 groups based on K-means clustering, which are consistent with factor analysis results. Octagon radar plots suggest the highest-risk group is distinguished by high neurocognitive problems and higher drinking problems than other two; moderate-risk and low-risk group share a similar level of drinking symptoms. Regression analysis of group membership showed the highest-risk group is predicted independently by combat level (OR=5.76, CI 1.09-30.32, p=0.04) and childhood violence (OR=4.25, CI=1.01-17.86, p=0.05).
Conclusions: Our findings support the utility of assessing a range of TSD symptoms for a study involving a traumatized population. Assessing both recent and distant past trauma exposure would improve subsequent prognosis on substance abuse in such a population.
Financial Support: W81XWH-11-2-0108, T32DA007313, BJHS/ISTS Clinical and Translational Sciences Research Program

538

CORRELATES OF MARIJUANA USE IN AFRICAN-AMERICAN WOMEN: THE IMPACT OF CULTURALLY RELEVANT FACTORS.

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Aims: Though marijuana is the most commonly used illicit drug among African Americans, there has been insufficient attention to its use among African American women. While some have argued that marijuana usage is normalized in African American communities, it is unclear if there are risk and protective factors specific to African American women that influence choices to engage in or abstain from marijuana use. The purpose of this study is to examine how various factors, including those that are uniquely culturally relevant like racism, sexism, social support, and level of criminal justice supervision, impact marijuana use among African American women.
Methods: Data used in this study were collected from community, probation, and prison samples of African American women at two time points (intake and 6 month follow-up; N=437). Logistic regression is used to regress the binary dependent variable of marijuana use at the 6 month follow-up on selected independent variables determined at baseline. A stepwise approach is used to test groups of related independent variables and to determine the degree to which these groups improve model fit.
Results: Results indicate that chronic pain in the year prior to baseline and experiencing gendered racism – the combination of racist and sexist life events – predict marijuana use at 6 month follow-up (OR=1.97, p<0.05; OR=1.03, p<0.05, respectively). However, results of the final model including all variables indicate that being married and having social support from family, friends, and significant others have a protective effect above and beyond these risk factors (OR=0.34, p<0.05; OR=0.78, p<0.05, respectively).
Conclusions: Findings suggest the fundamental importance of social integration in reducing marijuana use among African American women. Results indicate that though African American women may use marijuana to self-medicate, experiencing social support may provide a healthier outlet for coping with stressors.
Financial Support: This research is funded by the National Institute on Drug Abuse (R01-DA022967, PI: Oser).

539

RELATIONSHIPS BETWEEN DECISION MAKING, TYPE OF ADDICTION AND ADDICTION SEVERITY.

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Aims: Previous studies suggest possible pre-existing cognitive impairment across addiction type. Relationships between decision making in Iowa Gambling Task (IGT) and addictive behaviors were examined among individuals seeking treatment for addiction. We compared performances in IGT according to severity and type of addiction.
Methods: Participants were recruited from an outpatient addiction treatment center. A computerized version of IGT was used to assess decision-making. Performance in IGT was compared among subjects according to type of addiction and addiction severity measured by ASI Interviewer Severity Ratings. IGT statistics were calculated on total net score and net scores per block of 20 cards. To control personality characteristics that could influence IGT performances, adjustments were made based on the Temperament and Character Inventory and the Sensation Seeking Scale.
Results: 125 participants were recruited. Type of addiction was alcohol (n=38), cannabis (n=21), opiates (n=17), tobacco (n=17) and behavioral addiction (n=16). Performances in IGT did not differ according to type of addiction (p=0.09), but all groups showed poor final performances in comparison with non-dependent controls from the literature adjusted on age and sex. Performances in IGT were sensibly worse in the more severe group of patients, but this difference did not reach statistical significance (p=0.53).
Conclusions: Deficits in decision-making, could to be independent of type of addiction (type of substance or non-substance). This result supports the idea that lower performances in decision making tests are not only a consequence of substance use, but could be more related to the addictive process.
Financial Support: PHRC 2006, MILDT 2010, CRA 2009, PRA-CNRS-CHU 2008

540

THE EFFECT OF MIFEPRISTONE ON CORTISOL SECRETION IN MALE COCAINE-DEPENDENT TREATMENT-SEEKERS.

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Aims: Stress increases cortisol and elevated cortisol activity has been associated with poor cocaine treatment outcomes. Mifepristone, a CNS and PNS glucocorticoid receptor antagonist, blocks the effect of cortisol. As such, a concern with mifepristone is the onset of hypoadrenalism or Addison's disease. However, mifepristone has also been shown, in non-drug abusers, to increase cortisol by blocking cortisol's inhibition of CRF and ACTH secretion. We investigated if a similar rise in cortisol could be measured in cocaine-dependent men after three consecutive doses of 600mg.
Methods: Fourteen cocaine-dependent men enrolled in a double-blind placebo-controlled trial of mifepristone, provided basal serum cortisol, and another sample after randomization at week 2. Cortisol samples were collected for 7 patients in the AM and 7 patients in the PM.
Results: Cortisol levels rose significantly at week 2 when compared to baseline readings for the entire un-blinded sample (p<0.01; Wilcoxon Signed-ranks test). PM cortisol levels were significantly different at week 2 as compared to baseline (p<0.05). AM cortisol rose at the trend level (p=0.07).
Conclusions: Cortisol rose as expected for cocaine-dependent men on mifepristone. The rise occurred at both PM and AM levels. Increase in cortisol affords protection against hypoadrenalism since cortisol competes with mifepristone for occupancy of the glucocorticoid receptor. This property of mifepristone in cocaine dependent men lends supports to the safety of this novel approach.
Financial Support: NIDA grant: K23DA027044-01 and K24022412

541

EFFECTS OF A MORPHINE CONJUGATE VACCINE ON HEROIN PHARMACOKINETICS IN RATS.

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Aims: Morphine conjugate vaccines can mitigate heroin-induced behaviors in rodent models of addiction. However, the effects of immunization on the distribution of heroin and its active metabolites 6-acetylmorphine (6-MAM) and morphine are not clear.
Methods: Rats were vaccinated with morphine conjugated to keyhole limpet hemocyanin through a tetraglycine linker. Opiate concentrations were measured 5 minutes after administration of a single intravenous dose of 0.26 mg/kg heroin.
Results: Immunization elicited serum antibody concentrations from 0.5 to 1.2 mg/ml with high specificity towards heroin, 6-MAM, morphine, and morphine-6-glucuronide. Heroin retention in plasma was increased 40-fold in vaccinated animals compared to controls, while 6-MAM and morphine retention in plasma was increased 8-fold. In control rats, brain 6-MAM concentration was markedly higher than that of either heroin or morphine. Vaccination did not reduce heroin distribution to brain, but reduced the distribution of 6-MAM and morphine to brain by 70 and 65% respectively. There was a significant correlation between serum antibody concentrations and heroin metabolite concentrations in plasma or brain.
Conclusions: These data are consistent with literature suggesting that 6-MAM, in the absence of vaccination, is the major mediator of acute heroin effects after i.v. dosing. The large effect of vaccination on 6-MAM distribution to brain supports and provides a pharmacokinetic basis for its potential use as a treatment for heroin abuse. Serum antibody concentrations may be useful as a biomarker for the pharmacokinetic effects of opiate vaccines.
Financial Support: National Institute on Drug Abuse Grant DA026300, PharmacoNeuroImmunology Training Grant T32-DA07097

542

AVAILABILITY OF MENTAL HEALTH SERVICES IN ADOLESCENT TREATMENT FACILITIES IMPACTS CLIENT OUTCOMES.

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Aims: There is variability in the availability of psychiatric services across adolescent substance abuse treatment facilities. This study aimed to examine whether the availability of such services improve outcomes for young clients.
Methods: Client-level data at intake and 12-months data were collected among youth attending outpatient treatment facilities funded across multiple discretionary programs run by the Centers for Substance Abuse Treatment. An additional survey was sent to all funded facilities that inquired about their provision of psychiatric services. Propensity scores were applied to estimate how youth who attended facilities offering comprehensive psychiatric services would have fared had they received less intense or no such services.
Results: 932 youth attended a site that could treat all psychiatric conditions (i.e., reported having a psychiatrist and/or licensed social worker or psychologist on staff), 1375 attended a site that could treat psychiatric conditions except for severe/persistent mental illness, and 1210 attended a facility that could not treat psychiatric conditions. There was evidence that at 12-months post-intake, youth who attended facilities that could treat all psychiatric conditions had lower mean levels of substance use problems (SUP=1.03) and substance use frequency (SUF=0.06) relative to groups weighted to look similar offering less intense (SUP=1.29, SUF=0.07) or no (SUP=1.61, SUF=0.08) services. There was also evidence that mean levels of internal mental distress (IMDS) and behavior complexity (BC) were lower among youth attending facilities that could treat all psychiatric conditions (IMDS=1.18, BC=1.65) than among comparable youth attending facilities that could treat only a limited number of psychiatric conditions (IMDS=2.30, BC=3.31).
Conclusions: These results suggest that youth attending facilities with comprehensive psychiatric care fare better than they would at sites that do not offer such care.
Financial Support: NIDA R01 DA017507-05 (Morral, PI).

543

NEUROBIOLOGICAL MECHANISMS OF COCAINE ADDICTION IN FEMALES.

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Aims: This study examined the influence of estradiol as a mechanism underlying sex differences in vulnerability at an early and a late stage of cocaine addiction.
Methods: Rats were given access to cocaine under either short (ShA) or extended (ExA) conditions to model these respective stages. Importantly, ExA is characterized by high levels and binge patterns of self-administration (SA) producing subsequent increases in motivation for cocaine. Adult female ovariectomized (OVX) rats (n=6-9/group) were trained to SA cocaine (1.5 mg/kg) under a fixed-ratio 1 (FR1) schedule with a maximum of 20 infusions/session. Once rats acquired SA, they were given either ShA (3 more FR sessions) or ExA (10 days of 24h access under a discrete trial procedure of 4 infusions/hr) to cocaine. Following 14 days of abstinence, motivation to obtain cocaine was assessed by measuring responding under a progressive-ratio schedule.
Results: Data show that following ExA SA, OVX female rats demonstrate higher motivation for cocaine as compared to following ShA administration. Additionally, following ExA, OVX female rats supplemented with estradiol show significantly higher motivation for cocaine SA as compared to OVX female rats receiving vehicle.
Conclusions: The underlying mechanisms by which estradiol acts remain unknown. Research with males indicate that DA and BDNF-mediated signaling are critically involved in the development and maintenance of cocaine addiction with evidence to suggest that adaptations in each pathway contribute to long-term motivational and molecular changes that occur following chronic use. Importantly, evidence indicates that estradiol enhances DA signaling and increases BDNF levels. Therefore, we are currently examining the hypothesis that estradiol enhances vulnerability to addiction in females by enhancing DA and BDNF-mediated signaling in the reward pathway. We will examine DA and BDNF pathway markers in OVX females supplemented with estradiol and receiving vehicle in both ShA and ExA following 1 or 14 days of withdrawal using western blot analysis. Together, these results will begin to uncover underlying mechanisms of cocaine addiction in females.
Financial Support: R01DA024716(WJL)

544

SUBSTANCE USE SERVICE DEVELOPMENT IN IRAQ.

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Aims: As part of the Drug Demand Reduction Initiative in Iraq, UCLA ISAP has been awarded a grant from SAMHSA and U.S. Department of State/INL to work with Iraqi Ministry of Health (MOH) to strengthen substance use disorder (SUD) treatment and prevention capacity in Iraq. Two aims: 1) conduct direct clinical training to selected Iraqi professionals and stakeholders with a train-the-trainer emphasis, and 2) establish a Community Epidemiology Workgroup (CEWG) to develop a program for monitoring substance use trends in Iraq.
Methods: For the clinical training piece, a carefully selected core group of Iraqi medical professionals and other stakeholders will be trained in order to create a well-prepared cadre of professionals who can themselves disseminate knowledge and skills in the area of screening and brief interventions (SBIRT) for SUD more broadly into the larger nationwide SUD service systems. In order to establish the Iraqi Community Epidemiology Workgroup (CEWG), a group of regional representatives will participate in a Rapid Assessment and with US expert support will initiate efforts to identify individuals in the university and public health systems interested in a career in SUD research.
Conclusions: Collaboratively, with selected Middle Eastern subcontracted organizations, the goal of this effort is to establish a sustainable and functional Center of Excellence on Substance Abuse Services at Baghdad's Medical City site. At the present time, services operating under the MOH are insufficient to deal with the extensive problems of substance use, abuse, and dependence in Iraq, where rapidly developing trends—use of amphetamine-type stimulants and prescription drugs—cannot be countered by current resources and methods. This is a crucial initiative to improve the identification, monitoring, and treatment of the problematic use of drugs in Iraq with an emphasis on training and technology transfer.
Financial Support: Substance Abuse and Mental Health Services Administration (SAMHSA) and U.S. Department of State – Narcotics & Law Enforcement (State/INL); Grant #1U79TI023450-01

545

EXPLICIT AND IMPLICIT MEMORY OF DRUG-RELATED AND NEUTRAL VISUAL CUES IN COCAINE ABUSERS AND COLLEGE ATHLETES.

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Aims: Aim: Prominent theories of addiction point to the heuristic value of implicit /explicit information processing distinction for understanding the development and maintenance of problem drug use behaviors. Prior research has examined implicit and explicit memory for drug related verbal, but not visual information in cocaine abusers. We examined explicit and implicit memory for drug-related (cocaine, ecstasy) and neutral picture cues in young adults 19-22 yrs: 20 cocaine abusers (3 females) and 21 college athletes (14 females) who did not use cocaine. We hypothesized that cocaine abusers (vs. athletes) will have enhanced free recall for drug cues.
Methods: Methods: Participants completed a cue learning phase followed by an explicit free recall task and implicit repetition priming task (picture/non-picture decision, PND). During learning, participants viewed polydrug and neutral cues. Later, they recalled the cues verbally. In PND task, participants gave picture/non-picture decisions for viewed and non-viewed cues from same categories, and non-pictures. Recall and priming for each cue category was calculated.
Results: Results: Repeated measures ANOVA of recall data showed a significant main effect of cue type, $F(1,39)=10.31$, $p<.01$, and group, $F(1, 39)=7.30$, $p=.01$. Recall of drug-related cues was greater than recall of neutral cues; compared to college athletes, cocaine abusers had enhanced recall performance. There was a trend for interaction between cue type and group, $F(1,39)=3.51$, $p=.069$, suggesting no difference between groups' recall of neutral cues ($p=.30$), but enhanced recall for polydrug cues by cocaine abusers, $t(39)=3.11$, $p<.01$. For priming, only the main effect of cue type was significant, $F(1,39)=4.98$, $p<.05$. Repetition priming of drug related cues was greater than that of neutral cues.
Conclusions: Conclusion: Cocaine abusers showed a trend of enhanced explicit, but not implicit memory for cocaine and ecstasy visual cues compared to athletes. Results may have implications for developing individually tailored prevention and intervention techniques.
Financial Support: Research supported by NIDA P20DA017552.

546

TEXT MESSAGING REDUCES HIV RISK BEHAVIORS AMONG METHAMPHETAMINE-USING MEN WHO HAVE SEX WITH MEN.

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Aims: This pilot study assessed the utility of a real-time text-messaging intervention to reduce methamphetamine use and high-risk sex behaviors among out-of-treatment MSM.
Methods: At baseline, participants completed an ACASI assessment, received a urinalysis test and a rapid oral HIV antibody test. Following baseline, participants engaged in a two-week text-messaging intervention; social support and health education messages were transmitted in real-time. 400 text messages were developed based on the behavioral change theories of Social Support Theory, Health Belief Model, and Social Cognitive Theory. Follow-up evaluations were conducted two months following the two-week text-messaging intervention.
Results: Fifty-two participants enrolled in the study; mean age was 36.5 years (SD=8.86). Race/ethnicity was Hispanic/Latino (38.5%), Caucasian/white (34.6%), and African American/black (21.2%). 59.6% were HIV infected and 28.9% were homeless. At follow-up, participants (48/52) reported significant decreases in frequency of methamphetamine use and unprotected sex while on methamphetamines (both $p < .01$) and a significant increase in those who reported abstinence from methamphetamine use ($p<.001$). Additionally, participants reported reductions of unprotected anal intercourse with HIV-positive partners ($p < .01$); with their HIV-negative partners, participants reported fewer insertive and receptive episodes (both $p < .05$).
Conclusions: The pilot demonstrated preliminary efficacy of a text-messaging intervention in reducing meth use and HIV risk behaviors, and in transmitting health-promoting and social support messages to out-of-treatment meth-using MSM.
Financial Support: Centers for Disease Control and Prevention, grant #UR6PS000312.

547

ALCOHOL CONSUMPTION AS A FUNCTION OF DIETARY RESTRAINT AND THE MENSTRUAL CYCLE IN MODERATE/HEAVY ("AT-RISK") FEMALE DRINKERS.

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Aims: Despite research suggesting that women who report dietary restraint tend to consume alcohol in greater quantity, most studies use retrospective data collection, which are often unreliable, and no studies have accounted for this relationship with respect to changes in alcohol consumption due to the menstrual cycle. The purpose of the present study was to investigate the relationship between prospectively monitored drinking patterns and dietary restraint across the menstrual cycle among females from the general population whose drinking level places them at-risk for developing alcohol use disorders. "At-risk" drinking was defined as the consumption of seven to 20 drinks per week.
Methods: Using the median split of the cognitive restraint scale scores of the Three-Factor Eating Questionnaire (TFEQ), 51 participants were classified as restrained eaters (RES group) and 56 participants were classified as unrestrained eaters (UN-RES group). Each participant provided 45 days of prospective ratings measuring mood, alcohol consumption, and consequences of alcohol use across one full menstrual cycle.
Results: Although dysphoric mood increased during the late luteal and menstrual phases in both groups, the RES group drank on fewer days and consumed less drinks than the UN-RES group across the menstrual cycle.
Conclusions: This suggests that increased binge drinking in restrained eaters found in prior studies, mainly in college students, may be due to the cohort sampled. Future research should replicate prior studies in samples where irregular eating and drinking patterns are more prevalent and potentially problematic, such as a college-aged population, using the current design of prospective data collection.
Financial Support: Supported by NIDA grants DA009114 (SME) and DA022282 (SCR).

548

OXYTOCIN ATTENUATES METHAMPHETAMINE-INDUCED LOCOMOTOR ACTIVITY IN MALE AND FEMALE RATS: IMPLICATIONS FOR METH SEEKING.

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Aims: Men and women differ in the epidemiology of methamphetamine (meth) use and treatment response outcomes. The nonapeptide oxytocin decreases meth seeking in both male and female rats; however, whether this decrease results from non-specific behavioral effects is unclear. Here, we describe sex differences in meth-induced locomotor activity and oxytocin mediation of these sex differences.
Methods: Male (n=28) and female rats (n=23) were pretreated with oxytocin (1 mg/kg, IP) or saline (SAL), challenged with meth (1 mg/kg) or SAL, and locomotor activity was assessed. In Experiment 1, rats received oxytocin or SAL in a novel test chamber (30 min), followed by meth and activity was monitored (90 min). In Experiment 2, rats were habituated to the test chamber (10 min), administered oxytocin or SAL in the home cage (30 min), and challenged with either meth or saline in the activity chamber.
Results: In Experiment 1, oxytocin blunted motor activity in the novel environment in both males and females [treatment main effect, $F(1,14)=18.19$, $p<0.05$]. Meth increased motor activity more in females relative to males; however, meth-induced activity for both sexes was attenuated by oxytocin [sex x treatment interaction, $F(1,14)=4.75$, $p<0.05$]. In Experiment 2, meth-induced greater activity in female rats and oxytocin decreased motor activity in both males and females [sex x treatment x condition interaction, $F(1,35)=7.45$, $p<0.05$]. This reduction was equivalent to control rats in males only. Oxytocin did not completely block meth-induced motor activity in female rats.
Conclusions: Acute systemic oxytocin reduced meth-induced locomotor activity in both male and female rats. This attenuation differed in male and females in that oxytocin completely inhibited meth-induced locomotor activity relative to control levels in male rats. In contrast, oxytocin partially inhibited meth-induced activity in females. These findings demonstrate that sex specific interpretations of behavioral data may be required for studies using oxytocin to alleviate drug seeking.
Financial Support: P50DA016511 and K12HD055885

549

TRANSACTIONAL SEX AND LIFETIME SEXUALLY TRANSMITTED DISEASES AMONG DRUG USERS.

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Aims: Drug use is related to risky sexual behavior, particularly transactional sex (i.e., exchanging sex for drugs or money) and frequent causal partners. These situations create a power imbalance between the drug or money provider and the recipient, reducing the potential for condom use negotiation. We hypothesized that transactional sex participants are more likely to have STD diagnoses than non-participants.
Methods: Data were obtained from 631 sexually active adult drug users recruited from St. Louis, Miami, Sydney, AU; and Taiwan. Chi-squared and logistic regression procedures were used to examine the association between transactional sex and (1) condom non-use; (2) rationale for condom non-use, (3) STD diagnosis. Transactional sex was defined as: (1) giving or receiving drugs or money for sex; or (2) receiving income from prostitution.
Results: Nearly 10% of the sample reported transactional sex. Those who reported sex transactions were more likely to have been diagnosed with HIV, Chlamydia, and trichomonas than non-participants. Among those who did not always use condoms during sex, transactional sex participants were more likely than non-participants to have unprotected sex because their partner objected or because condoms did not taste good during oral sex. Multivariate analyses identified transactional sex as a risk factor for condom non-use (OR = 2.10).
Conclusions: Results from this study suggest that transactional sex is more common among drug users than the general population (10% vs. 6%). These transactions appear to increase unprotected sex and diagnoses for HIV, Chlamydia, and trichomonas than non-transactional sex participants. Overall, transactional sex is associated with unprotected sex and STD acquisition among drug users.
Financial Support: NIDA grants DA-14854, DA-14854-02S1, DA-14854-02S2 and HHSN 271200477521C (Cottler, PI).

550

NOVEL C1-COCAINE ANALOGS UNLIKE COCAINE OR BENZTROPINE.

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Aims: The hypothesis was tested that C1-cocaine analogs, not previously available, have a novel pharmacological profile.
Methods: By a novel method of asymmetric synthesis (FAD), we generated (-)-C-1 cocaine analogs. By published procedures we measured their uptake into mouse brain, their effects in vitro on uptake activity of human dopamine (DAT), serotonin, and norepinephrine transporters expressed in HEK 293 cells, and their effects in vivo on mouse locomotion, forced-swim mobility, and conditioned place preference (CPP).
Results: C-1-methyl-, ethyl-, and phenyl-cocaine were 2-, 3-, and 10-fold, respectively, more potent at DAT than cocaine, but had little or no locomotor stimulatory activity ($P<0.05$, Student's t-test, drugs compared at same dose of 10 or 30 mg/kg ip). The lack of stimulation was not due to poor brain penetration as C-1-methyl-cocaine (Me-COC) was taken up into mouse brain as rapidly as cocaine itself. Moreover, in the forced swim test at 30 mg/kg (ip) (3x) it decreased immobility time compared with saline ($P<0.05$, ANOVA, post-hoc Bonferroni), and in the CPP test at 10 mg/kg (ip) it increased the post-conditioning time in the non-preferred side ($P<0.05$, paired Student's t-test), i.e. produced CPP by itself; but it did not affect cocaine-induced CPP when given together. Me-COC, as cocaine (but unlike benztropine), was shown to interact preferably with outward-facing DAT expressed in HEK cells, and by its virtual docking into the substrate site in a DAT homology model.
Conclusions: The results support the conclusion that C-1 cocaine analogs, as cocaine, are taken up into the brain, but are not cocaine-like in that they are not stimulatory; they are not benztropine-like in that they do not prefer inward DAT. The present data warrant further consideration of these novel cocaine analogs for antidepressant or cocaine substitution potential.
Financial Support: Support: P30 DA13429 (EMU), R01 DA019676 (MEAR) from NIH.

551

FACTORS ASSOCIATED WITH UNPROTECTED SEX IN A SAMPLE OF YOUNG CLUB DRUG USERS.

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Aims: The present study assessed demographic characteristics, psychiatric symptoms, substance use and sexual risk behaviors in a sample of club drug users to identify factors associated with unprotected sex in the 12 months.
Methods: This cross-sectional study was carried out in 2010 and relied on targeted sampling and ethnographic mapping via face-to-face interviews conducted in bars and electronic music festivals using a semi-structured questionnaire.The sample comprised 240 male and female ecstasy and/or LSD users who had used any of the drugs in the 90 days preceding the interview and not currently participating in treatment for drug or alcohol problems.
Results: None of the variables assessed (demographic characteristics, drug use behaviors or psychiatric symptoms) showed correlation with unprotected sex. After we performed a multivariate logistic regression analysis and calculated adjusted Odds Ratio (OR) for all variables, two of the sexual risk behaviors assessed were significantly associated with unprotected sex, namely having had sex involving anal intercourse (OR = 2.1; 95%CI: 1.1 to 3.9) and having used alcohol/drugs to make sex last longer (OR=4.1; 95%CI: 1.5 to 11.5).
Conclusions: Findings suggest that users of club drugs that had sex involving anal intercourse and used alcohol / drugs to make sex last longer tend to present higher prevalence for unprotected sex. The implementation of intervention strategies aimed at reducing sexual risk behaviors should take into consideration the specific features of drug users and include the development of safer sex negotiation skills(either anal or vaginal).
Financial Support: This study was partially funded by Fogarty International Center (grant number 1R03TW007612-01A1) and by Fundo de Incentivo à Pesquisa (FIPE) from Hospital de Clínicas de Porto Alegre (GPPG-HCPA number 07-391).

552

INTERACTION BETWEEN DELAY AND EFFORT ON A BEHAVIORAL REGULATION TASK IN RATS: EFFECTS OF METHAMPHETAMINE.

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Aims: A number of studies have reported that drug abuse is associated with rapid discounting of delayed rewards. Delay discounting (DD) is involved in normal day to day decision making and is an important component of behavioral regulation. DD refers to the finding that the value of a immediate reward is greater than the value of the same reward received after a delay. For example, individuals may prefer to buy an item for $12.00 immediately rather than wait a year to buy the same item for $10.00. In another example, a consumer in a shopping mall may choose to buy an item immediately for $12.00 rather than walking for 15 minutes to buy the same item for $10.00. In the second example, both delay and effort may have altered decision making. Both effort and delay are involved in real world behavioral regulation. Here we describe a behavior regulation task for rats that provides independent measures of delay and effort.
Methods: Rats (n=16) were trained to shuttle between two water feeders. Rats received precisely measured amounts of water every 4 s by remaining at the water feeder. The amount of water was initially 0.15 ml and was decreased by 10% after each delivery in the same feeder. The rats could reset the amount of water to 0.15 by shuttling to the other feeder. However, shuttling to the opposite feeder resulted in a delay to activation of the feeder and a barrier was sometimes placed between the two feeders increasing effort required to shuttle between feeders. The time spent at each feeder before switching, and the amount of water available immediately before switching were measured as function of all possible combinations delay (0, 8, 16s) and effort (barrier, no-barrier). This experimental design allowed the effects of delay and effort to be separately measured. Effects of methamphetamine (Saline, 0.5, 1.0 mg/kg, i.p.) on performance of the task are reported.
Results: The results indicate that both delay and effort cause the rats to titrate water to lower levels before switching.
Conclusions: Methamphetamine increased switching and this effect was mediated by effort not delay.
Financial Support: DA10588

553

POWER AND HIV RISK AMONG OUT-OF-TREATMENT WOMEN USING METHAMPHETAMINE.

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Aims: To test the reliability of and relationship between variables created to assess multiple levels of power among non-injecting methamphetamine (MA) using women in Denver, Colorado.
Methods: Based on qualitative data collected during the first phase of this project, a 49-item quantitative instrument assessing five types of power was created: structural power, cultural power, social power, interpersonal power, and individual power. Between April 2010 and November 2011,162 MA using women were recruited using street and community outreach techniques. All eligible participants completed a structured interview.
Results: The average age of participants was 37 years. Almost a third (31%) had less than a high school graduation/GED and 35% considered themselves to be currently homeless. The majority were White (67%) and 19% reported Hispanic/Latina ethnicity. All participants had used MA in the recent past as verified by urinalysis. Most reported smoking MA (88%) an average of 21 (S.D. 8) days in the last month and having used MA for an average of 9 years. Pearson correlational analyses were conducted to examine each of the five subscales. Overall, the questions appeared to have relationships that were predicted a priori. Initial confirmatory factor analyses that included all 49-items and 5 subscales yielded poor model fit indices. Therefore, several analytical techniques were used to make decisions on which variables to retain. A final CFA provided adequate model fit indices and 6 subscales were identified: cultural power, social power, individual power, power over others, interpersonal power and drug culture. The relationship between these power scales and the woman's HIV sex risk and MA use behavior will also be presented.
Conclusions: Previous studies with women suggest that power within a relationship is strongly related to sex risk behaviors. However, the construct of power is typically defined at an interpersonal level. This instrument can be used to further empirical investigation of power and risk among women.
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554

PREVALENCE OF ALCOHOL AND DRUG USE DISORDERS AMONGST HOMOSEXUAL POPULATIONS IN AUSTRALIA: COMPARISON WITH THE USA LITERATURE.

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Aims: There is an existing body of literature which documents elevated rates of alcohol and/or drug use in gay, lesbian, and bisexual (GLB) populations. This can often be explained with reference to the cultural norms associated with these sexual minority populations, and in itself is not a cause for concern. However, what is important is the increased risk of developing disorders from heightened consumption. Previous research, predominantly from the US, has shown elevated rates of drug use disorders in GLB populations. The extent of this effect outside the US is largely unknown. This study was the first undertaken in Australia to examine the prevalence of DSM-IV alcohol and drug use disorders in GLB compared to heterosexual counterparts.
Methods: Australian data from the 2007 National Survey of Mental Health and Wellbeing were analysed to compare the lifetime prevalence of DSM-IV alcohol and drug use disorders amongst homosexual/bisexual respondents and heterosexual respondents. Chi square analyses were conducted in SUDAAN to gauge statistical significance, with a Bonferroni correction applied to account for multiple comparisons.
Results: Analyses indicated a higher prevalence of alcohol use disorder amongst homosexual respondents compared to their heterosexual counterparts (31% vs. 22%), though this difference was not statistically significant. Similarly, a higher prevalence of drug use disorders was observed amongst homosexual respondents compared to heterosexual respondents (17% vs. 7%), though this difference also did not reach statistical significance.
Conclusions: Consistent with USA findings, Australian research has failed to detect significant differences in rates of alcohol use disorders amongst GLB people when compared to their heterosexual counterparts. Higher rates of drug use disorders did not reach statistical significance, a finding somewhat at odds with the majority of the published USA literature.
Financial Support: This study was conducted with funding from NSW Health. No restrictions were placed on publication.

555

DEMOGRAPHIC AND RISK FACTOR CHARACTERISTICS OF HOMELESS VETERANS WITH CO-OCCURRING MENTAL HEALTH AND SUBSTANCE USE IN MISSION.

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Aims: This study extends previous findings by more comprehensively characterizing homeless veterans with co-occurring mental health and substance use disorders presenting for MISSION services.
Methods: Veterans (n=239) participated in a baseline assessment, which included the Structured Clinical Interview for DSM Disorders, Addiction Severity Index, BASIS 32, and GPRA Questionnaire. Baseline assessments characterized the sample by mental health/substance use diagnoses, medical comorbidity, employment, legal difficulties, and homelessness.
Results: Veterans met diagnostic criteria for cocaine (54%), alcohol (47%), and opiate (25%) abuse or dependence. Most mental health diagnoses were related to mood (75%) and anxiety disorders (42%). MDD (55%) and PTSD (27%) were most common. Consistent with other published data, participants endorsed a chronic medical condition (42%), unemployment (90%), history of arrests that led to charges (88%), and a history of homelessness (81%) at baseline. Self-reported acuity of problems and service needs by domain will also be included in the presentation.
Conclusions: Homeless veterans with co-occurring disorders are at an increased risk for negative outcomes related to physical health, employment, and legal difficulties. The current findings are consistent with and extend prior research by offering more specificity and a description of service needs. These findings provide important information to researchers and clinicians seeking to implement programs that will successfully address these negative outcomes and facilitate President Obama and Secretary Shinseki's 5-Year plan to end veteran homelessness.
Financial Support: SAMHSA-CSAT Grant # TI16576

556

DISCRIMINATIVE STIMULUS EFFECTS OF VARENICLINE, A NICOTINIC ACETYLCHOLINE RECEPTOR (NACHR) AGONIST, IN MICE.

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Aims: Varenicline is reported to be a partial nAChR agonist with lower efficacy than nicotine. The effectiveness of varenicline as a smoking cessation aid is proposed to result from attenuation of withdrawal symptoms (i.e., agonism) and attenuation of smoking satisfaction (i.e., nicotine antagonism). In mice discriminating nicotine, varenicline was demonstrated to have a lesser maximum effect than nicotine, consistent with low agonist efficacy.
Methods: To test the hypothesis that nicotine produces the same maximum effect as varenicline when varenicline is the training drug, C57BL/6J mice (N=8) were trained to discriminate varenicline (3.2 mg/kg s.c.) from saline under a fixed ratio 10 schedule of food delivery.
Results: The median number of training sessions to acquisition was 72 among mice. Varenicline dose-dependently increased drug-appropriate responding; the ED50 value was 1.9 mg/kg. The nAChR antagonist mecamylamine (3.2 mg/kg) antagonized the discriminative stimulus effects of varenicline, shifting the dose-response curve of varenicline rightward 2.9-fold. Nicotine dose-dependently increased varenicline-appropriate responding, with a dose of 1 mg/kg producing 93% drug-appropriate responding. The ED50 value of nicotine was 0.33 mg/kg. In contrast, cytisine (the parent compound of varenicline and a smoking cessation aid in Europe) produced a maximum of 52% varenicline-appropriate responding up to a dose that disrupted responding.
Conclusions: These results are consistent with the nAChR agonist efficacy of nicotine being equal to or greater than that of varenicline. Failure of cytisine to substitute for varenicline could be due to low agonist efficacy at varenicline-sensitive nAChRs or actions of cytisine at varenicline-insensitive receptors.
Financial Support: USPHS grant DA25267

557

LIFE STRESSORS ASSOCIATED WITH INTERPERSONAL VIOLENCE AMONG ADULT METHAMPHETAMINE USERS.

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Aims: Numerous studies have linked assault and interpersonal violence with methamphetamine (meth) use. The purpose of this study is to explore life stressors and background factors of adults with long meth use histories who have experienced recent violence.
Methods: Data are from a follow-up interview in an intensive natural history study of adults who had used meth regularly at recruitment in 1999-2003. Respondents (N=398) initiated meth use an average of 23 years prior to the 2009-11 follow-up interview, and 24% were using in the past 30 days. Those who reported being physically assaulted in the past year were compared to those who reported no past-year assault.
Results: Overall, 9% of the sample reported a past-year assault, perpetrated by the respondents' spouse/partner (41%), relative (11%) or other person (47%). Past-year marijuana ($p<.05$) and meth use ($p<.01$) were associated with assault. Those who reported being sexually or physically abused before age 15, or report their emotional state was fair/poor (vs. good/very good/excellent) were more likely to be assaulted, as were those who reported physically assaulting someone else in the past year. Younger respondents (39.1 vs. 42.6; $p<.05$), and those who had never received substance abuse treatment at study recruitment were more likely to have been assaulted. Although a higher proportion of assault victims were women, gender differences were not observed ($p=.098$). Likewise, ethnicity, income, employment and housing status were not associated with assault. Multivariate analyses further examine the relationship of physical assault, life stressors and substance use severity.
Conclusions: These preliminary findings suggest assault victims may have a greater need for substance abuse and mental health treatment than those who do not experience assault. Understanding characteristics associated with greater risk for violence among individuals with meth use histories may assist in developing and targeting violence prevention strategies.
Financial Support: NIDA DA025113

558

HYPERAROUSAL IN INSOMNIA AND CHRONIC HYPNOTIC SELF-ADMINISTRATION.

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Aims: Insomnia is hypothesized to be a disorder of hyperarousal shown by elevated mean daily sleep latency on the Multiple Sleep Latency Test (MSLT). But elevations are not seen in all insomniacs. This study evaluated whether hyperarousal in insomnia is predictive of increased hypnotic self-administration in chronic use.
Methods: Insomniacs (N=58), ages 32-65, meeting DSM-IVR criteria and a polysomnographic sleep efficiency of <85%, no other primary sleep disorders, no psychiatric diseases or drug dependency and in good health were recruited. All received a MSLT (1000, 1200, 1400, 1600 hrs) at baseline. Participants took 10mg zolpidem or placebo, double-blind, nightly for 12 consecutive months. In months 1, 4 and 12, self-administration assessments occurred. The zolpidem group had a color-coded zolpidem (10mg) or a placebo capsule on sampling nights 1 and 2, counter balanced. Then on 5 nights, participants chose 1, 2, or 3 zolpidem (5mg each) or placebo capsules. The placebo group choose color-coded placebo capsules, up to 3 nightly. All medications were taken 30 min before bedtime.
Results: The placebo group increased the number of capsules taken over months (M1: 8.2, M4: 9.9, M12: 9.7) ($p<.004$), while the zolpidem group did not (M1: 8.7, M4: 8.9, M12: 9.0) (NS). Across both insomnia groups those with Hi MSLTs (>15 min) took a greater number of capsules (placebo or drug) in months 1, 4, and 12 than those with Lo MSLTs (<10 min) (M1:9.4 vs 8.4, M4:10.4 vs 8.7, M12:10.7 vs 8.0) ($p<.05$). Finally, there was a trend showing those with Hi MSLTs were more likely to increase from month 1 the number of capsules taken in months 4 (1.0 vs 0.3) and 12 (1.4 vs -0.5) compared to those with Lo MSLTs ($p<.08$).
Conclusions: Hyperarousal among insomniacs, as defined by MSLT, is predictive of higher rates of self-administration (both placebo and active drug) during 12 months of nightly use.
Financial Support: NIDA, grant#: R01DA17355 awarded to Dr. Roehrs.

559

ASSESSING THE PENETRATION OF SBIRT TRAINING: A SURVEY OF COUNSELING EDUCATORS.

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Aims: While mental health counselors often see clients with substance use disorders (SUDs), pre-service education rarely includes substance abuse-related content, or only offers it as a specialty track. Emphasizing the gap between education and practice, research shows that counselors who feel unprepared to work with clients who have SUDs may be uneasy dealing with mental health and substance use comorbidity, or may avoid working with SUD clients altogether (Cellucci et al., 2001). This can result in misdiagnosis, referral to inappropriate levels of care, or SUDs being left untreated (Madison et al., 2008; Washton et al., 2006). Since studies show that medical professionals receive SBIRT training, it seems implausible that pre-service counselor education programs do not train students to identify, screen, intervene, refer, and treat clients with SUDs. The purpose of this study was to examine the amount of substance abuse-specific content, including SBIRT, taught in counseling education programs.
Methods: A web-based survey of CACREP accredited counselor education programs was conducted with educators in university-based school counseling, marriage and family therapy, and mental health counseling programs. An initial recruitment and three reminder emails were sent at one week intervals, and 38 educators participated (43% response rate).
Results: Less than half (47%) said all students are required to take a substance abuse course, with 53% having only one course that included an average of one hour of related content. When asked if their program teaches SBIRT, most (71%) responded "I don't know" and 21% said "No". Programs that said they did include SBIRT devoted less than one hour to teaching it, do not use video demonstrations, and only use student-to-student role play "sometimes" to teach counseling skills.
Conclusions: Counselors are likely to see clients who have SUDs. However, results from this study raise concerns about their preparation to identify, screen, intervene, refer, and treat those clients.
Financial Support: Center for the Application of Substance Abuse Technologies (CASAT), University of Nevada, Reno

560

AN EMPIRICAL SPIN HISTORY CORRECTION FOR MOTION EFFECTS IN FMRI.

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Aims: To develop a correction method for fMRI that will accommodate studies with localized motion effects and motion that closely correlates with experimental stimulation. This is a persistent challenge in drug related fMRI.
Methods: fMRI data from 6 subjects was used to develop this spin history correction method. Subjects were male, nicotine dependent, and abstinent before scanning. At 10 min into a 40 min fMRI scan they were injected with .02 mg/kg nicotine in an IV bolus. Subjects had blood samples taken every two minutes. Each subject participated in a sham (saline) and active (nicotine) scan. fMRI analysis was performed using a pharmacokinetic model of nicotine plasma concentrations fit to the measured blood data. fMRI analysis was performed using the drug model as experimental variable in a GLM, along with 6 globally detected motion derivative confound regressors (FSL software, Oxford Univ). Subject-wise analyses were combined in a paired analysis of differential response (placebo – sham) and the group mean presented as final result.
A 4D spin history regressor was constructed from a running image-image difference, which was then thresholded to 5% of the mean image, and z- transformed. In method 1 this 4D correction image was included as a voxelwise regressor in the GLM. In method 2 the fMRI data had this component fit and removed before GLM analysis. Both correction methods fit within the standard GLM analysis procedures and programs.
Results: Both methods produced fMRI results that were more spatially sharply defined, and that lacked motion artifact around the edges of the brain and other motion sensitive boundaries. They did not significantly change activation in cortical regions.
Conclusions: This method can be applied using existing data, and improves the removal of motion related artifact. Especially in fMRI studies with drug challenges, there may be motion that correlates strongly with stimulus and is difficult to separate statistically, This method presents a solution that is arrived at phenomenologically and may aid in future studies.
Financial Support: NIDA 5R01DA025065-02

561

ABUSE LIABILITY: ENHANCE THE QUALITY OF ADVERSE EVENTS (AE) REPORTS IN A NEW DRUG APPLICATION.

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Aims: To describe how to improve the usefulness of premarket assessment AE reports.
Methods: AEs collected during clinical drug development are a signal for the risk of postmarketing abuse liability but their reliability and predictive utility is suspect. At a recent CPDD meeting (Science of Abuse Liability Assessment, Nov. 2011) we proposed ways to improve the quality of AE information.
Results: Best practices to improve usefulness of AE data include: using pre-determined AE terms probing sedative, stimulant, perceptual, cognitive domains; using algorithm driven AE causality assessment; preparation of structured narratives driven by clinical terms with summary graphical presentations; use of structured and open symptom/sign inquiry after drug discontinuation (e.g. Drug Emergent Symptoms & Signs). Greater use of independent, consensus approaches to assess causality and severity are needed. Sole reliance on study investigator expert assessment is problematic if quality data are wanted. Standardizing these approaches could be a joint process involving industry, FDA and CPDD. Another potential initiative would be to develop an SMQ for "abuse potential symptoms/signs detected during clinical development". We know little about how patients think a drug's effects might influence their future behavior. Questions could be included in patient clinical trials to assess future behaviors using balancing and subjective effect questions e.g. bipolar VAS "overall liking", "use again for purpose other than pain relief, i.e. to help sleep" or unipolar VAS for "bad, good, high effects". Inclusion of instruments like Screener and Opiate Assessment for Patients with Pain (Inflexxion) and Current Opiate Misuse Measure in clinical trials would capture data about patient characteristics and behaviors. Recent laboratory data (Comer et al, 2010) suggest clinical trials including operant testing components may directly assess risk of reinforcing effects.
Conclusions: A CPDD, FDA and Industry Working Group could develop tools to improve the usefulness of AE reports as part of assessing abuse liability of new drugs.
Financial Support: None.

562

THE RELATIVE CRASH RISK OF DRUGGED AND DRINKING DRIVING: FATAL CRASHES (PRELIMINARY RESULTS).

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Aims: There is a growing interest in the extent to which the use of drugs by drivers is related to crash involvement. We evaluated the hypotheses that drugged driving contributes to crash risk, but not as much as drinking and driving.
Methods: We matched the 1998–2009 Fatality Analysis Reporting System (FARS) and the 2007 National Roadside Survey. Only states in which more than 79% of the drivers in the FARS file were tested for drugs and had a known result were included. A (0,1) dummy variable identified the presence of any drug. A total of 1,068 fatally injured drivers and 3,139 non-crash involved roadside survey sampled drivers satisfied the matching criteria. We ran two separate logistic regressions (main effects only) to estimate relative-risk estimates for drug-involved driving alone, and/or with alcohol as a covariate, for different demographic groups. To account for crash-responsibility, only single-vehicle crashes were included.
Results: About 66% of the non-crash-involved drivers were negative for both alcohol and drugs; 7% were positive only for alcohol; and 2% were positive for both. For fatally injured drivers, the percentages were 11%, 55%, and 16%, respectively. The odds ratio (OR) for crash involvement was significantly higher for males and underage drivers than for females and drivers aged 21-34. Drugs contributed to crash risk (OR=1.68) when BAC was not included in the model. With alcohol in the model, the contribution of drugs to crash risk was no longer significant.
Conclusions: These results present evidence in support of both hypotheses, namely that both drugs and alcohol contribute to crash risk, which such contribution being much higher for alcohol. Partition of the drug measure into components and the analyses of alcohol by drug interaction should add clarity to these results.
Financial Support: Support for data collection was provided by NHTSA (Contract No. DTNH 22-06-C-00040) and NIAAA (Grant No. R01 AA016407). Data analyses were supported by NIAAA (Grants No. R21AA018158-01A2 and P20 AA017831)

563

A NEW MODEL FOR THE APOMORPHINE TEST AS A BIOLOGICAL MARKER IN COCAINE-DEPENDENT PATIENTS.

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Aims: Until now, no reliable biological markers of risk and relapse in cocaine-dependent patients have been identified. The yawn-inducing Apomorphine test has been proposed as a marker for predicting relapse during cocaine withdrawal. Studying the Apomorphine Test as a predictor of relapse in intranasal cocaine dependet-patients performed the first day and 11 or 12 day after abstinence.
Methods: 39 (35 men) cocaine addicts were recruited and included in an addiction program involving 2 weeks in-patient setting and a 23 follow-up weeks. Dependence was diagnosed according to DSM-IV-TR criteria and other axis I comorbid main diagnosis were excluded. We performed the Apomorphine Test (including an Apomorphine Test plus a Placebo Test) at the beginning (day 1) and end (day 11 or 12) of a detoxification program. Patient received 0.005mg/kg of apomorphine and 0.005mg/kg of placebo subcutaneously each test.
Results: The patients who relapse prematurely (before 4 weeks), yawn more 18.85 (2-45) in the sum of the Apomorphine Test performed day 1 and 11 or 12 day of the detoxification process compared with patients that relapse no prematurely (after 4 weeks of follow-up), 10.71 (0-41), Z -1.89, p <0.05.
Conclusions: The increased number of yawns in relapse-patients could be proposed the sum of yawning-induced in Apomorphine Test as a biological marker of early relapse.
Financial Support: Supported by FIS Grant

564

JUST SAY KNOW: AN EXAMINATION OF SUBSTANCE USE DISORDERS AMONG OLDER ADULTS IN GERONTOLOGICAL AND SUBSTANCE ABUSE JOURNALS.

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Aims: The goal of this article is to examine the extent to which studies of alcohol abuse, illicit drug use, and prescription drug abuse among older adults appears in the leading gerontological and substance abuse journals between 2000 and 2010.
Methods: Publications were retrieved for the 10 social science gerontological journals and the 10 social science substance abuse journals with the highest 5-year impact factors. Data were obtained for these journals from PubMed (the National Library of Medicine) using Medical Subject Headings (MeSH) terms.
Results: From the years 2000 through 2010, of the 19,953 articles published in top ten gerontological and substance abuse journals, 181 articles met the inclusion criteria of reporting findings related to substance use disorders among older adults. Specifically, 0.9% (102 of 11,700) of articles from the top ten gerontology journals and 1.0% (79 of 8,253) of articles in the top ten substance abuse journals met the criteria. Most published articles addressed alcohol misuse/abuse or polysubstance abuse with few articles addressing illicit drug use or the misuse of prescription medications.
Conclusions: The number of older adults abusing alcohol, illicit substances, and prescription medications is growing, as is the number of older adults seeking treatment. Practitioners treating health and/or mental health problems are at a disadvantage in accurately identifying and treating these conditions in older adult populations without a proper understanding of the role of comorbid substance use disorders.
Financial Support: None

565

EFFICACY OF "DUAL FOCUS" MUTUAL AID FOR CO-OCCURRING DISORDERS: PRELIMINARY SUBSTANCE USE OUTCOMES.

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Aims: To determine whether adding a 12-step mutual aid group (Double Trouble in Recovery; DTR), designed to meet the specialized needs of persons with substance use and mental health problems, improves substance use outcomes of outpatient treatment.
Methods: Patients (N=146) with a mental health disorder who had used drugs/alcohol in the past 3 months and met lifetime criteria for a substance use disorder were recruited from eight mental health/dual diagnosis clinics in New York City and Grand Rapids, MI. The subjects were interviewed and randomly assigned to attend weekly DTR groups or placed on a waiting list for DTR (control condition). Outcome variables at 3 to 6 month follow-up were: days used any alcohol, any illicit or unprescribed drugs, and any alcohol or drugs in the past 30 days. To control for clustering within clinics, multilevel regression modeling was used in an intent-to-treat analysis to compare changes in substance use between the cohorts. Dependent variables were log-transformed and the baseline equivalent of the dependent variable was used as a covariate.
Results: Subjects were: male, 68%; mean age, 43 years; African-American, 30%; Hispanic, 14%; public assistance, 69%. At baseline, mean (M) past 30 day use was: days any alcohol (M=4.12; SD=7.54); days any drugs (M=3.95; SD=8.28), and days any substance use (M=6.94; SD=10.16). At follow-up (77% follow-up rate), the DTR cohort compared with the control group, respectively, reported significantly fewer days of alcohol use (2.05 vs. 5.40, $p<.05$), and significantly fewer days of any alcohol or drug use (4.11 vs. 8.19, $p<.05$).
Conclusions: Adding dual-focus mutual aid recovery groups to formal treatment can reduce patients' substance use.
Financial Support: NIDA grant # R01DA023119

566

ADOLESCENT ACCESS TO CONTROLLED MEDICATIONS AND PARENTAL SUPERVISION.

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Aims: National studies have demonstrated that nonmedical use of prescription medications is an increasing problem among adolescents in the U.S. The aim of this study was to determine adolescents' access to four classes of prescription medications that are typically controlled (i.e., pain, stimulant, anti-anxiety, and sedative medications).
Methods: The data for this research were collected as part of the qualitative arm of a 5 year longitudinal NIH-funded study. Enrolled students are interviewed every 6 months, starting in the 7th/8th grades, up to 8 times over the 5 year period of the project. In the second year of the study (Wave 2, academic year 2010-2011), 501 students participated in the interviews. Students were asked what medications they had been prescribed in the past 6 months, and whether the storage of their medications was supervised.
Results: The sample was 50.9% male, 72.9% Caucasian, 21.6% African American, 3% Asian, and 2.5% other. Fifty percent of respondents were in the 8th grade, and 50% in the 9th. Slightly less than half of the respondents (46.5%, n=233) reported having been prescribed medications during the past 6 months. Of this group, 15.5% (n=36) were prescribed pain medicines, 9.4% (n=22) were prescribed stimulants, 1.7% (n=4) were prescribed anti-anxiety medications, and 0.9% (n=2) were prescribed sedatives. Of those who were prescribed medications, 83.4% (n=191) stated that the storage of their medicines was not supervised, and that they had ready access to them. Of the 64 students who were taking medications typically controlled, 76.6% (n=49) had unsupervised access.
Conclusions: This study identifies that the overwhelming majority of adolescents have unsupervised access to their prescribed medications, approximately one-third of which are controlled. Lack of parental supervision of prescribed medications may be a factor in the nonmedical use and diversion of prescription medications by adolescents.
Financial Support: This study was supported by NIDA grant R01 DA024678 (Boyd, PI).

567

HEPATITIS C INFECTION IN NON-TREATMENT SEEKING HEROIN USERS: THE BURDEN OF STIMULANT USE.

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Aims: The prevalence of Hepatitis C virus (HCV) remains high in drug users population. The objective of this analysis was to identify the correlates of being HCV-positive in heroin-dependent individuals.
Methods: Data were collected from 5 inpatient studies conducted at the New York State Psychiatric Institute. The same standardized questionnaire was used to collect data concerning socio-demographic data, recent and past drug use. The diagnosis of HCV infection was based on analysis of plasma using the method of Enzyme-linked immunosorbent assay (ELISA). A logistic regression was used to identify correlates of being HCV-positive at baseline.
Results: Among the 120 heroin-dependent healthy volunteers, 42 were HCV-positive. Participants who had heavier alcohol use, a longer duration of heroin use or who reported using heroin by injection were more likely to be HCV-positive. Interestingly, participants who had injected cocaine during the previous month had a 9-fold greater risk of being HCV-positive (OR[95%CI]=8.52[2.58-28.21]) compared to non-cocaine users and those who used cocaine by a non-injecting route. The model showed an excellent discrimination [AUC = 0.83 (95%CI: 0.75–0.91)].
Conclusions: These findings confirm the risk of being HCV-infected through intravenous drug use. Furthermore, heroin users who also use cocaine by injection have a high risk of being HCV-positive. These results underscore the importance of rethinking interventions to prevent HCV infection.
Financial Support: These studies were supported by DA09236, as well as investigator-initiated grants from Schering-Plough and Grunenthal USA awarded to Dr. Comer. Funding for the writing of this paper was provided by a NIDA INVEST Research Fellowship awarded to Dr. Roux.

568

BRIEF TRAUMA ASSESSMENT FOR SCREENING PRISONERS IN SUBSTANCE ABUSE TREATMENT.

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Aims: Systematic and efficient data collection in high-volume drug offender populations is particularly important. Assessments that offer rapid diagnostic screening of selective needs and risks are necessary for treatment planning and placement. Screeners have typically focused on motivation, psychosocial functioning, criminal thinking, and engagement, but few have addressed symptoms of post-traumatic stress disorder (PTSD). This study focuses on a brief 1-page assessment, TRMAFORM (based on PCL-C, Weathers et al, 1994) addressing trauma symptoms at admission and discharge from treatment.
Methods: Offenders from six prison-based substance abuse treatment programs were assessed (N=5071), including three facility's serving "special needs" clients. The TRMAFORM includes 17 symptom-severity items representing post-traumatic stress disorder including subscales for re-experiencing, avoidance, and hyperarousal.
Results: Results indicated that both male and female offenders in the "special needs" facilities reported higher rates of PTSD symptoms at admission compared to offenders in the regular facilities. Women in the "special needs" facility showed the largest decrease in trauma symptoms from admission to discharge. Of interest, women in this facility had the opportunity to participate in "Seeking Safety"- a targeted trauma intervention.
Conclusions: Findings support the use of a targeted trauma screen to help identify treatment needs at admission and suggest the need for targeted interventions to reduce PTSD symptoms. Applications of the TRMAFORM as a tool for monitoring progress and change over time will be discussed.
Financial Support: Funding was provided by the National Institute on Drug Abuse, National Institutes of Health (NIDA/NIH) through a grant to Texas Christian University R01DA025885.

569

A MICRODIALYSIS AND BEHAVIORAL COMPARISON OF LISDEXAMFETAMINE AND METHYLPHENIDATE IN FREELY MOVING RATS.

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Aims: Lisdexamfetamine (LDX; Vyvanse®) is a prodrug that is metabolised to d-amfetamine (d-AMF) in red blood cells (Pennick 2010, Neuropsychiat Dis Treat 6:317), while methylphenidate (MPH) is a stimulant. Both compounds are used to treat ADHD.
Methods: The Culex Bambino automatically collects samples from dual microdialysis probes and simultaneously measures locomotor activity in freely-moving rats. The effects of pharmacologically equivalent doses of LDX (d-AMF base = 0.5, 1.5 and 4.5mg/kg po) and IR-MPH (3, 10 and 30mg/kg po) on locomotor activity and extracellular levels of norepinephrine (NA), dopamine (DA) and 5-HT in prefrontal cortex (PFC) and striatum (STR) were compared 5hr post-dose.
Results: In the PFC, LDX dose-dependently and significantly ($p<0.05$) increased efflux of NA (≤529% of baseline) and DA (≤296%), and at the highest dose, 5-HT (≤284%). IR-MPH increased DA efflux (≤202%) at the low dose and both DA (≤217%; ≤343%) and NA (≤261%; ≤289%) at the mid and high doses; it had no effect on 5-HT. In the STR, LDX dose-dependently increased extracellular DA (≤364%) and at the high dose, 5-HT (≤359%). IR-MPH (3.0mg/kg) did not increase DA or 5-HT in STR. IR-MPH produced small (≤131%) and substantial (≤243%) increases in DA at 10 and 30mg/kg. IR-MPH (30mg/kg po) only increased 5-HT efflux at 1 time-point. The actions of LDX and IR-MPH in PFC and STR reached a plateau at 45-60min, but the effects of LDX were larger and more sustained. LDX did not significantly enhance locomotor activity at 0.5mg/kg or 1.5 mg/kg except at 2 time-points. A small sustained increase (≤3.6/15min) was seen at 4.5mg/kg. All doses of IR-MPH significantly increased locomotor activity (≤4.7/15min).
Conclusions: These data show that LDX has larger and more sustained enhancing effects on NA and DA neurotransmission in PFC and STR than IR-MPH. The finding that substantial increases in STR DA can be achieved without causing unacceptable locomotor activation predict that LDX will have a greater separation between efficacy and stimulant adverse events than IR-MPH.
Financial Support: Shire Pharmaceuticals Ltd

570

MOTOR VEHICLE CRASHES AMONG FORMER DRINKERS: MALE-FEMALE DIFFERENCES.

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Aims: Driving under the influence of alcohol is an established cause of motor vehicle crashes (MVC), but little is known about how past drinking affects MVC risk after periods of abstinence. The aim of this study is to estimate the odds of MVC among never, former, and current drinkers, with a null hypothesis of no difference between former and never drinkers, and with local area matching for road conditions and other socially shared environmental determinants of MVC and drinking.
Methods: Data are from the 1988-91 United States surveys on drug use and health (NHSDA;NSDUH) with nationally representative samples of recent drivers age 16+ years (n=64, 913). A standardized interview schedule assessed MVC in the past year, as well as drinking history. Conditional logistic regression for matched sets yielded odd ratio estimates for weighted clustered data.
Results: Among the MVC cases (8% of drivers), an estimated 13% were former drinkers (3+ years of abstinence); most had recent drinking histories. With never drinking drivers as the reference subgroup, there was a modest association that links being a former drinker with excess odds of MVC, with and without statistical adjustments for covariates (e.g. miles driven on an average week, other drug use, age, sex) at $p<0.05$. The association was present for both male and female drivers, but the association for females was statistically more precise.
Conclusions: Rejecting the null hypothesis, and with a possible stronger association for female drivers, we found that former drinkers had excess risk of motor vehicle crashes as compared to never drinkers, even with covariate adjustments. Limitations include some important omitted variables (e.g., chronic health conditions that might affect driving, but that might be part of the mechanism of residual effects of past drinking). Residual effects on neurocognitive function can be considered in future research on the potential mechanisms, if there is a cause-effect relationship.
Financial Support: D43TW005819 (PR); T32DA021129 (JT); K05DA015799 (JCA).

571

PEERS, MONITORING, AND EXTERNALIZING BEHAVIOR ASSOCIATED WITH SEVERITY OF ADOLESCENT MARIJUANA USE.

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Aims: To examine deviant peers as a mediator of relations between monitoring and externalizing behavior and severity of marijuana use for African American (AA) and Caucasian (C) youth.
Methods: Youth enrolled in a randomized clinical trial for marijuana use and their parents (N=216) were included. Parent and youth scores on externalizing behavior and deviant peer affiliation were standardized and averaged. Structural equation modeling tested whether deviant peers mediates relations between parent monitoring and externalizing behavior and severity of marijuana use. Analyses controlled the effects of age and SES. Multiple group models were estimated using AMOS 18.
Results: A model constraining relations between the covariates (age, SES), the other variables, and predictive relations across race (AA, C) was the most parsimonious, best fitting model, $\chi^2(20)=32.08$, $p<.05$; CFI=.91; RMSEA=.053. According to this model, poor monitoring was directly related to severity of marijuana use ($B=.39$, $p<.001$), but unrelated to number of deviant peers ($B=.00$, $p=.64$). In contrast, externalizing problems were related to deviant peers ($B=.47$, $p<.001$), which, in turn, was related to marijuana use severity ($B=3.60$, $p<.001$).
Conclusions: Deviant peers mediates relations between externalizing problems and severity of marijuana use, but not relations between poor monitoring and severity of marijuana use. Results show that youth with externalizing problems have higher rates of marijuana use if they associate with deviant peers, indicating the importance of helping youth, especially those with conduct problems, build prosocial relationships. Results also show that poor monitoring is directly related to higher rates of marijuana use, regardless of the level of externalizing problems. Findings suggest that treatments should focus on externalizing problems in the context of peer associations and parent monitoring, and that programs that focus on monitoring alone may miss a significant risk factor for some adolescents. Targeting these risks may not need to be tailored based on race.
Financial Support: T32DA022981;R01DA015186;1UL1RR029884

572

SAFETY AND EFFICACY OF A NOVEL ANTI-(+)-METHAMPHETAMINE (METH) VACCINE.

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Aims: Active immunization against drugs of abuse is a promising treatment for abuse and addiction. While vaccine efficacy is a focal point in preclinical studies, safety testing is frequently understudied. Therefore, we investigated both safety and efficacy during active immunization with a control and METH-conjugate vaccine (MCV).
Methods: Vaccine safety was assessed by monitoring health and stability of responding in food maintained behavior over 16 weeks of testing. For the food maintained behavioral studies, rats were trained under a second-order schedule to lever press for food reinforcers until baselines were stable. Rats (n=9/group) were immunized with 100 μg of MCV or a control vaccine (carrier protein only) with booster injections at 4, 8 and 12 weeks. Food maintained behavior was assessed daily throughout the study. Starting two weeks after the last boost, rats received progressively higher sc METH doses (0.3 – 3.0 mg/kg) every 3-4 days, followed immediately by testing of the ability of the vaccines to blunt METH effects on food maintained behavior.
Results: The safety assessment profile of the control and MCV prior to the METH challenges showed there were no differences or apparent adverse effects. Results from METH-challenge efficacy studies (weeks 14-16) showed important differences between the two vaccine groups. At lower METH doses (0.3 -1.0 mg/kg), food behavior was not different between the groups. However, at the 3.0 mg/kg dose METH substantially inhibited the ability of rats in the control group to maintain stable food maintained behavior, resulting in significantly reduced response rates and number of reinforcers earned ($p<0.05$). Importantly, the MCV group was not affected. METH serum levels (and antibody titers) in the MCV group were significantly higher ($p<0.05$) than those of controls at all METH doses.
Conclusions: These findings suggest the MCV vaccine is safe and effective against METH, even at a high dose of the drug.
Financial Support: NIDA 5U01DA023900.

573

NICOTINE RESEARCH CIGARETTES FOR THE NIDA DRUG SUPPLY PROGRAM.

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Aims: To manufacture Nicotine Research Cigarettes for the NIDA Drug Supply Program for distribution to research investigators

Methods: Nicotine Research Cigarettes (NRCs) with the brand name Spectrum have been manufactured for the National Institute on Drug Abuse Drug Supply Program (NIDA DSP) for use in research programs. In consultation with NIDA, research investigators, and 22nd Century, Ltd, 24 batches of NRCs were selected for manufacturing. These include cigarettes with nicotine delivery levels from <0.05 to 1.5 mg/cigarette with variation in design features such as the menthol, tar levels, and ventilation. RTI collaborated with 22nd Century, Ltd in the manufacture of more than nine million cigarettes. Cigarettes are packaged in standard packs of 20 cigarettes each, similar to commercial cigarette packaging. The packs and cartons were labeled with a barcode and a human readable integrated code to facilitate the conduct of blinded studies if necessary. These NRCs are distributed according to the NIDA DSP procedures. All batches were tested by the supplier for nicotine content, nicotine yield, CO, moisture, tar and TPM. RTI tested the cigarette batches for nicotine content and yield, menthol, and minor alkaloids. Moisture content was also determined. RTI will continue to analyze these NRC batches on an annual basis to monitor the shelf life during distribution and use by investigators.

Conclusions: Nicotine Research Cigarettes are available for research following the NIDA drug supply guidelines upon NIDA approval.

Financial Support: This work was funded by NIDA.

574

NEW YORK'S CENTER FOR EXCELLENCE IN INTEGRATED CARE: "GETTING TO CAPABLE" — STATUS OF THE SYSTEM.

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Aims: Since November 2008, the Center for Excellence in Integrated Care (CEIC) has been assessing and providing technical assistance to New York State substance abuse and mental health outpatient programs. This is a statewide effort to improve the ability of these outpatient clinics to deliver integrated substance abuse and mental health services in the areas of Screening, Assessment, and Evidence-based Interventions to persons with co-occurring conditions. CEIC fosters improved and integrated services through on-site, "hands on" technical assistance.

Methods: Using the Dual Diagnosis Capability in Addiction [or in Mental Health] Treatment (DDCA[MH]T), CEIC has evaluated 447 addiction or mental health programs to date, generating an analysis of the system's capability to provide integrated services.

Results: These evaluations revealed a system average of 2.69 (on a 5-point scale), which indicates a level closer to Dual Disorder Capable (DDC) than to basic (Addiction or Mental Health Only Services) and that there is a need for further improvement to achieve a "capable" (DDC) status. Follow-up on a preliminary sample of 39 clinics indicates a significant increase in capability from 2.62 at Time 1 to 3.10 at Time 2, with significant increases shown in all seven dimensions of the measurement instrument.

Conclusions: At the conclusion of CEIC's 4-year term, it is expected that the majority of New York State's outpatient programs will have achieved "capable" (DDC) status. This initiative is significant in its potential to increase access to care, to enhance the health of New York State residents with co-occurring conditions, to promote system transformation, and to inform future developments consistent with Health Care Reform.

Financial Support: New York State Health Foundation awards 2008-2496857 & 2009-3426912

575

THE INFLUENCE OF NEUROCOGNITIVE IMPAIRMENT ON HIV RISK-REDUCTION OUTCOMES AMONG OPIOID-DEPENDENT PATIENTS.

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Aims: We examined the association between cognitive impairment and primary outcomes following a HIV risk reduction intervention among HIV negative opioid-dependent patients. Preventable drug- and sex-related HIV risk behaviors can threaten individual and community health. In order to successfully participate in behavioral interventions, however, a relatively high level of cognitive abilities may be required.

Methods: We examined the association between scores on the Neuropsychological Impairment Scale (NIS) - a 95-item self-report assessment instrument designed to measure neurocognitive impairment among drug users – and HIV risk reduction outcomes. Participants were 87 high risk HIV-negative opioid-dependent methadone maintained patients who reported drug- or sex-related HIV risk behaviors. The intervention involved 4 brief weekly group sessions of the Community-friendly Health Recovery Program (CHRP), an adapted evidence-based intervention approach that was designed to be integrated into drug treatment settings.

Results: Participants with higher levels of cognitive impairment tended to benefit less from the intervention content in terms of (1) learning drug-risk reduction skills and (2) learning sex-risk reduction skills that were taught during the group sessions compared with participants with relatively lower levels of cognitive impairment.

Conclusions: Higher levels of cognitive impairment were associated with lower levels of sex- and drug-related HIV risk reduction skill aquisition. Our results support prior research suggesting that the NIS may be a helpful screening tool to detect cognitive difficulties that may impede intervention participation among opioid-dependent methadone patients. Future research is needed to determine whether such interventions may be tailored to accommodate cognitive difficulties and promote optimal skill development among this population.

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576

UNODC-WHO PROGRAMME ON DRUG DEPENDENCE TREATMENT AND CARE: EFFECTIVE AND HUMANE TREATMENT FOR ALL PEOPLE WITH DRUG USE DISORDERS.

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Aims: Substance abuse and dependence is a public health, developmental and security problem both in industrialized and developing countries. It is associated with health problems, poverty, violence, criminal behavior and social exclusion. The United Nations Office on Drugs and Crime (UNODC) and the World Health Organization launched the UNODC-WHO Programme on Drug Dependence Treatment and Care in 2009 at the Fifty-second session of the Commission on Narcotic Drugs in Vienna with the goal of promoting and supporting worldwide, with a particular focus on low- and middle income countries, evidence-based and ethical treatment policies, strategies and interventions to reduce the burden caused by drug use and dependence

Conclusions: The poster will present an overview of the early implementation phase of the UNODC-WHO Programme as well as plans for the future.

Financial Support: UNODC and WHO would like to thank the donors of the programme: France, Italy, USA

577

THE ABILITY OF SINGLE SCREENING QUESTIONS FOR UNHEALTHY ALCOHOL AND OTHER DRUG USE TO IDENTIFY DEPENDENCE IN PRIMARY CARE.

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Aims: Single Screening Questions (SSQs) are recommended to screen for unhealthy alcohol and other drug use (from risky use through dependence). But SSQs may provide information on severity needed to inform brief intervention, thought to be obtainable only from longer questionnaires. We assessed SSQ accuracy for identifying patients with dependence.
Methods: In a cross sectional study in an urban primary care practice, subjects were administered the SSQs ["How many times in the past year have you had 5 (4 for women) or more drinks in a day?" & "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?"], the Alcohol Use Disorders Identification Test-Consumption items (AUDIT-C), the Drug Abuse Screening Test (DAST), & the Composite International Diagnostic Interview reference standard for current dependence. All possible cutoffs were evaluated by receiver operating characteristic (ROC) curve. Sensitivity (Ss), specificity (Sp), and positive predictive value (PPV) were assessed at cutpoints maximizing the sum of Ss and Sp (alcohol screening tests for alcohol dependence (AD), drug screening tests for drug dependence (DD)).
Results: Of 286 patients, 9% had AD and 12% DD. The area under the ROC curve (AUC, the probability of distinguishing those with and without dependence) was high for the SSQs (alcohol 88%, drug 93%), AUDIT-C (87%) and the DAST (96%). At the optimal cutpoints (OCs) characteristics of the alcohol SSQ for AD (OC ≥8 times) were Ss 88%, Sp 84% and PPV 35%; for the 3-item AUDIT-C for AD (OC score≥3) Ss 92%, Sp 71%, PPV 23%; for the drug SSQ for DD (OC ≥3 times) Ss 97%, Sp 79%, PPV 38%; for the 10-item DAST for DD (OC score ≥4) Ss 100%, Sp 84%, PPV 46%.
Conclusions: SSQ results, similar to results from longer screening tools, may be useful for identifying substance dependence, providing needed information, and overcoming a barrier to dissemination of screening and brief intervention (lengthy questionnaires) in primary care settings.
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578

EVIDENCE THAT PROPRANOLOL MAY ALTER CLINICALLY RELEVANT MEMORY RECONSOLIDATION PROCESSES IN COCAINE-DEPENDENT HUMANS.

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Aims: There is mounting preclinical evidence that β-blocking agents may alter the memory reconsolidation processes that follow retrieval of memories for drug-reinforced learning. The primary aim of this study was to examine the effects of propranolol vs. placebo, administered immediately after a 'retrieval' session of cocaine cue exposure (CCE), on craving and physiological responses occurring during a subsequent 'test' session of CCE. It was hypothesized that (a) compared to placebo-treated cocaine-dependent (CD) individuals, propranolol-treated CD individuals would evidence less craving & physiological arousal during the test session, and (b) group differences identified in the test session would be evident in a 1-week follow-up CCE session.
Methods: CD participants (N=50) received either 40 mg propranolol or placebo immediately following a 'retrieval' CCE session. After remaining overnight in a drug-free environment, participants received a 'test' session of CCE that was identical to the 'retrieval' session except no medication was administered. Participants returned 1-week after the 'test' session to undergo a follow-up CCE session. Craving and physiological reactivity were measured prior to, during, and following all CCE sessions.
Results: Propranolol- vs. placebo-treated participants evidenced significantly greater attenuation of both mean and peak craving during the test session (p's < .05). Additionally, propranolol-treated participants exhibited dampened cardiovascular reactivity (i.e., heart rate & blood pressure responses) relative to placebo-treated counterparts. Preliminary analyses indicate that these effects were not maintained at follow-up.
Conclusions: This study provides the first evidence that propranolol administration following CCE may modulate memories for learning processes that subserve cocaine craving/cue reactivity in CD humans. Implications for basic neuroscience and drug addiction treatment will be noted.
Financial Support: This research was supported by NIDA grant R21DA025155 (M. E. Saladin, PI).

579

MEDICAL MARIJUANA USE AMONG ADOLESCENTS IN SUBSTANCE TREATMENT.

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Aims: Colorado currently has the highest per capita rate of medical marijuana use, with 3.4% of adults possessing a medical marijuana registration. Little is known about how the widespread use of medical marijuana among adults is related to medical marijuana diversion and use among adolescent patients in substance treatment. Two research questions were addressed: what is the prevalence of medical marijuana diversion among clinical adolescents and what factors are related to clinical adolescents who use others' or their own medical marijuana compared to those who do not?
Methods: The prevalence of medical marijuana diversion was examined among adolescents in substance treatment (n=164), ages 14–18, in the Denver metropolitan area in 2010 and 2011. Multiple logistic regressions were completed to compare adolescents who used medical marijuana to those who did not.
Results: 73.8% of clinical adolescents used someone else's medical marijuana. After adjusting for gender and race/ethnicity, adolescents who used medical marijuana reported more severe behaviors including earlier age of regular marijuana use (OR=0.79, 95% C.L.: 0.62, 0.99; p=0.039), more marijuana abuse and dependence symptoms (OR=1.31, 95% C.L.: 1.13, 1.51; p=0.0005), and more conduct disorder symptoms (OR=1.16, 95% C.L.: 1.01, 1.33; p=0.040) in comparison to those who did not use medical marijuana.
Conclusions: Medical marijuana diversion among adolescent patients in substance abuse treatment is very common. Policy changes in the past few years have resulted in transformations in the origins of the marijuana used by clinical adolescents. Whether this holds true for general population adolescents is currently unknown. Monitoring adolescents' attitudes toward marijuana is needed because labeling marijuana as "medicinal" may result in a shift in adolescents' perceptions of the risk of marijuana use and their willingness to use marijuana.
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580

IMPACT OF DRUG USE ON HIV DISEASE PROGRESSION.

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Aims: To estimate the effect of drug use on HIV disease progression, as measured by CD4 cell count in the absence of antiretroviral therapy (ART)
Methods: We assessed 77 HIV-infected Russians not on ART at baseline and 12 months later to estimate the effect of any illicit drug use on change in CD4 cell count. Median regression analyses were performed adjusting for depressive symptoms, age, gender, risky drinking, and baseline CD4 count. In secondary analyses, individual drugs (i.e., opioids, stimulants, cannabis) were examined as main independent variables. The study was not designed to test for an association but to estimate the effect size of this association.
Results: The adjusted median decline in CD4 cell count was 112 cells/mm3 from baseline to 12 months for those with and 126 cells/mm3 for those without drug use; difference between groups was 14 cells/mm3 (95%CI: -160, 188; p=0.87). The only covariate that reached statistical significance was baseline CD4; higher baseline CD4 cell count was associated with a greater change in CD4 (p=0.005). Secondary analysis revealed the following: for *opioid use*, CD4 decline was greater in the no opioid use group (median difference 40 cells/mm3 95%CI: -144, 244; p=0.67); for *stimulant* use, CD4 decline was greater in the no stimulant use group (median difference 127 cells/mm3 95%CI: -172, 426; p=0.40); for *cannabis use*, CD4 decline was smaller in the no cannabis use group (median difference 37 cells/mm3 95%CI: -388.9, 314.6; p=0.83).
Conclusions: Among HIV-infected Russians not on ART, clinically important differences in CD4 cell count changes were not found between those reporting current drug use compared to those not reporting drug use. Notably, the observed associations, although not statistically significant, were not in the hypothesized direction for any drug use, nor specifically for opioids or stimulants. These findings do not suggest either a strong effect or positive association between drug use and HIV disease progression as measured by CD4 cell count for those not on ART.
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581

MALE-FEMALE DIFFERENCES IN FREQUENCY OF CANNABIS SMOKING AND ONSET OF NEWLY INCIDENT DRINKING.

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Aims: In a new line of research on polydrug use, our aim was to compare and contrast the cannabis smoking (CS) frequency across subgroups defined by recency of onset of drinking alcoholic beverages ('drinking'). In the long run, we seek to estimate the degree to which onset of drinking might displace cannabis smoking, whether there might be male-female differences in this displacement effect, if it exists, and whether there is a stronger effect at the legal minimum drinking age.
Methods: Data are from the 2004-2008 United States National Surveys on Drug Use and Health, which yield nationally representative samples of community residents (n=277,960 age 12+ years), all assessed with a standardized interview schedule to identify cannabis smokers (CS), and users of alcohol or other drugs. In our analyses, we compare CS frequency for newly incident drinkers (all with drinking onset <90 days before survey) versus other drinkers, with a null hypothesis of no difference in CS frequency, with sex (M/F) as a possible effect modifier, and with a sub-analysis focused on those who delayed drinking onset to the legal minimum age. Analyses take into account the complex sample design and weights.
Results: Newly incident drinkers had lower CS frequency as compared to other drinkers, with and without statistical adjustment for covariates (e.g., age, sex, race-ethnicity, education, use of other drugs) at $p<0.05$. In males, the inverse association was statistically more precise ($p<0.01$). The sub-analysis was not statistically reliable; there were too few newly incident drinkers with CS smoking to warrant estimation.
Conclusions: In this preliminary cross-sectional study, the evidence suggests some possible displacement of cannabis smoking in the initial months after onset of drinking, and that this displacement might occur for both sexes, although perhaps to a greater extent for males. With new survey data, sample size may become large enough to study those who delay drinking to the legal age. We hope to pursue this interesting hypothesis in future research.
Financial Support: NIDA K05DA015799 (JCA) & D43TW005819.

582

SEX DIFFERENCES IN THE EFFECT OF EXERCISE DURING AN ABSTINENCE PERIOD ON SUBSEQUENT NICOTINE SEEKING.

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Aims: Cigarette smoking is the leading cause of preventable death in the US followed closely by obesity. Most smokers initiate use during adolescence and those that do find it more difficult to quit than those that begin later in life, suggesting that adolescents are exceptionally vulnerable. Recent preclinical and clinical work suggests that exercise may be effective in prolonging abstinence in adults, with results to suggest that it may be particularly effective in females. The purpose of this study was to determine if voluntary exercise during an abstinence period would decrease subsequent nicotine seeking in male and female rats that had extended access to nicotine self-administration during adolescence.
Methods: Beginning on postnatal day 30, male (n=15/group) and female rats (n=6/group) were trained to self-administer saline or nicotine (5 μg/kg/infusion) under a fixed ratio 1 schedule with a maximum of 20 infusions/day for 5 days. After training, access to nicotine was unlimited for 23-hr/day for a total of 10 days. Rats were then moved to polycarbonate cages where they either had access to a locked (sedentary group) or unlocked (exercise group) running wheel for 2 h/day. Nicotine seeking was examined following the 10th day of abstinence/exercise under a within-session extinction/cue-induced reinstatement paradigm.
Results: Females self-administered more nicotine under extended access conditions, but no differences were observed in total nicotine intake within the two groups prior to exercise. In males, exercise during abstinence significantly reduced subsequent nicotine seeking. In contrast, in females, access to a locked or unlocked running wheel both caused a decrease in subsequent nicotine seeking with levels of responding under both conditions similar to those observed among saline controls.
Conclusions: These findings suggest that exercise reduces nicotine seeking in both males and females and females are more sensitive to the environmental enrichment provided by the wheel.
Financial Support: Virginia Foundation for Healthy Youth Award: VFHY 8520667 (DHB)

583

EFFECTS OF GABAPENTIN IN OPIOID-DEPENDENT INDIVIDUALS DURING A 10-DAY BUPRENORPHINE DETOXIFICATION.

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Aims: Opioid dependence is a significant public health issue, yet detoxification strategies are limited by an inability to suppress withdrawal symptoms and high relapse rates. Thus, this pilot study examined the efficacy of the N-type calcium channel blocker gabapentin (GBP) to improve outcomes during a brief detoxification protocol with buprenorphine (BUP).
Methods: Treatment-seeking opioid-dependent individuals were enrolled in a 5-wk, double blind placebo-controlled trial examining the effects of GBP during a 10-day detoxification from buprenorphine (BUP). Opioid-dependent volunteers were inducted onto BUP (12 mg/day) during week 1 and randomized to receive GBP (1600 mg/day) or placebo during weeks 2-5. The BUP taper started at the beginning of week 3 and the GBP taper occurred during week 5. Assessments included weekly craving and use measures and thrice-weekly opioid withdrawal scales, vitals, and urine drug screens (UDS). Thus far, 16 participants (7 male, 13 Caucasian, mean age 29.6 yrs) have completed this ongoing study (GBP, N=7; placebo, N=9).
Results: Baseline characteristics did not differ between groups. Preliminary analyses indicate that GBP produced a significant decrease in ratings of "desire for opiates" (GBP= 2.29±1.33, PLA=7.27±1.98; F=9.95, p=0.007) and an increase in the percentage of participants reporting an average length of daily cravings of ≤ 5 minutes (GBP=56.3%, PLA=35.3%; χ^2=3.99, p=0.05) over the course of the BUP detox. Self-reported opioid withdrawal ratings were relatively low and did not differ between groups during the BUP taper. In the GBP and PLA groups, 21.7±7.6% and 39.6±13.2%, respectively, of urines were positive for opiates during weeks 3-4 ($p>0.1$).
Conclusions: These very preliminary results suggest that GBP reduces craving for opiates during a 10-day BUP detox.
Financial Support: Supported by NIDA grant DA10017, 5T32DA022981-03 and CTSA grant 1UL1RR029884. The authors have no disclosures.

584

GROUP MOTIVATIONAL INTERVIEWING ENHANCES TREATMENT ENGAGEMENT IN DUALLY DIAGNOSED VETERANS .

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Aims: Despite improved outcomes when participating in aftercare treatment, many substance abusing patients with DSM-IV-TR Axis I co-existing psychiatric disorders do not participate in aftercare treatment following the initial treatment phase. Group Motivational Interviewing (GMI) is an adaptation of Motivational Interviewing, which has been shown to promote treatment engagement and lower substance use. Little prior research has investigated GMI for dually diagnosed patients. The aim of this study was to evaluate whether GMI resulted in enhanced treatment engagement compared to treatment-as-usual (TAU).
Methods: Veterans (n = 46) with current alcohol and drug dependence/abuse and a co-existing Axis I psychiatric disorder were randomized to GMI or TAU through the Charleston VAMC Substance Abuse Treatment Center. Using electronic medical records, researchers counted the number of outpatient encounters (e.g., number of SATC group and individual meetings) that occurred 6 months prior to and following the patient's first treatment session. Data analyses were conducted using Generalized Estimating Equations (GEE) module of SPSS. Since data were in the form of discrete 'counts', a Poisson model was used within the GEE procedures.
Results: Mental health/substance use treatment utilization changed over time, as indicated by a main effect for treatment month, Wald $\chi2 = 298.1$, $p < .001$. Although there was no main effect for treatment group, patients in the GMI group attended significantly more treatment sessions than participants in TAU, as indicated by a significant treatment group x treatment month interaction, Wald $\chi2 = 27.6$, $p < .01$.Post hoc tests using a Poisson model indicated significance at month 3 ($p < .05$) and at month 4 ($p < .01$).
Conclusions: Results indicate significantly enhanced treatment engagement among participants in GMI compared to those in TAU. This report is a preliminary analysis of a larger RCT evaluating treatment utilization and substance use outcomes.
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585

MEDIATORS OF INCARCERATION AND SEXUAL RISK BEHAVIORS AMONG ADULTS IN DRUG INVOLVED RELATIONSHIPS.

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Aims: Although incarceration has been consistently found to be associated with sexual risk behaviors among drug using adults, few have thoroughly examined interpersonal level mediation chains linking criminal justice involvement and sexual risk outcomes. This study represents an examination of relationship dependencies (or the degree of dependence on a sexual partner for drugs and resources) as a mediator linking prior incarceration and sexual risk outcomes among a sample of adults in drug involved sexual partnerhsips where at least one partner has reported a history of drug abuse.
Methods: Baseline data from 689 HIV negative adults in sexual partnerships recruited for a randomized clinical trial testing the effectiveness of a couple-based HIV prevention intervention were analyzed for the current investigation. Participants' reported sociodemographics, incarceration history, dependencies on intimate on sexual partner, number of sexual partners, episodes of unprotected sex and drug use in the past 30 days was collected.
Results: Most participants reported use of crack/cocaine (88.3%) marijuana (74.6%), heroin (52.8%) in the 30 days prior to the study. 57% of participants reported ever being incarcerated while 33% of the sample reported engaging in sex with concurrent partners. 26% reported that their partner paid for most expenses, while 19% reported that their partner supplied most of their drugs. Results are reported on a multivariate model where the mediation effects of resource dependency are tested, linking incarceration to sexual risk outcomes.
Conclusions: Results from the current study will underscore the role that interpersonal power dynamics play in fueling HIV infection among drug involved adults who have been formerly incarcerated. Findings will also inform the development of interpersonal level HIV prevention programs as well as policies that facilitate the reintegration of adults being released from correctional institutions.
Financial Support: This research was supported by the Social Intervention Group at the Columbia University School of Social Work with a grant from the National Institute of Drug Abuse.

586

CHANGE LANGUAGE AND SUBSTANCE ABUSE TREATMENT OUTCOMES AMONG INDIVIDUALS WITH SERIOUS MENTAL ILLNESS.

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Aims: The primary mechanism underlying the effect of Motivational Interviewing (MI) on substance use behavior change is hypothesized to be the selective reinforcement of client change language by the therapist. As such, change language has been found to predict substance use treatment outcomes. Nevertheless, it is unclear if change language has similar predictive utility among individuals with serious mental illness, a unique psychiatric population that often presents with significant motivational deficits and poor substance use treatment outcomes. Therefore, the current study sought to examine the reliability of change language and its predictive utility among individuals with serious mental illness and co-occurring substance use disorders.
Methods: Participants were 45 individuals with serious mental illness and co-occurring substance use disorders who received MI as part of a larger randomized clinical trial comparing the Behavioral Treatment for Substance Abuse in Schizophrenia to treatment as usual. Two independent raters coded MI sessions for change language frequency and strength.
Results: Change language exhibited good reliability in this sample. Of the six change language categories coded, Ability language (i.e., statements regarding lack of self-efficacy) emerged as a unique predictor of long-term substance use treatment outcomes above and beyond negative symptoms, depressive symptoms, and substance use severity.
Conclusions: Findings were counterintuitive, wherein elicitation of client statements regarding lack of self-efficacy to reduce or stop substance was predictive of outcome. Potential reasons for this unexpected finding are discussed. These findings suggest that the investigation of client language during MI represents a promising avenue for understanding motivational processes underlying substance use treatment outcomes among individuals with serious mental illness.
Financial Support: None.

587

THE IMPACT OF DEPRESSION ON PRIMARY CARE OFFICE-BASED BUPRENORPHINE TREATMENT OUTCOMES.

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Aims: Current major depression is prevalent among opioid dependent patients seeking treatment. Research suggests that major depression at treatment initiation can adversely impact treatment outcomes in patients receiving methadone. The extent to which this finding extends to those initiating primary care office-based buprenorphine treatment (BNT) is unclear. The aim of this study is to examine the impact of a diagnosis of current major depression and depressive symptoms on treatment outcomes among patients initiating BNT.
Methods: Current major depression was evaluated at treatment initiation using specific modules from the Structured Clinical Interview for DSM-IV. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D). Urine samples were collected weekly; missed samples were considered positive. Kaplan-Meier survival analysis was used to evaluate patient retention; ANOVA and ANCOVA were used to evaluate substance use outcomes.
Results: Participants were 202 opioid dependent patients enrolled in a 24 week clinical trial of BNT. Buprenorphine/naloxone doses ranged from 2 to 24 mg (M = 17.8, SD = 2.7). Patients ranged in age from 18 to 62 years old (M = 33.7, SD = 10.0); 150 (74%) were men; 173 (86%) were white. 35 (17%) met criteria for current major depression. Patients without current major depression were retained longer in treatment (M = 117.9 days) than depressed patients (M = 91.7, p = .03). Major depression was not associated with opioid use (or other drug use) as assessed by urine toxicology results (p = .16). CES-D scores were not associated with retention (p = .83).
Conclusions: Current major depression is inversely associated with retention in BNT and supports the need for clinicians to assess for and address this psychiatric condition. A measure of depressive symptoms was not associated with retention; suggesting that diagnostic criteria may be more informative in identifying patients at risk of attrition.
Financial Support: NIDA K23 DA024050, K24 DA00445, K01 DA022398, and R01 DA019511.

588

RELATIONSHIPS AMONG REVICTIMIZATION, PTSD, HIV RISK BEHAVIOR, AND DRUG USE ONSET IN INJECTING DRUG USERS.

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Aims: Injection drug users (IDUs) experience high rates of violence exposure in childhood, adulthood, or both (i.e., revictimization). Compared to adult-only assault, revictimization is associated with higher rates of PTSD and other psychiatric disorders, increased HIV risk behavior, and earlier onset of drug use. However, revictimized individuals also experience larger numbers of assaults than those assaulted only as adults, raising the possibility that the qualitative behavioral differences associated with revictimization could be due to quantity, rather than timing, of assaults.
Methods: We collected data from 208 active IDUs (30% women; 67% black; M [SD] = 41.6 [8.3] years) enrolled in a syringe exchange program. Measures included the Traumatic Life Events Questionnaire, Addiction Severity Index, the Baltimore Risk Assessment Battery, and the Modified PTSD Symptom Scale-Revised (MPSS-R). Participants were classified as having no assault history (NA; n = 21), adult assault only (AA; n = 111; 4.3 [3.2] assaults) and child and adult assault (CAA; n = 76; 7.8 [8.6] assaults).
Results: CAA participants' MPSS-R scores were significantly higher than all others' (25.3 [28.3]; p < .01). AA participants' MPSS-R scores were significantly higher than NA participants' (18.2 [23.1] vs. 11.4 [18.2]; p < .01). Group differences in MPSS-R scores became nonsignificant when adjusted for number of assaults (p = .49). There were no group differences in HIV risk behavior or age of drug use onset in any analyses (ps > .05).
Conclusions: In this sample of IDUs with high rates of violence exposure, timing of assault – childhood vs. adulthood – was not associated with differences in PTSD symptoms, HIV risk behavior, or age of drug use, when results were adjusted for quantity of assaults. These findings contrast with past findings of significant differences in outcome attributed to revictimization and suggest that assault timing may be less important than overall quantity of assaults in predicting clinical outcomes.
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589

THE ROLE OF PROBLEMATIC ALCOHOL USE ON SEX RISK BEHAVIOR AND HIV EXPOSURE AMONG ILLICIT DRUG USERS.

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Aims: Aim: Previous literature in the field has begun to examine the role of alcohol on sex risk behaviors, but has not differentiated between severity of alcohol use among illicit drug users. The current study examines how drinking severity among injection drug users (IDU) and non-injection drug users (NIDU) is associated with sex risk behaviors and HIV exposure.
Methods: Design: The study was a cross-sectional, retrospective study of baseline data from the NEURO-HIV Epidemiologic Study focusing on self-reported alcohol use, IDU and NIDU as well as sex risk behaviors. Participants also provided blood samples to verify HIV status.
Method: The present study used a subset of participants (N = 557) who disclosed their alcohol use in the prior 30-days. Participants reported sex risk behaviors including (a) condom use, (b)alcohol use before/during sex, and (c) IDU and NIDU during/before sex. Sixty-three percent of participants reported lifetime IDU and 8.3% tested positive for HIV. Participants were divided into three groups based on NIAAA definitions of problem drinking and their past 30-day alcohol use: abstainers, moderate users, and problematic users.
Results: Results: Chi-squares and one-way ANOVAs revealed significant differences between drinking severity conditions on age of first IDU, alcohol use during/before sex, and IDU during/before sex. After controlling for age and sex, problematic drinkers were almost five and three times more likely than moderate drinkers and abstainers respectively to use alcohol during/before sex, and almost six times more likely than abstainers to engage in IDU before/during sex. Among Black participants, problematic alcohol users were almost three times more likely than moderate users to be HIV+.
Conclusions: Conclusions: These results outline the necessity for research and clinical intervention among this population to reduce sex risk behaviors and potential HIV exposure, while highlighting the need to examine drinking severity as a meaningful predictor of sex risk behaviors.
Financial Support: This research was supported by NIDA R01DA014498 and T32DA007292.

590

CHARACTERISTICS ASSOCIATED WITH RECURRING DUI OFFENSES IN A STATE IN BRAZIL.

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Aims: This study aim to compare characteristics of DUI repeat offenders to those of one-time offenders in 2009 in the state of Rio Grande do Sul (RS). Additionally, characteristics of DUI offenders were compared to those of all registered drivers.
Methods: Data on 6,388 DUI offenders were obtained from the State Department of Traffic and analyzed using the Habermann test of adjusted residuals. This cross-sectional study considered drivers' age, sex, education, duration of licensure, and license category among other variables. Drivers were considered a repeat offender if they were convicted of DUI more than once within 2009
Results: Repeat DUI offenders are older, have less education, and have been licensed for more years when compared to one-time offenders. DUI offenders when compared to general drivers were more likely to be male, between the ages of 21 and 30, and to have only a basic education. Professional drivers represented 73.5% of DUI offenders but accounted for only 17.9% of all drivers in RS. However, recurrent DUIs among professional drivers were much less likely than among non-professional drivers
Conclusions: The decreased probability of repeat offenses among professional drivers suggests that increased consequences of losing employment influences future behavior among this group. Additionally, because drivers licensed for more than 13 years are more likely to commit one or more DUIs, refresher courses required for this group should focus on DUI prevention
Financial Support: Fundação de Apoio a Pesquisa do Estado do Rio Grande do Sul -FAPERGS

591

SCREENING MEDICATIONS FOR COCAINE DEPENDENCE TREATMENT USING A PRE-RANDOMIZATION, ABSTINENCE-INDUCTION PROCEDURE.

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Aims: Trials of cocaine pharmacotherapies often observe considerable variability in baseline level of cocaine use; with recent evidence suggesting that this is potentially an important predictor of medication effects. We screened three candidate medications to determine whether response to treatment differed as a function of cocaine use/abstinence at baseline.
Methods: Eligible treatment-seeking cocaine dependent subjects entered a 4-week abstinence-induction period using contingency management (Phase I), followed by a 12-week medication trial (Phase II) with random assignment to one of the following four treatment conditions stratified on baseline abstinence status: naltrexone (50mg/d), levodopa/carbidopa (800/200mg/d), modafinil (400mg/d), or placebo. Twelve weeks of treatment consisted of thrice weekly clinic visits for urine benzoylecgonine testing and weekly behavioral therapy targeting medication compliance.
Results: Of the 120 subjects enrolled, 39 (32%) achieved abstinence during Phase I, defined a priori as 6 consecutive cocaine-negative urines. Tests of the interaction of medication (active vs placebo) by baseline status (abstinent vs nonabstinent) evaluated the moderator effect. Overall, baseline abstinence predicted better outcome. Response to levodopa and naltrexone differed as a function of baseline use status, showing reduced cocaine use for nonabstinent subjects receiving active versus placebo medication. There was no evidence of an interaction effect for modafinil.
Conclusions: Evidence of differential treatment response was found for levodopa and naltrexone, favoring these medications for nonabstinent subjects. Among subjects abstinent at baseline, the screened medications failed to demonstrate relapse prevention effects. This research supports the feasibility and utility of examining baseline cocaine use status as a moderator of treatment outcome.
Financial Support: National Institute on Drug Abuse Grant P50 DA09262

592

SCIENTIFIC COLLABORATION ON DRUG ABUSE BETWEEN LATIN AMERICA AND EUROPE (2001-2011).

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Aims: The importance of collaboration among research groups in the drug abuse field has been increasedly reinforced. These collaborations consolidate the scientific activity and guarantee the improvement of methods and outcomes. This study aims at analysing the collaboration networks on drug abuse between Latin American and European countries by means of applying bibliometric methods and collaboration networks analysis.
Methods: The search was conducted through the Science Citation Index Expanded database. A total amount of 228 articles were found by using a specific drug abuse search strategy based on previous studies.
Results: The European country with a higher amount of collaborative articles was Spain (n=199) and Brazil was the Latin American country with the highest production (n=170). United States of America had an active role in the collaboration networks. The collaborative work between Latin America and Europe has increased from 2001 (4 articles) to 2010 (50 articles). The collaboration networks analysis showed that Spain and Colombia (25 articles) as well as Spain and Brazil (24 articles) were the countries with the highest joint production. Alcoholism-Clinical and Experimental Research was the preferred journal for collaborative articles (n=11).
Conclusions: Collaborative scientific production has increased during the last decade between Latin America and Europe, and countries from other continents, especially United States. Spain and Brazil were the most representative countries for scientific collaboration.
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Plan Municipal de Drogodependencias. Ayuntamiento de Valencia (Spain)

593

DEFINING CLINICALLY IMPORTANT DIFFERENCES IN SUBJECTIVE ABUSE POTENTIAL MEASURES.

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Aims: Subjective measures are used in human abuse potential studies. While such measures show good sensitivity, 'clinically important' differences (CID) have not been well defined. A preliminary analysis was undertaken to identify CIDs in human abuse potential studies.
Methods: Data from several measures (eg, 100-pt bipolar Drug Liking, Overall Drug Liking; unipolar Take Drug Again, High, Good Effects VAS) were combined from multiple double-blind, randomized, crossover human abuse potential studies in recreational drug users (N>300). Descriptive data (eg, effect size, ½ standard deviation [SD], pooled standard error [SE], 95% confidence intervals [CI]) for placebo, positive control drugs of abuse (opioids, dissociatives, stimulants, depressants, cannabinoids) and negative controls (non-abused drugs) were investigated using anchor- and distribution-based approaches. Several sources of post-market data (eg, DAWN, AERS) were used to identify rates of abuse for the different drugs.
Results: On most measures, average difference from placebo and effect sizes for positive control drugs were larger than those of negative controls. On Drug Liking VAS, effect sizes ranged from 2-4 with opioids and were <0.5 for most negative controls. Average difference from placebo was >20 pts on Drug Liking/Overall Liking for positive controls and ≤10 for negative controls. The ½-pooled-SD and pooled-SE ranged from ~5 to 15 points and were similar between positive and negative controls (distribution-based approach). Patterns of effects across classes generally corresponded with post-market abuse data, although exceptions (eg, ketamine) were observed.
Conclusions: Non-abused drugs showed a distinct range of responses compared to high doses of drugs with established abuse liability, suggesting that negative control data may be a useful clinical anchor in establishing CIDs for investigations of abuse potential.
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594

OPIOID-INDUCED HYPERALGESIA – CAN IT BE REVERSED? A STUDY OF ACTIVE AND FORMER OPIOID ADDICTS AND DRUG-NAïVE CONTROLS.

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Aims: Compelling evidence has shown that opioids can elicit hyperalgesia (OIH). Recently, we examined the response to cold pain in opioid addict subjects (OA's) and found that the OA's mean time for hand withdrawal (tolerance) was significantly shorter than that of drug naïve controls. In addition, their altered pain perception did not reset four weeks subsequent to the cessation of the opioid use. The aim of this study was to explore if OIH is a reversible phenomenon that may require a long time of abstinence to reset.
Methods: The study included three groups: Addicts to heroin or methadone (OA's, n=60); former OA's for at least six months of drug abstinent who live at therapeutic communities (FOA's, n=43); drug naïve controls (C, n=70). All subjects were exposed to the cold pressor test (CPT). Latency of pain onset (sec) and tolerance were measured.
Results: Mean±SD time of latencies were 10.8±7.7, 6.9±3.9 and 6.8±3.5 sec for the OA's, FOA's and C, respectively ($p<0.001$). Mean±SD tolerance were 30±36.2, 64±58.1s and 56.4 ± 51.4 sec for the OA's, FOA's and C, respectively ($p<0.001$). Post hoc analyses revealed that the significant changes were between the OA's and the other two groups in each of the pain variable.
Conclusions: It is suggested that altered pain perception in OA's is a drug-related, reversible phenomenon that may require a long time of abstinence to reset, rather than an individual long-term stable trait.
Financial Support: This study was supported by a grant from the Israeli Anti-drug Authority.

595

EFFECTIVENESS OF ADOLESCENT SUBSTANCE ABUSE TREATMENTS: IS DRUG SCREENING SUFFICIENT?

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Aims: To assess the relative effectiveness of three treatment modalities for adolescent substance abuse treatment relative to no treatment: urine drug screening (UDS) only, Motivational Enhancement Therapy-Cognitive Behavioral Therapy (MET-CBT5), and MET-CBT5 combined with UDS.
Methods: Data are from a longitudinal observational study of 5186 adolescents enrolled in substance abuse treatment programs funded by the Centers for Substance Abuse Treatment. Treatment groups were defined by and outcomes were assessed in terms of self-reported questions on the GAIN survey, administered at baseline and 3, 6 and 12 month follow-up visits. Adolescents were classified into four treatment groups: UDS only, MET-CBT5, MET-CBT5 combined with UDS, and no treatment. Outcomes of interest were substance use frequency and substance use problems, as assessed by the GAIN. Multinomial propensity score weighting was used to adjust for pretreatment covariate imbalances between the four treatment groups. Propensity score weights were estimated using Generalized Boosted Models (GBM). Weighted regression analyses were used to estimate the treatment effect on each outcome.
Results: Relative to the no treatment group, adolescents in the UDS only group showed a significant decrease in both substance use frequency and problems through 12 months of follow-up. MET-CBT5 showed a (non-significant) trend of reducing frequency of substance use. Combining UDS and MET-CBT5 does not appear to result in more favorable outcomes than UDS alone.
Conclusions: This study offers preliminary evidence that standalone urine drug screening is associated with reduced substance use and substance problems. Further work should explore whether standalone UDS would be an effective treatment modality for adolescents, and the conditions necessary for it to achieve its potential effects.
Financial Support: NIDA DA015697

596

WEB-BASED TRAINING AND DISSEMINATION OF THERAPEUTIC GOALS MANAGEMENT (TGM).

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Aims: The aim of this presentation will describe and demonstrate the newly developed web-based "TGM eLearning Course" and "TGM MetaCM" supported by SAMHSA and ChipRewards, Inc.
Methods: Therapeutic Goals Management (TGM) is a person-centered, behavioral, multi-life area, goal management intervention established in previous empirical research of behavioral day treatment plus contingency managed housing and work therapy for homeless persons who are cocaine dependent.
Results: TGM has the potential for wide use in community substance abuse treatment programs not only to improve clinical outcomes, but add therapeutic precision and evaluate treatment outcome, and incorporate the participant more in the treatment process. Barriers to scalable implementation include demanding personal-to-person training and tedious paper and pencil implementation.
Conclusions: It is concluded that these training and implementation products provide opportunities for scalable dissemination of TGM.
Financial Support: SAMHSA, NIDA

597

BENZODIAZEPINE USE AND BUPRENORPHINE TREATMENT OUTCOMES: A RETROSPECTIVE STUDY.

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Aims: Benzodiazepine(BZ) use is common among patients receiving opioid treatment. Some feel prescription(Rx) BZ use impedes addiction recovery. Overdose from BZ abuse is a safety concern during buprenorphine/naloxone(B/N) treatment. Our aim was to examine the effects of BZ misuse and Rx BZ use on retention and adverse events during B/N treatment.
Methods: We retrospectively examined intake records from a community outpatient B/N treatment program. We excluded cases with psychosis,intracranial injury,pregnancy,or without a complete intake assessment(substance abuse history,urine toxicology,and physician evaluation). We divided the sample into patients with and without evidence of past-year BZ misuse. We also identified patients with an approved BZ Rx at intake. Primary outcomes included 12-month retention and frequency of adverse events (i.e. emergency department(ED) visits).
Results: Subjects (n=328) were 40% female and 93% Caucasian,with 40% retention in B/N treatment at 12 months; lifetime history of BZ use was 82%. Past-year BZ misusers (n=156, 48%),compared to those without past-year BZ misuse,evidenced increased lifetime prevalence of alcohol ($p<0.001$),amphetamine and cocaine abuse ($p<0.005$). Those with an approved BZ Rx at intake (n=58, 18%) were more likely to be female and to have multiple psychiatric hospitalizations,history of psychotropic use,and disability income ($p<0.01$). We found no association of past-year BZ misuse on 12 month B/N treatment retention,nor any interaction effects on retention due to prescription BZ use. We found no association of past-year BZ misuse on ED visits. Yet,ED visits were more frequent during B/N treatment among patients with an approved BZ Rx compared to those without Rx (RR= 2.02, $p<0.005$),even after adjusting for gender,BZ misuse,and addiction & psychiatric severity.
Conclusions: Patients receiving B/N and a BZ Rx had more ED visits during treatment than those without a BZ Rx,irrespective of BZ misuse history. Past-year BZ misuse and BZ Rx were not associated with B/N treatment retention.
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598

NEUROCOGNITIVE CORRELATES OF RISKY SEXUAL BEHAVIOR AMONG YOUNG ADULT CANNABIS USERS.

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Aims: Rates of risky sexual behavior (RSB) are high among cannabis users. However, little is known regarding the underlying mechanisms of this association. We examine the relationships among neurocognitive measures of episodic memory and inhibitory control on several indices of RSB among young adult cannabis users.
Methods: Sixty-six cannabis-users (ages 17-24) completed inventories of their cannabis use and RSB. Neurocognition was assessed via: Hopkins Verbal Learning Test—Revised (HVLT), Iowa Gambling Task (IGT), Balloon Analogue Risk Task (BART), Go-Stop Task (GST), and Monetary Choice Questionnaire (MCQ). Participants identified cannabis as their drug of choice, used cannabis in the last 45 days, and had minimal mental health, medical, and other substance use confounds.
Results: Fewer words recalled after a delay on the HVLT ($\beta=-.35$, $p=.006$) and poorer performance on the BART ($\beta=.28$, $p=.04$) were both associated with higher overall sexual risk. Poor HVLT delayed recall also predicted decreased use of protection ($\beta=-.41$, $p=.005$). Furthermore, more cannabis use was associated with more overall sexual risk among those who performed more poorly on the IGT ($\beta=.50$, $p=.006$), but not among those with better performance ($\beta=-.02$, $p=.91$). Similarly, more cannabis use was associated with more sex-related consequences among those who evidenced more risk-taking on the BART ($\beta=.73$, $p=.03$), but not among those who performed better ($\beta=.08$, $p=.82$). No other significant effects emerged.
Conclusions: Preliminary support is provideed for the adverse influence of neurocognitive deficits on RSB among cannabis users. In addition to the direct effects between episodic memory and risk-taking on RSB, we found that the relationship between amount of cannabis use and RSB is influenced by decision-making and risk-taking. However, these relationships varied according to the dimension of neurocognition and parameter of RSB in question. Longitudinal methodologies are needed to establish temporal relationships between cannabis use, neurocognitive dysfunction and RSB.
Financial Support: F31DA032244-01(Schuster);K23DA023560(Gonzalez)

599

THE RELATIONSHIP BETWEEN EXPANSION OF OPIOID AGONIST TREATMENT AND REDUCTION IN HEROIN OVERDOSE DEATHS IN BALTIMORE, MARYLAND: 1995-2009.

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Aims: Over the last 15 years, Baltimore City, MD (USA) expanded opiate agonist treatment to reduce the negative impact of the city's widespread heroin addiction problem. This archival data study examined the association between the expansion of methadone and buprenorphine treatment and heroin overdose deaths in Baltimore City from 1995 through 2009.
Methods: Annual data were obtained on the number of heroin overdose deaths, the purity of seized heroin, and the number of methadone and buprenorphine patients for the period of 1995-2009, inclusive, in Baltimore City. Time series analysis of heroin overdose deaths was conducted using Newey-West regression.
Results: Starting in 2003 and adjusting for heroin purity and the number of methadone patients, heroin overdose deaths decreased as more individuals were treated with buprenorphine ($p<.001$). Heroin overdose deaths over this period were not significantly associated with heroin purity. From 1995 – 2009, the relationship to methadone treatment was complex. Average annual overdose deaths decreased by 37% following the availability of buprenorphine in 2003 (262 vs. 165; $p<.05$).
Conclusions: Starting in 2003, increased access to buprenorphine in Baltimore may have significantly reduced heroin overdose deaths. Policies that expand access to such treatment can potentially have a substantial impact on heroin-associated mortality.
Financial Support: NIDA 1R01DA013636 and 2R01DA15842

600

PREDICTORS OF CRACK COCAINE USE IN THE HOMELESS POPULATION IN BRITISH COLUMBIA, CANADA.

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Aims: An increase in crack cocaine use in the injecting population in Vancouver, BC from 1996 (7.4%) to 2005 (42.6%) has been reported. A high level of crack cocaine use characterizes our provincial severe concurrent disorder treatment program frequented mainly by homeless. It thus seemed pertinent to study crack cocaine use among homeless in BC. We hypothesized that socio-demographics, region, and childhood adversity would predict crack cocaine use.
Methods: Individuals were randomly recruited from 3 urban regions in BC. Standard assessments included the MINI International Neuropsychiatric Assessment, and the Mausdley Addition Profile. Analyses were conducted using bivariate tables and logistic regressions (SAS).
Results: 499 individuals provided sufficient information. 382 (76.6%) reported a history of crack cocaine use. In bivariate analysis age ($p=0.013$), incarceration ($p<0.0001$), lower education ($p=0.011$), lack of employment ($p=0.038$), involvement with sex-trade ($p=0.013$), heroin use ($p<0.0001$) and a history of depressive episode(s) ($p<0.0001$) were significantly associated with crack cocaine use. Not associated were sex, ethnicity, region, mania, psychosis, childhood abuse, foster care or alcohol use. A logistic regression model indicated three factors to be independent significant predictors: heroin use ($p<0.0001$), depressive episodes ($p=0.0027$) and incarceration ($p=0.021$).
Conclusions: The level of crack cocaine use in the homeless population in BC is extremely high. Predictors identified were different from those hypothesized: 1.) heroin use, but not use of other substances; 2.) a history of DSM IV depressive episode(s), but no other mental disorders; 3.) a history of incarceration. The cross-sectional character of the study constitutes its main limitation. Additional analysis will be presented to further probe these findings and test post hoc explanations of these findings.
Financial Support: BCMHA (PHSA)

601

THE FIRST 90 DAYS FOLLOWING RELEASE FROM JAIL: PRELIMINARY FINDINGS FROM THE RECOVERY MANAGEMENT CHECKUPS FOR WOMEN OFFENDERS (RMCWO) EXPERIMENT.

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Aims: To examine the direct impact of monthly Recovery Management Checkups (RMC) vs. control in the first 90 days post release from jail on receipt of community-based substance abuse treatment and the indirect effect of RMC on abstinence (via treatment), HIV risk behaviors and illegal activity/re-incarceration (via treatment and abstinence).
Methods: Women were recruited from Cook County's Department of Women's Justice Services (DWJS), which operates jail- (residential) and furlough- (outpatient) based programs as alternative sentencing for women offenders incarcerated for drug problems and who are considered nonviolent. Of 492 women eligible, 98% agreed to participate. Of the 480 randomized women, 100% completed the intake and release interviews, and over 90% completed the 30-, 60-, and 90-day post-release interviews. Half the women were randomly assigned to get monthly RMC using motivational interviewing regarding substance use, HIV risk behavior or illegal activity, HIV intervention, and assistance accessing and engaging in treatment. Of the women assigned to RMC, 83% attended all three session for RMC.
Results: During the 90 days following release from jail, women in the RMC condition (vs. control) were significantly more likely to participate in substance abuse treatment and returned to treatment significantly sooner. Women who received any treatment were significantly more likely than those who did not to be abstinent from any alcohol or other drugs. Those abstinent were significantly less likely to engage in unprotected sex, illegal activity, and to be re-incarcerated.
Conclusions: The study documented the high relapse rates during the first 90 days post-release and demonstrated the effectiveness of aggressively linking them to community-based treatment in terms of directly increasing initiation. These results also demonstrated the indirect impact of RMC on abstinence, illegal activity, and re-incarceration for the women offenders.
Financial Support: NIDA grant number R01 DA 021174

602

HIGH-RISK BEHAVIORS AND INFECTIOUS DISEASE SPREAD AMONG ADOLESCENTS.

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Aims: Prior work has linked behaviors to infectious disease risk but results have been limited by inadequate female representation. With girls abusing alcohol/drugs and committing violent crimes at similar levels to boys, they face elevated risk of HIV/STD infection. Our aims: 1) examine the prevalence of risk behaviors and infectious disease among youth, 2) discover what behaviors are most predictive of disease, 3) delineate behavior and disease status patterns that differ by gender.
Methods: Data are from adolescents (n = 195; 52% female, ages 14–18) court-referred to residential treatment for chemical dependency. Assessments spanned various domains (e.g. demographic, drug, and behavioral variables) at intake and discharge. Differences between subjects were evaluated using Fisher's exact test for binary variables or Kruskal-Wallis Chi-Square Test. Random effects regression analysis was performed to identify predictor variable associated risk conditions. Gender by risk condition interaction terms were included to explore differential effects of predictors by gender.
Results: Several variables emerged as predictors: For example, gender ($F=23.91, p<0.0001$), minority status ($F=11.59, p<0.0008$), sexual abuse ($F=6.88, p<0.0095$), contraceptive use ($F=4.38, p<0.0140$), prior felonies ($F=3.78, p<0.0472$), age at 1st intercourse ($F=3.76, p<0.0442$), age at first drink ($F=6.37, p<0.0126$), and nicotine use ($F=3.92, p<0.0493$) was predictive of STD status. Further, order in which participants first used substances and first engaged in sexual activity indicated that for both women (77.45%) and men (77.42%), substance use preceded sexual activity.
Conclusions: Risk behaviors associated with disease spread differ by gender. Gender-oriented recovery programs must improve protocols by addressing differing patterns in behavior by gender and their impact on health.
Financial Support: NIAAA K01AA015137, John Templeton Foundation Award

603

IMPLEMENTATION AND ADAPTATION OF CONTINGENCY MANAGEMENT TREATMENTS FOR COCAINE ADDICTS IN COMMUNITY SETTINGS.

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Aims: Cocaine use is an increasingly serious problem in Spain. Thus, the development and dissemination of effective treatments for cocaine dependence is an important public health priority in this country. There is extensive clinical evidence that Contingency management (CM) treatments are effective in the treatment of this addiction. Further research is needed to demonstrate the adaptation of CM interventions in natural settings. The main objective of the present study was to analyze the effectiveness and the applicability of one of the most widely researched and most highly rated psychological treatments, the Community Reinforcement Approach (CRA) plus Vouchers, in a Spanish public general healthcare context.
Methods: Ninety-one cocaine dependent patients enrolled on an outpatient program for cocaine dependence were assigned to one of three treatment conditions, CRA plus vouchers, CRA or standard care.
Results: At the 6-month assessment, 16.1% of patients assigned to standard treatment were abstinent, compared to 28.2% in the CRA condition and 47.6% of patients assigned to the CRA plus vouchers condition. Retention rate at six months was 32.3% in the standard treatment group, 41.00% in the CRA group, and 62.00% in the CRA plus vouchers group.
Conclusions: This study showed that treating cocaine addiction by combining CRA with vouchers was more effective than CRA only and standard treatment in community outpatient programs in Spain. Our study suggests the generalizability of CRA plus vouchers in natural contexts, with similar levels of effectiveness than in experimental settings. Further research is necessary to support these findings.
Financial Support: Spanish National Plan on Drugs (Ref. MSC-06-01) and the University of Oviedo, Spain.

604

CARE COORDINATION OF PRESCRIBED PSYCHOTROPIC MEDICATION IN A METHADONE PROGRAM.

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Aims: Methadone Maintenance patients suffer from multiple comorbidities. Patients are prescribed psychotropic medication which may cause impairment or sedation with methadone. Care coordination with outside prescribing professionals is essential to ensure safety. A quality improvement project was developed to assess patients being prescribed psychotropics, educate patients regarding risks of drug interactions, assess for impairment/sedation and coordinate care with prescribers.
Methods: Nurses created a list of patients. Counselors met with patients to discuss the risks of methadone with prescribed medications and requested a consent to release information regarding their methadone treatment to medical providers and an update of the patients current medications and treatment plan. Patients were assessed for illicit drug use or impairment. Patients declining consent were required to meet with the physician.
Results: 88(21%)of the 421 clinic patients were prescribed psychotropic medications. The demographics reflected the population served, 44(50%)were >50yrs. 16(18%) were positive for illicit drug use and 4 were believed impaired, all 4 used illicit drugs. No patients prescribed medications but not using illicit substances were impaired. 88(100%)received counseling, 78 (89%) signed a consent for release of information and care coordination, 10(11%) refused consent. 4(33%) patients of the total refusing to consent were using illicit substances. 31(40%)of consults requested were returned. No patients had a dose decrease or were discharged from the MMTP.
Conclusions: Patients were receptive to counseling on the risks of methadone and psychotropic medications. The majority were willing to sign consents allowing for coordination of care, however responses from less than half of the providers indicates a need for improved communicaton. No patients declining consent required a decrease in their methadone dose or were discharged from the program for non-compliance, indicating an ability to indiviualize care based on pateint need. Impairment from prescribed psychotropic medication was not problematic.
Financial Support: BIMC
NYS OASAS

605

RELATIVE ATTRACTIVENESS OF REFORMULATED OXYCONTIN®: COMPARATIVE ASSESSMENT OF TAMPERING POTENTIAL AND RECREATIONAL DRUG USER PREFERENCES FOR OPIOID FORMULATIONS.

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Aims: Reformulated OxyContin® (oxycodone HCl controlled-release) tablets (ORF) use a polyethylene oxide control-release formulation that imparts resistance to physical and chemical manipulations. Original OxyContin® tablets (OC) provided no tamper resistance. Information on how in vitro tamper-deterrent properties translate into real-world decrease in attractiveness to abusers is provided.
Methods: This was a non-interventional, single-session study in abusers/users experienced in tampering with prescription formulations. Subjects were presented with opioid formulations in a randomized manner using information cards and placebos. Subjects attempted to tamper with placebo tablets using commonly available supplies (eg, hammer, pill crusher, mortar and pestle). Subjects responded to questions about the products and their tampering potential. The following endpoints were assessed: Opioid abuse/tampering history and preferences, Opiate Attractiveness Scale, Value of Product Scale, Likelihood to Tamper Scale, Value of Product - Likelihood to Tamper Index, Overall Desirability ranking, and Estimated Street Value.
Results: OC had the highest mean score on the Opioid Attractiveness Scale and a hypothetical oxycodone/naltrexone oral product and ORF were ranked lowest. Both a hypothetical oxycodone/naltrexone oral product and ORF had properties that rated them as unattractive. Mean scores were approximately 5.0 to 6.4 (on a 7-point Likert scale) for Value of Product and from 5.4 to 6.6 for Likelihood to Tamper for OC, OxyIR®, Percocet®, Percodan®, and a hypothetical oxycodone transdermal patch. On Overall Desirability and Estimated Street Value, OC was ranked first and ORF was ranked just above a hypothetical oxycodone/ naltrexone oral product.
Conclusions: ORF was among the least attractive of the opioid products for purposes of tampering while OC was the most or among the most attractive. The characteristics of the ORF formulation may constitute significant deterrents against tampering.
Financial Support: Purdue Pharma L.P.

606

PERIPHERAL SELECTIVITY AS AN APPROACH TO CIRCUMVENT DYSPHORIC EFFECTS OF CANNABINOID CB1 RECEPTOR INVERSE AGONISTS.

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Aims: To design, synthesize and test antagonists/inverse agonists of the cannabinoid CB1 receptor (CB1R), that do not cross the blood-brain barrier (BBB) while exhibiting suitable affinity and selectivity for CB1R vs. CB2R and metabolic stability.
Methods: 1) SAR study incorporating charge and topological polar surface area (tPSA) that are associated with restricted BBB permeability, 2) synthesis, 3) calcium flux functional assay to determine efficacy and selectivity at CB1R and CB2R, 4) CB1 and CB2 receptor binding assays vs. [3H]CP 55,940 and [3H]SR141716 for potency and selectivity, 5) MDCK-mdr1assay as a model of BBB penetration, 6) blood plasma and S9 liver enzymes to determine metabolic stability, and 7) mouse PK study in plasma and brain from i.p. and oral administration (10 mg/kg), 30-60 min.
Results: CB1 antagonists/inverse agonists were developed with increased tPSA (≥ 80 A2) that had high CB1 affinity (3-15 nM) and selectivity (>100 fold) and showed < 1% permeability across an MDCK-mdr1 cellular membrane model of the BBB in the best examples. Compounds were identified with good metabolic stability in blood plasma and S9 liver enzyme preparations (<20% degradation over 2 hr). Snapshot pharmacokinetics supported brain:plasma distribution at 1 h consistent with negligible brain penetration.
Conclusions: Structural modifications focusing on tPSA and balance with lipophilic moieties of the 3-carboxamide sector of the rimonabant template have been demonstrated to introduce peripheral selectivity and improve pharmacological properties of inverse agonists of the CB1R. In contrast to CB1R inverse agonists that cross the BBB (eg. Rimonabant), these analogs can be considered viable candidates for circumventing the psychological problems (ie. suicidal ideation) in therapies where CB1R antagonism would be beneficial.
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607

DECREASED VENTROMEDIAL PREFRONTAL ACTIVITY DURING STRESS EXPOSURE IS ASSOCIATED WITH EMOTION REGULATION DIFFICULTIES IN EARLY ABSTINENT ALCOHOL-DEPENDENT PATIENTS.

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Aims: Early abstinent alcohol-dependent (AD) patients often suffer from increased sensitivity to stress and emotion regulation difficulties. However, brain mechanisms underlying emotion regulation problems associated with chronic alcoholism remain unclear. The current study aims to examine neural correlates of difficulties in emotion regulation in early abstinent alcohol-dependent patients using functional magnetic resonance imaging.
Methods: The study compared demographically matched, 40 (9 women) AD patients and 40 (13 women) healthy controls. Brain activity was examined while participants were engaging in brief individualized script-driven imagery trials of stress, alcohol-cue and neutral-relaxing scenarios. Individual differences in emotion regulation ability were measured using the Difficulties in Emotion Regulation Scale (DERS).
Results: AD patients showed greater emotion regulation difficulties verified by higher DERS scores than healthy controls ($t=2.36$, $p<0.05$). During stress exposure relative to Neutral, AD patients showed negative correlations between DERS scores and activity in the ventromedial prefrontal cortex (VmPFC) and anterior cingulate cortex (ACC) ($p<.01$, whole-brain FWE corrected). DERS scores did not correlate with brain activity during Alcohol-cue or Neutral, indicating that this association is stress-specific. Healthy controls did not exhibit any correlations between their DERS scores and brain activity.
Conclusions: The VmPFC and ACC are core brain regions involved in emotion and stress regulation. These results suggest that decreased regulatory function in the VmPFC/ACC under emotional stress may partially account for emotional dysregulation in early abstinent AD patients. Current findings highlight stress-specific, altered response in core regulatory regions associated with emotion regulation problems in early abstinent AD patients.
Financial Support: This work was supported by NIH grants and the NIH Roadmap for Medical Research Common Fund: UL1-DE019586(RS), P50-DA016556(RS), R01-AA13892(RS), PL1-DA024859(RS).

608

THE ASSESSMENT OF DOPAMINERGIC INVOLVEMENT IN COCAINE-INDUCED TASTE AVERSIONS.

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Aims: Although cocaine readily induces taste aversions, little is known about the mechanisms underlying this effect. It has been suggested that its inhibitory effects at one of the monoamine transporters may be mediating this suppression. The present series of studies examined a possible role of dopamine (DA) in this effect. Experiment 1: Animals were exposed to a DA reuptake inhibitor, GBR 12909 (GBR) prior to taste aversion conditioning with cocaine. Such preexposure generally weakens aversions if the two drugs share a common mechanism. Experiment 2: Animals were injected with the DA antagonist haloperidol (HAL), immediately prior to aversion conditioning with cocaine.
Methods: Exp 1: Male Sprague-Dawley rats were exposed to GBR (32 or 50 mg/kg) prior to aversion conditioning in which a novel saccharin solution was paired with either cocaine (18 mg/kg), GBR (32 mg/kg) or vehicle. Exp 2: A non aversive dose of HAL (1 mg/kg) was administered prior to the pairing of saccharin with cocaine (10, 18, or 32 mg/kg) or vehicle.
Results: Exp 1: A 2 x 3 x 4 mixed-model ANOVA revealed significant effects of Trial, Preexposure and Conditioning, as well as significant Trial x Preexposure and Trial x Conditioning interaction. A One-way ANOVA on the Final Aversion Test revealed significant group differences. Fisher LSD post hoc analysis revealed that preexposure to GBR at 50 mg/kg, (but not 32 mg/kg) attenuated aversions induced by itself and cocaine. Exp 2: None of the doses of HAL tested were aversive in the CTA procedure. A 2 x 4 x 5 mixed-model ANOVA revealed significant effects of Trial, Pretreatment and Conditioning, as well as a significant Trial x Pretreatment x Conditioning interaction. Under these conditions, HAL blocked cocaine-induced CTAs (at the 18 and 32 mg/kg doses).
Conclusions: These results suggest that DA has a role in cocaine-induced CTAs. These data are discussed in the context of previous work demonstrating roles for both norepinephrine and serotonin in cocaine-induced CTAs.
Financial Support: This work was supported by a grant from the Mellon Foundation to ALR

609

FEASIBILITY AND VALIDITY OF ECOLOGICAL MOMENTARY ASSESSMENT IN ALCOHOL-, TOBACCO-, CANNABIS- AND OPIATE-DEPENDENT PATIENTS.

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Aims: Despite growing use of Computerized Ambulatory Monitoring (or Experience Sampling Method) in substance dependence research, little is known about the comparative feasibility and validity of these novel methods by type of substance dependence. This study compares the feasibility and validity of computerized ambulatory monitoring in outpatients seeking treatment for alcohol, tobacco, cannabis or opiate dependence.
Methods: : Participants were recruited from an outpatient addiction treatment center. Patients completed standard clinical instruments followed by two weeks of computerized ambulatory monitoring of their daily life experiences including mood states, behaviors and substance use.
Results: 109 participants were recruited. The main substance dependence was alcohol (n=38), opiates (n=27), tobacco (n=23), cannabis (n=21). Individuals with cannabis dependence had the lowest rates of study acceptance (31%) as well as compliance with the repeated electronic interviews (79.9%), while those with tobacco dependence had the highest rates (62% and 91.0%, respectively). Strong concurrent validity was found between scores from standard clinical instruments and similar constructs assessed in daily life, with no difference by substance group. While no fatigue effect was observed, changing patterns in responses indicated possible reactivity to the repeated assessments.
Conclusions: Computerized ambulatory protocols are feasible and provide valid data in dependent subjects treated for alcohol, tobacco, cannabis or opiate dependence.
Financial Support: PHRC 2006, MILDT 2010, CRA 2009, PRA-CNRS-CHU 2008

610

ADOLESCENT RISK-TAKING AND COCAINE SELF-ADMINISTRATION; A VICIOUS CYCLE?

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Aims: Chronic cocaine use is associated with maladaptive decision-making and elevated risk-taking, but it is unclear whether elevated risk-taking predisposes individuals to cocaine use, or whether cocaine-induced neuroadaptations promote risk-taking (or both). To address each of these possibilities, we used a behavioral task in rats (the Risky Decision-making Task - RDT) to assess relationships between both adolescent and adult risk-taking and cocaine self-administration.
Methods: Adolescent male Long-Evans rats (P26) were trained in the RDT. In this task, rats were given discrete-trial choices between two levers, one which delivered a small, "safe" food reward and the other which delivered a large, "risky" food reward accompanied by the risk of a mild footshock, the probability of which increased over the course of a test session in consecutive blocks of trials (0, 25, 50, 75, 100%). Upon reaching adulthood (P70), half the rats were implanted with intravenous jugular catheters. Following recovery, rats self-administered cocaine HCl (0.5 mg/kg/infusion) for 2h/day for 10 days, followed by a high-dose, long-access regimen (1.0 mg/kg/infusion for 6h/day) for 14 days. The remaining rats orally self-administered a sucrose solution as a control procedure. Rats then remained abstinent from cocaine (or sucrose) for 3 weeks before RDT retesting.
Results: There was substantial variability in adolescent RDT performance, which was associated with acquisition of cocaine self-administration (preference for the large risky reward was correlated with cocaine intake during the first 5 days of 0.5 mg/kg/infusion self-administration). In addition, upon RDT retesting, rats that self-administered cocaine showed greater risk-taking compared to controls that self-administered sucrose.
Conclusions: These data indicate that adolescent risk-taking is predictive of acquisition of cocaine self-administration, and that cocaine self-administration in turn also causes long-lasting elevations in risk-taking, indicating a possible "vicious cycle" between risk-taking and cocaine use.
Financial Support: DA024671 (BS)

611

REDUCTION IN OXYCONTIN® DIVERSION CASES FOLLOWING THE INTRODUCTION OF REFORMULATED OXYCONTIN.

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Aims: Reformulated OxyContin® (ORF), a formulation intended to deter crushing and that forms a gel when dissolved, was introduced in August 2010, with the goal of deterring abuse, particularly through routes that require tampering. This study examines whether there was a decline in drug diversion cases for OxyContin following the introduction of the reformulation.
Methods: The number of diversion cases using reports from law enforcement agencies participating in the RADARS® System were compared for the periods before and after introduction of ORF. Case count data from the 4Q2008 through the 3Q2010 was considered the pre-ORF period and 4Q2010 to 2Q2011 the post-ORF period. Poisson regression tested whether the number of OxyContin diversion cases declined post-ORF, adjusting for population coverage and for number of individuals filling a prescription for a given drug, a measure of drug availability. Trends were also estimated for eight other prescription opioid drug classes.
Results: A 45% decline in the expected number of OxyContin diversion cases (95% CI: 40-50%, $p<0.001$) was observed following transition to reformulated OxyContin. This decline was significantly greater than changes observed for immediate release oxycodone (10% increase, 95% CI: 5-16%), hydrocodone (20% decrease, 95% CI: 16-23%), tramadol (31% decrease, 95% CI: 19-41%) and other opioid drug classes with the exception of buprenorphine (34% decrease, 95% CI: 23-43%).
Conclusions: These findings indicate that introduction of reformulated OxyContin was followed by a decline in diversion of OxyContin and that the decline was greater than most other prescription opioids. The decreased diversion of OxyContin to illegal channels suggests a decline in demand for reformulated versus original OxyContin.
Financial Support: H Chilcoat & P Coplan are employees of Purdue Pharma L.P. The RADARS System provides post-marketing surveillance of medications to pharmaceutical manufacturers.

612

DEVELOPMENT OF INFORMATIONAL MATERIALS ABOUT MEDICATION-ASSISTED TREATMENT.

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Aims: Four non-experimental studies were conducted to inform the development of the informational materials, and subsequently to assess, the impact of the materials upon their targeted audiences. The purpose of the materials was to enhance patients' awareness and motivation to use MAT and to increase substance abuse treatment providers' knowledge about engaging and promoting patients' use of MAT as part of their treatment and recovery process.
Methods: Study 1 identified critical constructs affecting patients' interest, ease and ability to engage in MAT through 8 focus groups involving 68 patients. Study 2 assessed the attitudes, knowledge, and self-efficacy in promoting MAT among 510 substance abuse providers. Study 3, assesses the emotive and cognitive responses of patients in response to exposure to the developed informational and promotional MAT materials. Study 4, assesses changes in the attitudes, knowledge, and self-identified efficacy in promoting MAT among substance abuse providers upon completion of a self-paced online instructional program.
Results: Results from Study 1 indicated that elements of street or drug culture often supersede those of ethnic culture in determining attitudes toward and motivations for using MAT. Participants described MAT in nuanced ways suggesting a variety of perceived benefits and barriers to engaging in MAT. From Study 2, less than ½ of the respondents reported working for a treatment agency the provided MAT either directly or through affinitive agreements. While 78% of the respondents indicated that they have spoken to patients about MAT, these same counselors also report doing so with less than half of their patients.
Conclusions: In addition to summarizing the methodological approaches and challenges encountered with each of these studies, this poster will summarize key findings from each.
Financial Support: Project was supported by a cooperative agreement from the Substance Abuse & Mental Health Services Administration.

613

MOTIVES FOR CHANGING SUBSTANCE USE AMONG METHAMPHETAMINE-USING ADULTS.

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Aims: This study describes motives for restarting and stopping substance use after periods of abstinence/use, self-reported by adults with long histories of methamphetamine (meth) use.
Methods: Data are from an 8-year follow up interview in a natural history study (2009-11) of meth users in Los Angeles county (N=393); 59% had received drug treatment at study recruitment. One-fourth used meth in the past 30 days. Respondents answered open-ended questions about why they began or ended periods of use of meth, alcohol, and other substances in the past 8 years. Responses were coded (by each of 3 coders) into 15 categories; coding discrepancies were discussed until consensus was achieved. Interview data also provided demographics, substance use history, and days/months since last use of each substance.
Results: The 5 most commonly reported reasons for resuming meth use were: 1) to achieve desired physical effect (e.g., better sex, concentration; 40% of 284 providing reasons for change); 2) to cope with mental/emotional concerns (e.g., depression, stress, boredom; 38%); 3) the social context (e.g., friends used; 29%); 4) meth was available (27%); and 5) craving/addiction (e.g., had to have it; couldn't stop; 22%). With the exception of social context, these reasons were significantly related to using meth in the past year. The most common reasons for stopping use were related to self-awareness and an intrinsic need for a life change (e.g., lost too much; wanted a better life; realized I could do better; 25%); and entering treatment (16%). Analyses further explore motives for changing alcohol and illicit drug use and their relation (using chi-square and t-test) to demographics, substance use severity and abstinence.
Conclusions: Preliminary results suggest that relapse among adults with long histories of meth use is characterized by a wide array of individual differences in motivations. A better understanding of these motives may assist treatment providers in improving relapse prevention strategies.
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614

COMMUNITY-BASED SMOKING CESSATION PROGRAMS: LESSONS LEARNED FROM A RANDOMIZED CLINICAL TRIAL.

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Aims: Utilization and effectiveness of smoking cessation services are usually lower among underserved populations, indicating a need for more sustainable interventions. This study aims at exploring the possibility of community based cessation programs based on results of a Randomized Clinical Trial (RCT). A new intervention is being planned, implemented, and supported by the local community.
Methods: A total of 437 participants were recruited and randomly assigned to either a group-based or an individual-based smoking cessation intervention during the first phase of this program. Participants in both arms received training on smoking cessation according to the Fresh Start curriculum for twelve weeks and followed for nine months. The trial was based in a community health clinic under the supervision of medical providers.
Results: Intent to treat analyses indicate that success in smoking cessation was low (i.e., quit rates of about 10%), with a high level of attrition (i.e., 45% attended between 1 and 5 sessions, and only 14% attended 6-12 sessions). Attendance was strongly correlated with cessation. Withdrawal syndrome, stress, and "not being ready to quit" were among important barriers to quitting. There were no significant differences between the two arms; however, the group intervention was deemed to be more cost-effective.
Conclusions: Community based smoking cessation programs in underserved communities can be successful if they include proper incentives to retain participants and are supported by community organizations. The preliminary results of a new decentralized community model comparing group interventions with different incentives and intensity will be presented. The process of how the new intervention is informed by the facts of the previous trial in partnership with local community will be described with special attention to a new incentive program that includes non-monetary club membership awards and status.
Financial Support: Supported by grant 5 R24 MD002803 from the National Center of Minority Health and Health Disparities

615

EVALUATION OF PEPTIDE AND CONJUGATE MORPHINE VACCINES IN MICE.

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Aims: Vaccines against opiate addiction are not yet sufficiently characterized to proceed to clinical studies. In this study, we aimed to investigate conjugate and peptide morphine vaccines for production of antibodies with sufficient binding affinity to block morphine analgesia.
Methods: 6-succinyl-morphine-lipopeptide vaccine was generated by peptide synthesis. Conjugate vaccines were prepared by linking a hapten (6-succinyl-morphine or 6-amino-oxobutenoic-morphine) to a carrier protein (KLH or tetanus toxoid). Anti-morphine antibody levels in Balb/C mice were evaluated using ELISA. Antibody affinity was determined by inhibition ELISA. Morphine induced analgesia was assessed using a hot plate assay.
Results: All morphine vaccines evaluated were able to elicit anti-morphine antibodies with peaks at 6 to 8 weeks. Antibody levels varied depending on vaccine and adjuvant used. Adjuvant was needed for conjugate vaccines to produce satisfactory levels of antibodies (ranged from 800 to 1700 μg/ml). By contrast, adjuvant was not required for the peptide vaccine to elicit a similar level of antibodies. Addition of adjuvant to the peptide vaccine resulted in a 3 fold increase. Antibodies generated by conjugate vaccines had adequate affinity for morphine and for 6-acetyl morphine, and were effective for inhibiting morphine analgesia by 3 to 5 fold. However, the antibodies from the peptide vaccine had relatively lower binding affinity, which was associated with lower inhibition of morphine analgesia.
Conclusions: The peptide vaccine produced higher antibody levels than conjugate vaccines. The conjugate vaccine made from a 6-succinyl-morphine linked to tetanus toxoid elicited antibodies with highest binding affinity and the greatest inhibition of analgesia.
Financial Support: R01 DA026859, DA030338, DA023898, VA Merit Review Program.

616

REGULATION OF AKT AND GSK3 PHOSPHORYLATION BY DOPAMINE RECEPTORS IN MOUSE NUCLEUS ACCUMBENS.

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Aims: Previous studies demonstrate that dopamine receptors in the striatum can signal through the serine/threonine kinase Akt by a G-protein independent mechanism. Regulation of Akt and its downstream substrate glycogen synthase kinase-3 (GSK 3) by specific dopamine receptor subtypes in the nucleus accumbens remains poorly understood. This study investigated Akt- and GSK-3 phosphorylation in mouse nucleus accumbens by direct or indirect activation of dopamine receptors using the D1-like receptor agonist SKF82958, D2/D3 dopamine receptor agonist quinpirole, and indirect dopamine receptor agonist cocaine. Receptor specificity was characterized using selective dopamine D1 and D2 receptor antagonists.
Methods: CD-1 mice received a single injection of SKF82958 (1 mg/kg), quinpirole (2 mg/kg), cocaine (20 mg/kg) or saline and were euthanized at 15, 30, 60, or 90 min post-injection. Nucleus accumbens were dissected and processed for detecting phosphorylation of GSK3 and Akt by Western blotting.
Results: Levels of p-AktThr308 and pGSK3α/β-Ser21/9 in the nucleus accumbens were significantly elevated 15, 30, and 60 min after quinpirole, but not SKF82958, as compared to their corresponding saline-injected controls. In contrast, there was a rapid and transient increase in pAktThr308 and pGSK3α/β-Ser21/9 15 min after cocaine. Pretreatment with the selective D2 receptor antagonist, eticlopride (0.5 mg/kg) significantly blocked the upregulation of pGSK3α/β and pAkt produced by quinpirole. Experiments in progress will reveal the subtype(s) of dopamine receptors that mediate the phosphorylation of AktThr308 and GSK3α/β induced by cocaine.
Conclusions: These data indicate that phosphorylation of Akt and GSK3 in the nucleus accumbens is differentially regulated by D1 and D2 receptors in a time-dependent manner. Quinpirole-induced phosphorylation of GSK3α/β and Akt is a D2 receptor-dependent event.
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617

EFFECTS OF CHRONIC TREATMENT WITH ALCOHOL ON THE MORPHINE-INDUCED REWARDING EFFECTS.

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Aims: Morphine is an opioid receptor agonist, and has widely been used to control pain in the case of cancer. It is known that the psychological dependence on morphine is not induced under the pain state, and that the psychological dependence on morphine could be easily developed in patient who has alcohol dependence history. Chronic consumption of alcohol can alter the biochemical processes in the dopaminergic system. The neurochemical process of alcohol-induced physical dependence is supposed to result from adaptive changes in a number of neurotransmission systems, and several reports demonstrated the functional relationship between behavioral changes observed in alcohol-dependent animals and neurotransmission systems. On the other hand, many reports suggest alcohol increases the release of the endogenous opioid, and this increase significant part of the neurobiological mechanisms that are functionally involved in the drinking behavior of alcohol and development of alcohol dependence. However, the exact mechanism how alcohol treatment can affect the development of psychological dependence on morphine is not yet cleared. Therefore the aim of the present study was to examine the effect of chronic alcohol treatment on the rewarding effects of morphine in mice.
Methods: C57BL/6J mice were treated with 0%, 1% and 3% of alcohol in liquid diet for 5 days.
Results: We found that the chronic alcohol treatments dose-dependently enhanced the rewarding effects of morphine (5 mg/kg) using conditioned place preference paradigm. The DAMGO-induced stimulation of [35S]GTPγS binding in alcohol-chronic treated group was more potent than that in control mice in the ventral tegmental area.
Conclusions: These results suggest that prior alcohol treatment induces the up-regulation of μ-opioid receptor and enhances the acquisition of the rewarding effects of morphine.
Financial Support: This work was supported in part by Grants-in-Aid for Scientific Research from the Ministry of Health, Labor and Welfare and from the Ministry of Education, Culture, Sports, Science and Technology of Japan (No.23700453).

618

FEMALE VULNERABILITY TO SOCIAL STRESS AND ITS EFFECTS ON COCAINE TAKING.

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Aims: Cocaine addiction is sexually dimorphic. Women acquire habitual cocaine use in a shorter period of time, engage more in "binge"-like cocaine use, and are more prone to relapse relative to men. Significantly, stress disorders including major depression, increase the risks for substance use and relapse. Here we test the hypothesis that the vulnerability to cocaine addiction in females is due to neuroadaptation of dopaminergic neurons as a result of depressive-like social stress. We do so by using female social stress models in rats that behaviorally and neurochemically are activating or impairing.
Methods: Female Long-Evans rats exposed to maternal aggression for either 4 brief episodes (intermittent stress) or an extended confrontation twice a day for 21 days (chronic stress) were used. The experimental rats were tested for behavioral sensitization and DA release in the nucleus accumbens. In addition, the rats that self-administered cocaine were examined for performance during limited access (fixed ratio, FR5), progressive ratio (PR) schedule, and a 24-h continuous "binge". Following the "binge", the rats were studied in a reinstatement procedure after 2 weeks of abstinence.
Results: Only the rats that experienced chronic stress exhibited a significant attenuation in DA levels in response to cocaine, and attenuation of performance on a PR schedule of self-administration. On the other hand, intermittent stress showed a higher DA tone and longer-lasting behavioral and neurochemical sensitization. Intermittent stress attenuated the decrease in the "binge" when the rats were in estrus.
Conclusions: Neuroadaptations as a result of chronic social stress may attenuate subsequent cocaine taking. Intermittent stress induced sensitization and performance for cocaine taking varied by estrous cycle.
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619

PROBLEMATIC BEHAVIOR AND MDMA USE AMONG JAPANESE RAVE POPULATIONS.

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Aims: In Japan, the use of MDMA has emerged in the last decade. The fatal MDMA intoxication was reported, and the most of the cases were related to rave parties. In addition, the number of arrests and seizures of MDMA in Japan has drastically increasing. However, very little is known about the epidemiology of MDMA use among Japanese rave attendees. The purpose of this study was to examine the association between problematic behavior and MDMA use among rave attendees in Japan.
Methods: Participants were recruited between October 2010 and February 2011 from four rave parties at three different venues in Tokyo. The anonymous self-administrative questionnaire was conducted by laptop computers that installed all questionnaires. A total of 305 rave attendees (47.2% female) were included for data analysis.
Results: Among participants, 7.9% of total reported MDMA use in their lifetime. MDMA users were much more likely to experience aggressive behaviors and delinquent behaviors than non-MDMA users, such as bullying as perpetrator ($p=0.018$), reckless driving ($p=0.010$), and shoplifting ($p=0.012$). However, self-harm behaviors, such as self-injury ($p=0.272$) and having suicidal ideation ($p=0.796$), were not associated with MDMA use.
Conclusions: Compared to non-MDMA users, MDMA users were more likely to have experience of bullying as perpetrator, reckless driving, and shoplifting. Although the significant association between MDMA use and some of problematic behavior was found in our results, these data were based on cross sectional design, and it is limited to lifetime experience. Therefore, the results could not mention the causal relationship between the variables. However, our result may indicate potential risk for problematic behavior among MDMA users.
Financial Support: This study was supported by a Research Grant for Regulatory Science of Pharmaceuticals and Medical Devices, Health and Labour Sciences Research Grants from the Ministry of Health, Labour and Welfare of Japan.

620

DEVELOPMENTAL PATHWAYS FROM CHILDHOOD MALTREATMENT TO PROBLEMATIC ALCOHOL USE IN YOUNG ADULTHOOD.

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Aims: Childhood maltreatment has been linked to problematic alcohol use in young adulthood but there is a paucity of empirically-based knowledge about the developmental pathways linking childhood maltreatment and problematic alcohol use in later life. This study identified a unique and theoretically important, but little examined mechanism, personality trait of urgency, in accounting for the association between childhood maltreatment and later alcohol use.
Methods: Using a community sample of young individuals (N=257; mean age: 21.9; female 60%), we performed structural equation modeling to investigate how child maltreatment influences problematic alcohol use through the personality trait of urgency and to determine pathways for these effects in a multivariate context. We also examined variations in these pathways by characteristics of maltreatment including maltreatment subtypes (i.e., physical, emotional, and sexual abuse, neglect) and developmental timing of maltreatment (i.e., childhood vs. adolescence).
Results: The final models fit the data well. We found that emotional abuse was related to problematic alcohol use ($\beta = .22$) but this relationship was mediated to a great degree by urgent personality ($\beta = .41$) whereas sexual abuse was directly related to problematic alcohol use ($\beta = .15$). Our analyses also revealed that maltreatment occurred in childhood predicted problematic alcohol use, but this effect was mediated to a great degree by urgency ($\beta = .39$) whereas adolescent maltreatment had a direct effect on problematic alcohol use during young adulthood.
Conclusions: The present study suggests that personality trait of urgency may play a significant role in linking child maltreatment to problematic alcohol use in young adulthood. The results of this research suggested that urgent personality trait would be potentially useful targets to prevent problematic alcohol use among young people who have exposure to child maltreatment.
Financial Support: This research was supported by NIDA R03-DA030884 and the AMBRF/The Foundation for Alcohol Research.

621

ALTERED EXPRESSION OF α1 AND α2 SUBUNITS OF THE GABAA RECEPTOR AFTER LONG-TERM COCAINE SELF-ADMINISTRATION BY RHESUS MONKEYS.

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Aims: Recent research has shown significant changes in the GABA neurotransmitter system following chronic exposure to cocaine. The present study examined immunoreactivity (IHC) of α1 and α2 subunits of the GABAA receptor in reward-related nuclei (nucleus accumbens, NAc; anterior cingulate cortex, ACC; caudate, Cd; and putamen, Put) after long term cocaine self-administration.
Methods: Ten male rhesus monkeys either self-administered cocaine intravenously or received passive infusions of saline yoked to the cocaine injections (yoked control) for 100 days. Twenty-four hours after the last session, animals were sacrificed and their brains removed. The tissues were sectioned and IHC was conducted using a commercially available primary antibody to the α1- and α2- subunit of the GABAA receptor (α1GABAA and α2GABAA). Image analysis was conducted using ImageJ software.
Results: We found significantly higher immunoreactivity for α1GABAA receptors within the ACC and Cd in cocaine-exposed monkeys compared to yoked controls, whereas no corresponding effects were found in the NAc and Put. Within the VTA we found significantly lower immunoreactivity for α1GABAA in cocaine exposed animals. GABAA receptors containing α2 subunits showed a significantly decreased staining in cocaine self-administering monkeys when compared to yoked controls within the Cd and Put. No significant effects emerged across groups within the NAc, VTA and ACC.
Conclusions: Both the abundance of α1GABAA receptors and the fast ionophore kinetics suggest this receptor may play a greater role in neuroplasticity in comparison to α2GABAA, along with glutamate receptors, traditionally associated with synaptic restructuring. Our results raise the possibility that α1GABAA and α2GABAA receptors may contribute to the neuroadaptations that accompany chronic cocaine self-administration.
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622

VALIDITY OF PROPOSED CRITERIA FOR DSM-5 NICOTINE USE DISORDER IN 734 ISRAELI LIFETIME SMOKERS.

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Aims: Extensive evidence supports a proposal for DSM-5 to combine the criteria for substance abuse and dependence into one disorder, remove legal problems and add craving, resulting in Substance Use Disorder (SUD) defined by 11 criteria. Applied to Nicotine Use Disorder (NUD), these criteria indicate a single latent trait, but evidence is needed on their validity.
Methods: The relationship of each NUD criterion to nine external validators was examined in 734 lifetime smokers in an Israeli household sample evaluated with a structured interview. The validators included smoking soon after awakening, number of cigarettes/day, and withdrawal severity; regression analysis was used. Receiver operating characteristic (ROC) curve analysis was used to assess the association of the validators with the set of NUD criteria (number endorsed) and to identify whether DSM-5 NUD or DSM-IV nicotine dependence (ND) provided the most discriminating criterion set.
Results: All proposed DSM-5 NUD criteria were significantly associated with the validating variables; adjusted odds ratios for validators ranged from 1.26-10.93. Dependence, abuse and craving criteria showed similar magnitude of associations with the validators. The proposed DSM-5 NUD criterion set was also significantly associated with the validators, with significant ability to discriminate between the presence or absence of the validators (discrimination range, 63.9%-86.9%). ROC curve analysis indicated that the proposed DSM-5 set was significantly more discriminating than DSM-IV ND criterion set (p-value range, .036-<.0001).
Conclusions: Validation of each proposed DSM-5 NUD criterion, validity of the entire criterion set, and increased discrimination compared to the DSM-IV ND set all support the inclusion of nicotine abuse and craving criteria, allowing alignment of the nicotine criteria with those for alcohol and drug use disorders in DSM-5. The proposed changes should overcome some of the concerns expressed about nicotine disorders as defined in DSM-IV.
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623

SENSITIVITY AND PERFORMANCE OF DERIVED PARAMETERS FROM HUMAN ABUSE POTENTIAL STUDIES.

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Aims: Derived parameters are used to summarize large amounts of data from subjective measures in human abuse potential studies. This analysis describes distribution, variability, and inter-correlation characteristics of derived parameters for commonly used abuse potential measures.
Methods: Parameters for 100-pt Drug Liking and other VAS (peak effect [Emax], partial area under the effect curve [$AUE_{0\text{-}3h}$], AUE over 24 hours [$AUE_{0\text{-}24h}$] of each dose; Emax of all doses combined [$Emax_d$]) were derived for placebo and control data collected at multiple timepoints over 24 hours from 7 single-dose, randomized, double-blind, crossover studies in recreational drug users. Emax/$Emax_d$ were also calculated for global measures (Overall Liking/Take Drug Again VAS). Distribution was assessed using Shapiro-Wilk and skewness/kurtosis. Internal consistency and correlations were assessed with Cronbach's alpha and Spearman correlations.
Results: Drug Liking VAS Emax was very sensitive and showed large effect sizes (>1.0) for drugs of abuse, while treatment differences with $AUE_{0\text{-}24h}$ were modest. $AUE_{0\text{-}3h}$ was less sensitive compared to Emax but effect sizes were still reasonably large (>0.6 in most cases) and the 2 endpoints were significantly correlated ($p<0.001$) in most studies. Variability (%CV) was similar between $AUE_{0\text{-}3h}$ and Emax, although $AUE_{0\text{-}3h}$ was somewhat more likely to show normal distribution. $Emax_d$ showed a similar pattern compared to Emax of each dose but effect sizes were larger, even compared to Emax of the highest doses, and variability was slightly lower. Results were similar for other measures.
Conclusions: Derived parameters such as Emax, $Emax_d$, and $AUE_{0\text{-}3h}$ are sensitive and show similar performance characteristics, while $AUE_{0\text{-}24h}$ was less sensitive. These results have important implications for endpoint selection in human abuse potential studies.
Financial Support: INC Research and Pfizer Inc.

624

USING FINANCIAL INCENTIVES TO SUSTAIN SMOKING ABSTINENCE AMONG OPIOID-MAINTAINED PATIENTS.

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Aims: Approximately 90% of methadone and buprenorphine patients smoke cigarettes. Despite this, little progress has been made in developing effective treatments for these patients. We have shown that an intensive 2-week incentive intervention produced significant smoking abstinence in this group (Dunn et al., 2008, 2010) and are now conducting a 12-week trial aimed at sustaining the abstinence achieved in those initial weeks.
Methods: During Weeks 1-2 of this trial, subjects attend the clinic daily and earn voucher-based incentives for biochemical evidence of smoking abstinence. At the end of Week 2, subjects are randomized to an Extended Contingent (CONT) or Extended Noncontingent (NON) group for Weeks 3-12. Contingent subjects continue to receive vouchers contingent on smoking abstinence; Noncontingent receive vouchers independent of smoking status. We hypothesize that continued reinforcement of abstinence will be necessary in order to sustain the abstinence achieved during the initial two weeks of the cessation effort.
Results: Thus far, 44 subjects have completed the trial (32 yrs old, 41% male). During Weeks l-2, 58.8% of samples are smoking abstinent. In Weeks 3-12, CONT subjects are achieving significantly more smoking abstinence than NON (49.8% vs. 32.5% smoking-negative samples, respectively, $p<.05$). Similar patterns are seen in self-reported cigarettes per day, mean CO and urinary cotinine levels.
Conclusions: This treatment is producing relatively high levels of smoking abstinence during the initial two weeks that are consistent with our prior studies. Preliminary data suggest that ongoing reinforcement of abstinence may be important for sustaining the smoking abstinence achieved during the initial two weeks of the cessation effort, though there may be a subset of participants who can avoid relapse following a brief but intensive smoking intervention. Full data from the completed trial will be analyzed and presented at the June 2012 meeting, including analyses of baseline characteristics which may predict individuals who need brief vs. extended treatments for smoking cessation.
Financial Support: NIDA R01 DA019550 & T32 DA007242

625

VALIDATION OF BRAZILIAN VERSION OF INTERNALIZED STIGMA OF MENTAL ILLNESS SCALE ADAPTED FOR SUBSTANCE DEPENDENCE.

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Aims: The aim of this study was to translate and validate the Internalized Stigma of Mental Illness scale (ISMI) adapted for substance dependence for the Brazilian reality.
Methods: The ISMI is composed by 29 items grouped thematically in five subscales: Alienation, Stereotype Endorsement, Perceived Discrimination, Social Withdrawal and Stigma Resistance. The research was conducted with a sample of 299 substance dependents, patients from two public health institutions of Juiz de For a (MG), Brazil. The research instruments were: demographic questionnaire; MINI; ISMI; Rosenberg Self-Esteem Scale (RSES); Herth Hope Scale (HHS); and Center for Epidemiological Studies-Depression (CES-D) scale. The reliability analysis of ISMI was estimated by the Cronbach's alfa (α) and the split-half Spearman-Brown coefficient. Evidence of ISMI validity were analyzed by content and construct validity. For the construct validity, it was used the convergent validity and the exploratory factor analysis (maximum likelihood).
Results: The scale had an internal consistency reliability coefficient of alpha= 0.83 (and split-half=0.76). The construct validity showed a statistically significant correlation ($p<0.01$) between ISMI and CES-D (r=0.47), HHS (r=-0.19), and RSES (r=-0.48). The Brazilian version of ISMI adapted for substance dependence has satisfactory psychometric properties and promises to be a useful tool to measure internalized stigma.
Conclusions: Physicians and health professionals can encourage and include the reduction of stigma as part of treatment for substance dependence.
Financial Support: Supported by: FAPESP, AFIP, CAPES, CNPQ

626

PEER INFLUENCES ON ADOLESCENT SUBSTANCE USE: THE MODERATING ROLE OF PARENTING.

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Aims: The family environment and peer substance use are important factors in the development of substance use in adolescence. The present study examines the association between parenting behaviors and affect and substance use in adolescents with and without substance-using peers.
Methods: One-hundred twelve 10-16 year old adolescents and their parents participated in a Parent Adolescent Interaction Task (PAIT), in which they discussed a conflict topic for 10 minutes. Parent behaviors (negative affect, positive affect, shared parent-child positive affect, and supportive and structuring parenting) were coded throughout the interaction using a system (Chaplin, 2010) based on the parenting literature. Lifetime adolescent drug use was self-reported on the Youth Risk Behavior Survey (Brener et al., 2002) and peer substance use of any kind was reported by adolescents.
Results: Findings revealed a trend for an interaction between parent negative affect and peer use on adolescent substance use, B=-1.14, OR=.32, p=.09. For youth with peer use, higher parent negative affect was associated with *lower* odds of using substances, B=-1.12, OR=.32, p=.01. Findings also revealed a trend for an interaction between parent-adolescent shared positive affect and peer use on adolescent substance use, B=.680, OR=1.975, p=.06. For youth with no peer use, higher shared positive affect was associated with lower odds of using substances, B=-.59, OR=.55, p=.05. Associations between parent structure and support and adolescent substance use were not significant.
Conclusions: Findings suggest that high parent negative affect may be protective for youth who are in the higher-risk context with peers who use. For low-risk youth who do not have substance-using peers, positive affect in parent-adolescent interactions may be protective. Overall, our findings may aid in future research by identifying the specific contexts in which parenting factors prevent substance use.
Financial Support: NIH Grants (K01-DA-024759, UL1-DE19586) and ABMRF and AACAP Grants.

627

PREVALENCE OF TRAINING IN SUBSTANCE ABUSE TREATMENT IN APA-ACCREDITED CLINICAL AND COUNSELING PSYCHOLOGY DOCTORAL PROGRAMS.

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Aims: This research aims to assess the extent to which APA-Accredited Ph.D. and PsyD programs offer classes and have faculty expert in the area of substance use disorders (SUDs). Many psychologists reported feeling inadequate and unprepared by their graduate education and training when treating individuals with SUDs in their practice (Aanavi et al., 1999; Cardoso et al., 2006; Harwood et al., 2004).
Methods: We comprehensively surveyed curriculum webpages of all 243 APA-accredited clinical and counseling psychology programs [PhD (n=180), PsyD (n=53), and combined Phd/PsyD programs (n=10)]. We tallied the number of programs that offered courses in SUDs (required and electives) and the number of faculty members who listed addiction as one of their clinical and/or research interests. Chi-square was employed for a statistical analysis.
Results: Only 30.8 % (n=75) of all programs offered at least one course in SUDs, about 50% of which (n=38) were listed as core courses. Significantly more PsyD programs (49%) offered SUD training than PhD programs (23%; X2= 5.39, $p<.05$). 60% of combined programs offered a SUD course. Over 70% of the SUD courses offered in PsyD programs were required courses, compared with 32% in PhD programs (X2= 7.99, $p<.001$). 77% of PsyD programs listed at least one faculty member with clinical/research interests in SUDs, compared with 55% of Ph.D. programs (X2=7.25, $p<.001$). All combined programs listed at least one faculty member.
Conclusions: Consistent with previous studies, we found that the minority of APA-accredited psychology programs offered at least one SUD course and the majority of these courses were offered in PsyD programs, which are traditionally geared more toward clinical practice than PhD programs. The lack of training is of concern for many psychologists who increasingly encounter patients with SUDs in their practice but feel unprepared by their education to provide much needed addiction services.
Financial Support: NIDA grant(T32 DA007233)

628

ASSESSING DEVELOPMENT OF RECOVERY-ORIENTED SYSTEM OF CARE (ROSC) ENVIRONMENT IN IOWA.

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Aims: The goal of this initiative is to assess the progression towards implementation of ROSC principles and a recovery oriented environment in behavioral health treatment providers within the state of Iowa.
Methods: The RSA-R Provider Assessment developed by O'Connell, Tondora, Kidd, Stayner, Hawkins, and Davidson (2007) was adapted for use with Iowa treatment providers. Adaptations were based on input from key stakeholdes across the state, and pilot testers in programs participating in ROSC training. The adapted survey assessed wait time, policy and procedures, outcome data, and program descriptions related to treatment and prevention of substance abuse, problem gambling, and mental health.
Results: The adapted survey instrument will be used with all programs in Iowa who participate in ROSC training in preparation for Health care reform and Iowa transitioning to a ROSC system of care in Problem gambling and substance abuse prevention and treatment. 250 people have already completed the survey. Participating programs will complete the survey at baseline and 6 to 12 months later to track progress towards implementation of ROSC principles.
Conclusions: The adapted RSA-R Provider Assessment is a promising instrument to track the change of the behavioral health workforce in this time of transition to healthcare reform and movement towards ROSC environments. The state of Iowa plans to move to a ROSC environment by 2014, and the adapted RSA-R Provider Assessment should help providers to track the steps needed to transition to a ROSC environment.
Financial Support: Substance Abuse and Mental Health Services Administration

629

GENETIC AND ENVIRONMENTAL FACTORS UNDERLYING COMORBID BULIMIC BEHAVIORS AND ALCOHOL USE DISORDERS: A ROLE FOR PERSONALITY?

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Aims: Women with bulimia nervosa (BN) frequently have co-occurring alcohol use disorders (AUDs). Twin studies have been mixed as to whether there is shared genetic transmission of these disorders. Discrepant findings may be due to personality heterogeneity among individuals with BN. Cluster analytic studies have been used to characterize women with BN in groups based on personality profiles with the Dysregulated cluster emerging as a group that may be more closely linked etiologically to AUDs. The Dysregulated cluster is characterized largely by behavioral disinhibition and emotional dysregulation and has higher rates of AUDs compared to other clusters. The present study aimed to examine whether personality heterogeneity has contributed to discrepant findings by determining whether genetic associations between BN and AUDs are strongest among the Dysregulated cluster.
Methods: Participants were female twins assessed at ages 17 and 25 from the Minnesota Twin Family Study. Symptoms of BN and AUDs were assessed using clinical interviews and self-report scales. Personality clusters were defined using scores on the Multidimensional Personality Questionnaire.
Results: Twin moderation models suggested small-to-moderate common genetic transmission between BN and AUD symptoms. However, shared genetic effects did not differ by personality cluster. However, findings did indicate that unique genetic influences on AUDs are higher among the Dysregulated cluster compared to the Other clusters, suggesting an influence of personality on AUDs alone, but not on their association with BN symptoms.
Conclusions: Despite the presence of shared genetic transmission between BN and AUDs, cluster membership did not affect etiologic associations between the phenotypes. This suggests that although personality clusters may be associated with the etiology of BN, they are unlikely to account for associations between BN and AUDs.
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630

A LOW-INTENSITY TREATMENT ENGAGEMENT INTERVENTION FOR HOMELESS VETERANS WITH CO-OCCURRING MENTAL HEALTH AND SUBSTANCE ABUSE PROBLEMS: MISSION.

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Aims: This study examined the Maintaining Independence and Sobriety through Systems Integration, Outreach and Networking (MISSION) approach in homeless veterans with co-occurring mental health and substance use disorders transitioning from VA residential care to the community.
Methods: A quasi-experimental design was used. Homeless veterans (n=354) with a co-occurring mental illness and substance use disorder were recruited from the VA Domiciliary for Homeless Veterans Residential Program (DOM). 121 subjects received VA Treatment as Usual (TAU) alone and 233 received TAU along with MISSION. Group assignment was based on availability of MISSION treatment slots at enrollment.
Results: At 12-month follow up, subjects receiving either VA TAU or TAU with MISSION showed significant improvements on a number of mental health and substance use domains, which will be presented. Those in MISSION, however, performed better in a number of domains including 41% less likely than TAU alone to experience serious tension/anxiety and 55% less likely to drink to intoxication. Those in MISSION, compared to TAU also had a greater reduction in psychiatric hospitalizations (30% vs. 18%) and were more likely to be engaged in treatment (75% vs. 65%). Additional data will be forthcoming.
Conclusions: VA TAU was effective in improving outcomes among homeless veterans with a co-occurring disorder. However, the MISSION approach can further improve treatment engagement and certain behavioral outcomes compared to TAU alone. MISSION is currently being studied in a large VA multisite hybrid implementation and effectiveness trial within the VA HUD-VASH Program.
Financial Support: SAMHSA-CSAT Grant # TI16576

631

THERAPIST TRAINING IN MI DETERMINES PATIENT COMMITMENT STRENGTH: RESULTS FROM A RANDOMIZED TRIAL OF COMMUNITY-BASED COUNSELORS.

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Aims: Strengthening patient commitment to change is a central goal of motivational interviewing (MI). Strength of patients' language indicating commitment to change (e.g., substance use) in manualized treatment sessions has repeatedly been shown to predict outcome. However, the impact of therapist MI expertise on patient commitment strength (CS) is understudied. This study investigated patient commitment language from a randomized MI training trial (Smith et al., 2007, submitted).
Methods: Counselors based in community drug treatment centers completed a standard two-day MI training workshop and randomized to receive one of three post-workshop supervision programs: live supervision via telephone conferencing (TCS), standard tape-based supervision (Tape), or workshop training without follow-up supervision (TAU). TCS included simulated clinical interaction with an actor simultaneously monitored by a supervisor who provided real-time feedback using teleconferencing technology. METHOD Recordings for baseline (BL), one week post-MI workshop (PW), 8 week (FU1) and 20-week (FU2) follow-up sessions for 66 clinicians (23 TCS, 23 Tape, and 20 TAU) were coded for patient change talk using the DARNC system (Amrhein et al., 2003). Variables coded according to session decile epoch were strength of commitment, desire, ability, need, readiness and reasons to reduce or maintain current drug use. Three coders rated 264 session recordings (10% double-coded, kappa=.73).
Results: Relative to baseline (non-MI) sessions, patient CS increased after therapists had received the MI workshop, $F(9,567)=3.00, p<.002$. However, substantial erosion of patient CS at FU1 was observed for TAU counselors $F(1,22)=5.30, p<.001$, but not for TCS, $F(1,22)=2.33, p>.14$, or Tape counselors, $F(1,19)=0.67, p>.42$. At FU2, patients across counselor training groups exhibited CS similar to earlier patients at PW assessment, $F(9,567)=1.40, p>.25$.
Conclusions: Practicing MI skills learned at workshop eventually aids patients—but at a delay without follow-up therapist supervision.
Financial Support: Supported by DA016950-05A1

632

THE EFFECTS OF AEROBIC EXERCISE ON COCAINE SELF-ADMINISTRATION: IMPORTANCE OF TEMPORAL RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND INITIAL DRUG EXPOSURE.

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Aims: Previous studies have reported that aerobic exercise decreases cocaine self-administration in laboratory rats with long-term access (9+ weeks) to activity wheels. In most previous studies, rats had access to activity wheels for extended periods of time both before and after initial drug exposure. The purpose of the present study was to determine whether exercise retains its efficacy to reduce cocaine self-administration if access to activity wheels is confined only to the period of time (1) before or (2) after initial drug exposure.
Methods: Female rats were obtained at weaning and divided into four groups: (1) EXE-SED rats were housed in exercise cages (with activity wheels) for six weeks and then transferred to sedentary cages (no activity wheel) after the first day of cocaine exposure; (2) SED-EXE rats were housed in sedentary cages for six weeks and then transferred to exercise cages after the first day of cocaine exposure; (3) SED-SED rats remained in sedentary cages for the duration of the study; and (4) EXE-EXE rats remained in exercise cages for the duration of the study.
Results: Cocaine self-administration differed significantly across conditions, and the four groups were rank ordered on the basis of cocaine intake: EXE-SED = SED-SED > EXE-EXE = SED-EXE. Thus, exercise reduced cocaine self-administration if activity wheels were available only after initial drug exposure, but did not reduce cocaine self-administration if activity wheels were available only before drug exposure.
Conclusions: These data suggest that exercise may be effective at reducing cocaine use in drug-experienced individuals with no prior history of aerobic activity.
Financial Support: This study was supported by NIH grant DA027485.

633

CLINICAL AND DEMOGRAPHIC CHARACTERISTICS ASSOCIATED WITH THE USE OF OPIOID ANALGESICS IN PREGNANCY.

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Aims: Use of opioid analgesics for chronic noncancer pain has increased considerably among women in the United States in recent years. However, prior research has not determined the extent of prescription opioid use and its associated characteristics among pregnant women. The aim of the study was to examine characteristics associated with the use of opioids in pregnancy.
Methods: Data were derived from a prospective cohort study of pregnant women conducted between 2005 and 2009 in Connecticut and Massachusetts. Participants were administered the Composite International Diagnostic Interview to identify depressive and anxiety disorders and data on medication use were gathered at each assessment. Participants included 2,654 English or Spanish speaking pregnant women who had a singleton live birth.
Results: Six percent or 161 women used opioid analgesics at any point in pregnancy. More women using opioids met diagnostic criteria in pregnancy for major depressive disorder (16% vs. 8% for non users), generalized anxiety disorder (19% vs. 9% for non users), post-traumatic stress disorder (11% vs. 4% for non users) ($p<0.001$), and panic disorder (6% vs. 4% for non users). Women who reported opioid use were also significantly more likely than non users to report using illicit drugs as compares to non-users. Eight percent of opioid users reported marijuana use and 5% reported other illicit drug use as compared to 6% and 1% of non-users respectively ($p<0.001$). Opioid users were almost three times as likely to report smoking in the second or third trimester of pregnancy (22%) as compared to non opioid users (8%).
Conclusions: The use of opioids in pregnancy was associated with higher levels of psychiatric comorbidity and use of other substances as compared to non opioid users. The rate of use is similar to recent published data on long term use of opioid analgesics in the U.S. population of non-pregnant women of childbearing age (5.8%).
Financial Support: BIRWCH K12 from the National Institutes of Health (OD)
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634

ILLICIT DRUG USE AND RELATIONSHIP AGGRESSION AMONG NEWLY MARRIED COUPLES.

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Aims: This study aimed to examine whether illicit drug use (IDU) predicted physical relationship aggression (PRA) in a community sample of newly married couples.
Methods: Couples (n = 634) completed surveys at marriage and one, two, and three years later. The dependent variable, past year PRA, was dichotomized. Three IDU groups were created: no use, marijuana only, and other IDU regardless of marijuana. Odds ratio (OR) estimates for husband (H) and wife (W) PRA were calculated simultaneously using multi-level modeling. Estimates were adjusted for sociodemographics, antisocial behavior, and alcohol dependence. Models tested H and W IDU random effects and the following interactions: whether H IDU by W IDU predicted H and W PRA, whether H IDU by H alcohol dependence predicted H PRA, and whether W IDU by W alcohol dependence predicted W PRA.
Results: H and W marijuana use predicted both H and W PRA ($p < 0.05$) in unadjusted models, while H other IDU predicted H PRA, and W other IDU predicted W PRA. H marijuana use and H other IDU predicted H PRA after adjustment for sociodemographics, but not after adjustment for antisocial behaviors and alcohol dependence. None of the H by W IDU interaction effects or the random effects for IDU were significant and were dropped from the final models. W alcohol dependence predicted W PRA among marijuana non-users (OR = 1.09; $p < 0.05$), while the association was non-significant among marijuana users.
Conclusions: In this methodologically rigorous study, IDU did not increase the risk for PRA when analyses accounted for alcohol dependence and antisocial behaviors. For wives, marijuana use mitigated the risk associated with alcohol dependence. These findings suggest that, in the general community, alcohol dependence, antisocial behaviors and sociodemographic characteristics may be more relevant risk factors for PRA than IDU.
Financial Support: This project was funded by a pre-doctoral dissertation grant from the National Institute on Drug Abuse (1R36DA031996-01).

635

TEMPORAL PATTERNING OF PATHWAYS INTO THE CRIMINAL JUSTICE SYSTEM OF DRUG-ABUSING WOMEN.

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Aims: Prior feminist pathway research (mostly qualitative) posits that women in the criminal justice system follow a path where the presence of childhood abuse is rampant, followed by drug use and then arrest. The current research tests the certainty of this assumption by assessing the total number of temporal pathway patterns using the age of victimization, first drug use and arrest. In addition, the study explores the risks associated with following the two most common paths.
Methods: The data come from women mandated to a criminal justice drug treatment program (N=1,209). The pathways were created by temporally clustering the women by the ages of first victimization, drug use and arrest. Moreover a dichotomous variable was constructed from two of the most populated paths and a logistic regression was conducted to examine the risk factors associated with each path.
Results: There were a total of nine chronological pathway sequences. The most common path was drug use leading to arrest- path 1(45.7%) and the second was childhood abuse leading to drug use then leading to arrest-path 3 (36.3%). The logistic regression model ($X2=84.2$, $p<.001$; $R2 =.112$) found that experiencing familial drug use in childhood increases the odds of following Pathway 3 by a factor of 1.53 (logit=.427, $p<.05$). Also, having a parent in prison during childhood (logit=.753,$p<.001$), prior foster care (logit=.937, $p<.001$) and previous prescription of mental health medication (logit=.375, $p<.05$) increases the odds of following Pathway 3.
Conclusions: Results challenged feminist pathway research, which posits that childhood victimization is a key factor in propelling women into crime. This research challenges this notion by showing that there are multiple pathways and in fact the single leading path for women in this sample was a sequence where drug use preceded arrest in the absence of childhood victimization. However, women who followed a path where childhood victimization was present fared significantly worse, possessing more risk factors than women without childhood victimization.
Financial Support: NIDA grant (T32 DA007233)

636

METHYLPHENIDATE VS. ATOMOXETINE DURING ADOLESCENCE ON DOPAMINE TRANSPORTER FUNCTION AND CELLULAR EXPRESSION DURING ADULTHOOD IN AN ADHD MODEL.

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Aims: ADHD is characterized by medial prefrontal cortex (mPFC), orbitofrontal cortex (OFC) and striatal dysfunction. Methylphenidate (MPH), a DAT and NET inhibitor, and atomoxetine (ATO), a selective NET inhibitor, are prescribed for ADHD. Spontaneously Hypertensive Rats (SHR), an ADHD model, given MPH during adolescence, enhanced cocaine self-administration in adulthood. We hypothesize that MPH during adolescence will produce a lasting increase in DAT function and cell-surface expression in mPFC and OFC of SHR, while ATO will not.
Methods: SHR, Wistar-Kyoto inbred (WKY) and Wistar outbred (WIS) received MPH (1.5 mg/kg, po), ATO (0.3 mg/kg, ip) or vehicle on P28-55 (n=6-10/group). DAT function and cellular expression were assessed during P77-85. Saturation analysis of [^{3}H]dopamine uptake was performed using mPFC, OFC and striatal synaptosomes. Biotinylation assays determined DAT cellular expression.
Results: For each brain region, Vmax and Km values for control rats from each strain did not differ. MPH increased Vmax in SHR mPFC, decreased Vmax in WKY OFC and decreased Km in WIS OFC, and had no effect in striatum. MPH did not alter cellular distribution in any brain region. These results indicate trafficking-independent DAT functional alterations in response to MPH. ATO decreased Vmax and DAT surface expression in SHR OFC, suggesting that NET inhibition decreases DAT function and cell surface expression. Also, ATO decreased DAT Vmax, but not expression in WIS OFC, suggesting trafficking-independent regulation. ATO decreased Vmax in SHR, but not WKY, which was accompanied surprisingly, by increased DAT surface expression. Despite sparse NET expression in striatum, ATO altered DAT function and expression in this dopamine rich brain region.
Conclusions: In conclusion, adolescent treatment with MPH and ATO produce different brain region specific alterations in DAT function and cellular expression, and thus, may differently influence cocaine vulnerability in adults with ADHD.
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637

TRAINING MMT COUNSELORS IN PROVISION OF BEHAVIORALLY ORIENTED DRUG COUNSELING IN CHINA.

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Aims: Methadone maintenance treatment (MMT) programs were introduced in China in 2004 and continue to expand rapidly. However, they offer only very limited psychosocial interventions and MMT personnel is not extensively trained in provision of drug counseling.
Methods: During 2010 and 2011, we conducted a series of workshops to train drug counselors in behaviorally oriented drug counseling in several cities in China, including Wuhan, Hubei; Nanning, Guangxi; Guangzhou, Guangdong; and Guiyang, Guizhou. The training included multiday (2-4 days) didactic workshops and supervised provision of the learned counseling to 2 MMT patients.
Results: A total of 30 counselors were trained: 11 MDs, 14 nurses, 3 data clerks, and 2 pharmacists; 60% were females; their age ranged from 28 to 68. During the workshops we provided education on illicit drugs used in China, interactions of drugs with the brain, risk behaviors of drug users, drug dependence as a medical condition, effective treatments, basic pharmacology and the role of methadone in recovery, treatment goals, ground rules of counseling, communication skills, and specific behaviorally oriented counseling techniques. We used a variety of interactive teaching methods, including lectures, power point presentations, case discussions, and role plays. All counselors trained in Wuhan (n=7) successfully completed their training cases and are currently providing counseling to MMT patients. Other trainees are continuing with their supervised training cases.
Conclusions: MMT personnel in China are interested and motivated to learn evidence based counseling; they reported high levels of satisfaction with the training methods and improved ability to help MMT patients following the training. Future training programs will include structured assessments of satisfaction with specific training modules, evaluations of knowledge and skills gains, and the training impact on patient outcomes.
Financial Support: Supported by NIDA DA026797 & CMHC/DMHAS/State of Connecticut

638

PRE-EXISTING PSYCHIATRIC SEVERITY DID NOT AFFECT LIKELIHOOD OF SUCCESS IN THE PRESCRIPTION OPIATE ADDICTION TREATMENT STUDY (POATS).

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Aims: Psychiatric co-morbidities have been positively associated with severe opiate use and decreased probability of success in treatment for opiate addictions. The POATS, a multisite, randomized controlled trial conducted by the Clinical Trials Network of NIDA presents the first opportunity to evaluate the influence of psychiatric co-morbidities on treatment retention and outcome in patients addicted to prescription opiates.
Methods: The Addiction Severity Index Lite (ASI) was given to all 653 patients at baseline in the POATS study. All patients were treated with buprenorphine-naloxone and standard medical management, with half also receiving opioid dependence counseling. The dichotomous succeed/fail primary outcome was predefined as a composite of reduction in opiate use and completion of treatment. Proportions of successes and failures were compared to the Psychiatric Status (PS) domain of the ASI using 1) the TRI Composite score, 2) questions P1 or P2 for history of mental health treatment, and 3) questions P13 and P14 to capture concern regarding symptoms in the 30 days before randomization using Chi square and linear regression methods.
Results: One-third of all POATS patients reported psychiatric problems in the ASI. 220 patients in the POATS study were successes and 433 were failures. The proportions of successful and failing patients were not related to the PS composite score or to past treatment for mental health problems (P1 or P2). A greater proportion of successful patients were concerned about recent symptoms and desired to receive treatment for these symptoms than failing patients ($p < .02$; P13 and P14).
Conclusions: The self-reported psychiatric severity of POATS patients did not affect their likelihood of treatment success, but successful patients tended to express more concern about their psychiatric symptoms.
Financial Support: POATS study funded by NIDA U10 grants. Analyses reported here funded by contract with EMMES Corp.

639

CONTINUITY OF CARE AFTER DETOXIFICATION: USE OF THE WASHINGTON CIRCLE PERFORMANCE MEASURE TO EVALUATE PUBLIC SECTOR TREATMENT SERVICES IN CALIFORNIA.

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Aims: At the point of discharge from detoxification care (detox), patients are at high risk of relapse and vulnerable to system failures. This study applied the Washington Circle Public Sector Workgroup's (WC) measure of continuity of care after detox to determine the extent to which detox patients in California transition from detox to substance abuse treatment within 14 days of discharge.
Methods: Treatment episode data from the California Outcomes Measurement System were examined for all patients admitted to a detox service from 2008-2009 in 32 counties (N=26,209). The observation period included the first four treatment admissions.
Results: The vast majority of patients (71.9%) were treated in residential (non-hospital) detox facilities, while 28.1% were treated in outpatient detox facilities. Overall, 17.3% of patients transitioned to substance abuse treatment within 14 days of discharge from detox. The most common service after detox was residential treatment. Women were more likely to transition from detox to substance abuse treatment than men (21.4% vs. 15.6%, respectively). Patients who received treatment within 14 days were less likely to readmit to detox care within a year (15.8% vs. 24.9%, respectively).
Conclusions: Better coordination of care is needed to improve transitional care from detox to substance abuse treatment in California. Subsequent analyses will identify associations between continuity of care and both patient- and provider-level attributes.
Financial Support: NIDA 1F31DAO31509-01and UCLA Dissertation Year Award

640

CHARACTERIZING THE TRANSITION PERIOD FROM USE TO PROBLEM USE OF PRESCRIPTION OPIOIDS.

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Aims: The pathways to prescription opioid addiction are more varied than for other substances of abuse due to the therapeutic need for opioids. The transition period from use to problem use of prescription opioids has not been investigated. The objective of the full study was to determine the variety of pathways leading to addiction to pharmaceutical opioid products, including characterizing the transition period to self-identified problem use.
Methods: Adults with prescription opioid addiction were interviewed to retrospectively determine lifetime timelines related to prescription opioid use and addiction.
Results: A total of 347 interviews were conducted (mean age: 38 ± 10 years, range 18 – 63 years; 65% male). Mean age at first exposure to prescription opioids was 21±7 years. 44% were recreational users only, whereas 56% had periods of therapeutic and recreational use in their lifetime. The transition period from use to problem use occurred later (mean age: 27±11 vs 22±8 years, respectively, $p<0.001$) and lasted longer (mean duration: 3±4 vs 2±3 years, respectively, $p=0.03$) in the therapeutic user group (TG) compared to the recreational user group (RG). Patterns of use changed over this period, with more cases injecting opioids by the time they self-identified problem use (16% to 35%), fewer swallowing whole tablets (62% to 37%), and more using prescription opioids on a daily basis (69% to 85%). The most common significant events occurring during the transition period included family stress (43%) and relationship stress (39%), with more in the TG identifying physical health-related events compared to the RG (29% vs 4%, respectively). In only a minority of cases did an MD (12%) or other health care provider (6%) express concern during this period; although this was higher for family members (60%) and spouses (31%).
Conclusions: Characterizing the transition period from use to problem use is important as we strive to understand the unique nature prescription opioid abuse.
Financial Support: Health Canada

641

EFFECTS OF ADDICTIVE DRUGS ON DELAY DISCOUNTING IN RATS: A LABORATORY MODEL OF IMPULSIVE CHOICE.

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Aims: Research shows a strong, positive relationship between addictive drug use and impulsive choice. Impulsive choice can be defined as preference for a smaller immediate reward over a large delayed reward and measured using a delay discounting task. As part of a larger study of addictive drug action on impulsivity, we tested rats under acute and chronic methamphetamine and cocaine exposure to assess effects on delay discounting.
Methods: 24 Sprague-Dawley rats were trained to lever-press between two choice reinforcements: one food pellet immediately or three pellets after various delays. Once baseline delays (16 or 60s) were established, acute doses of methamphetamine or cocaine were administered prior to test sessions. Effective doses of methamphetamine (1 mg/kg) and cocaine (15 mg/kg) were determined and administered chronically for 30 consecutive days. Indifference points are calculated as the delay at which smaller and larger reinforcements are equally chosen. Shorter indifference points indicate increased impulsive choice.
Results: Preliminary results show that across all delays, methamphetamine decreased impulsive choice after both acute and chronic administration. Consistent with previous literature, chronic cocaine increased impulsive choice in 60s rats. However, rats that had shorter baseline delays (16s) showed a decrease in impulsive choice after acute and chronic cocaine exposure.
Conclusions: Data indicate that moderate-dose methamphetamine may increase the subjective value of delayed reward in rats, decreasing impulsive choice. Though cocaine typically increases impulsive choice, it may have variable effects in rats unable to tolerate longer delays. This suggests cocaine's actions on impulsive choice could possibly be related to baseline levels of impulsivity. Results of our study will help to understand relationships between impulsive choice and addiction.
Financial Support: National Institute on Drug Abuse Intramural Research Program (NIDA IRP)

642

BRIDGING FROM CONVENTIONAL MARKETED EXTENDED RELEASE FORMULATIONS TO NEW TAMPER-RESISTANT ALTERNATIVES.

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Aims: Tamper resistant formulations (TRF) may enhance patient safety by e.g. maintaining the intended release properties of oral dosage forms and preventing misuse e.g. by crushing. TRF may also raise the hurdle for intentional abuse by different tampering methods. Gruenenthal (GRT) has developed a TRF technology with increased tablet hardness using a high molecular weight polymer.
A switch from a conventional extended release (ER) formulation to these safer drug product alternatives requires bridging studies. Currently, clear guidance is not available. The aim was to provide an acceptable program of bioequivalence trials.
Methods: Following scientific advice the bioequivalence of 6 dose strengths of the GRT-TRF against reference marketed ER formulations of an analgesic product was investigated in a study program with healthy subjects in 8 randomized, 2-way crossover trials. Oral doses were administered as fasted and fed single doses as well as under multiple dose conditions. Serum drug concentrations were determined by a validated LC-MS/MS method. Non-compartmental PK analysis was performed and the usual 80-125% confidence interval acceptance criteria for bioequivalence were applied for the key pharmacokinetic parameters.
Results: The results reflect the minimum and maximum values observed for the whole set of 6 single (fasted and fed) and 2 multiple dose bridging trials.
The 90% Confidence intervals [%] for PK parameters Cmax or Cmin/max,ss and AUC0-t or AUC,ss were 91 – 119% and 92 – 109%, respectively.
Thus bioequivalence of the GRT-TRF to the reference formulations could be shown in all 8 trials.
Conclusions: Although GRT-TRF tablets are extremely hard, their in-vivo performance is comparable to the standard extended release formulations.
Bioequivalent TRF tablets enable physicians to simply switch patients from conventional to reformulated TRF products.
Financial Support: The authors are employees of Gruenenthal GmbH, Germany.

643

EFFECTS OF ENVIRONMENTAL ENRICHMENT ON NICOTINE-INDUCED SENSITIZATION AND CROSS-SENSITIZATION TO D-AMPHETAMINE IN RATS.

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Aims: The rodent environmental enrichment model has been shown to protect against the sensitivity to psychostimulant drugs in adulthood. The purpose of the present study was to determine if environmental enrichment can alter the ability of nicotine exposure during adolescence to induce both nicotine-sensitization and d-amphetamine cross-sensitization in adulthood.
Methods: Male Sprague-Dawley rats were received approximately at post natal day (PND) 21 and placed in one of two environments: an enriched condition (EC) or an isolated condition (IC) under a 12/12 hr. light/dark cycle, with lights on from 6:00-18:00 hr. After a seven day acclimation period (PND 28), all animals received seven daily injections of 0.4 mg/kg dose of nicotine (SC; free base) or saline. Following pretreatments was a 30 day wash out period in which the animals were raised in their respective environments. Over two different days (PND 69 and 73) the nicotine-and saline-treated animals were injected with 0.5 or 1.0 mg/kg (IP) of d-amphetamine in the cross-sensitization groups or with 0.2 and 0.4 mg/kg (SC) of nicotine for the nicotine sensitization groups. Separate groups of saline- and nicotine-treated animals were administered two saline injections over two different days. Immediately following the test injections, animals were placed in a locomotor chamber for 45 minutes to monitor ambulatory activity.
Results: Results suggest that exposure to 0.4 mg/kg dose of nicotine resulted in cross-sensitization in IC rats only following the low dose of d-amphetamine, while IC rats did not show nicotine-induced locomotor sensitization. However, following the high dose of d-amphetamine only nicotine-pretreated EC rats showed cross-sensitization, while EC rats did show nicotine-sensitization at low doses.
Conclusions: These results indicate that environmental enrichment may decrease the ability of nicotine exposure during adolescence to alter the sensitivity to low doses of amphetamine but does not protect against altered nicotine sensitivity in adulthood.
Financial Support: Supported by Creighton University

644

3-MONTH OUTCOMES FOLLOWING EVIDENCE-BASED ALCOHOL TELEMEDICINE THERAPY FOR RURAL OFFENDERS.

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Aims: This presentation describes an innovative approach of using telemedicine to deliver an evidence-based intervention (Motivational Enhancement Therapy) with at-risk alcohol users in real-world settings (rural probation and parole offices). The primary aim is to examine 3-month outcomes for the telemedicine-based therapy for alcohol use and community treatment utilization relative to the control condition.
Methods: Interviews were conducted with rural offenders under community supervision in four Kentucky districts. Eligible participants (N=125) completed a baseline interview focused on alcohol and other drug use, criminal activity, and treatment history. Participants were then randomly assigned to re-entry services as usual (n=65) or to telemedicine-based Motivational Enhancement Therapy (n=60) delivered via videoconferencing equipment in the rural parole office. All participants were followed 3 months post baseline.
Results: Data collection is on-going, and preliminary findings in this analysis are based on self-report data from 83 respondents at follow-up (80% of those eligible). Although not significant, a smaller percentage of MET participants reported using alcohol during the past 3 months than the control group (27% vs. 34%). MET participants did report significantly fewer days using alcohol to intoxication than the control group in the 3 month follow-up period (1.1 days vs. 2.8 days ($t(81)=5.1$, $p<.05$). MET participants were also significantly more likely to utilize community alcohol services during the 3 month follow-up period compared to the control group (77.8% vs. 25.8%, $\chi 2(1,N=83)=22.3$, $p<.000$).
Conclusions: This study demonstrates that telemedicine is a feasible option to deliver services with promising outcomes in real-world, accessible settings for rural offenders. This approach has potential to eliminate some of the barriers to access and utilization of effective, evidenced-based treatment for rural alcohol users.
Financial Support: Financial Support: Project supported by R21-AA017937.

645

SLEEP ARCHITECTURE IN ABSTINENT MARIJUANA-DEPENDENT VOLUNTEERS COMPARED TO CONTROLS.

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Aims: Sleep disturbances are commonly reported by chronic marijuana (MJ) users upon discontinuation of use and often identified as reasons for MJ relapse and/or other drug use. In the current study we compared the sleep architecture of 6 heavy MJ users to normal controls.
Methods: Participants in the marijuana group (4M/2F) were a subset of participants from a larger inpatient study of marijuana discrimination. All met DSM-IV criteria for cannabis dependence but were otherwise healthy individuals. Control group participants (10M/3F) had no history of illicit drug use or medical illness and were not shift workers. Neither group reported a history of sleep-related disorders. Polysomnography studies (PSG) were conducted at the Henry Ford Sleep and Research Center Hospital, using an 8-hr fixed time in bed (2300-0700 hr). PSG recordings were scored using Rechtschaffen and Kales standard criteria. Sleep measures included sleep efficiency (total sleep time/time in bed * 100), latency to persistent sleep, and percent of time spent in Stage 1, 2, 3/4, and rapid eye movement (REM).
Results: PSGs taken on the first night of inpatient stay showed that MJ users spent more time in Stage 1 sleep compared to controls (means 21.08 vs 8.95, $p<.03$) and less time in REM (means 11.82 vs 18.04, $p<.04$). During placebo MJ administration, MJ users showed a reduced sleep efficiency compared to controls (means 81.23 vs 90.32, $p<.02$), and increased latency to persistent sleep (means 52.17 vs 17.77, $p<.04$), percent of time in Stage 1 (means 22.42 vs 8.51, $p<.03$) and reduced percent of time in Stage 3/4 (means 6.05 vs 15.89, $p<.04$).
Conclusions: These data show reduced sleep efficiency and lightened sleep (increased stage 1 and reduced stage 3/4) in heavy MJ users during abstinence, findings that are predictive of relapse in other drug abuse populations.
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646

RISK OF HIV AMONG DRUG-USING AFRICAN-AMERICAN WOMEN: TRAUMA, CONDOM USE, AND SHARING PIPES.

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Aims: Research has linked traumatic life experiences to drug use. Further, evidence suggests trauma as a predictor of HIV status for African American women. The purpose of this study is to explore correlates of perceived risk for contracting HIV among drug-using African American women, while controlling for known HIV risk factors.
Methods: Data were derived from 206 drug-using African American women. Initial bivariate correlations were conducted, followed by a logistic regression. Cumulative interpersonal trauma was calculated using items from the Traumatic Life Events Questionnaire ($\alpha = .80$). Only 13% of the sample reported consistent condom use and 28% of the sample reported sharing pipes. The dependent variable of interest was perceived risk of contracting HIV. Approximately 69% of the women in the sample perceived themselves at risk for contracting HIV. Hypotheses are: women who report inconsistent condom use, sharing pipes, and have histories of trauma will perceive themselves at a greater risk for contracting HIV.
Results: The overall model correctly predicted 70% of the cases. Women who reported sharing a pipe to smoke drugs were 2.6 times more likely to perceive themselves at risk for contracting HIV (OR= 2.57). For every one unit increase in cumulative interpersonal trauma, women were 1.10 times more likely to perceive themselves at risk for contracting HIV (OR= 1.10). Condom use was not a significant correlate.
Conclusions: The study adds to the literature that drug-using African American women who have cumulative histories of interpersonal trauma and who share pipes perceive themselves at greater risk. The findings are also concerning with the low percentages of consistent condom use, it was anticipated that inconsistent condom use would result in a higher likelihood of perceived risk of contracting HIV. Future studies are needed to examine factors such as limited condom self-efficacy which may explain this relationship among this population of drug-using women.
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647

PREVALENCE OF EARLY TRAUMA IN CANNABIS-DEPENDENT PATIENTS.

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Aims: Childhood trauma has been associated with a greater likelihood of adult psychopathology, including substance abuse. We hypothesize that early trauma will be associated with greater cannabis use and current mood symptoms.
Methods: Forty-one participants who met criteria for current cannabis dependence were sampled from an ongoing 12-week, double-blind, placebo-controlled, treatment trial. Assessments in this analysis included the SCID for Axis I disorders, HAM-D, and Early Trauma Inventory (ETI). ETI results for each of the 4 domains (general, physical, emotional, sexual) were summed to yield a total trauma score. Participants were grouped into high-users (n=21), defined as smoking greater than or equal to 21 joints per week and low-users (n=20), defined as smoking less than 21 joints per week.
Results: Compared to low-users, high-users had significantly higher total trauma scores [$t(39) = 2.13$, $p = 0.040$] and physical trauma scores [$t(39) = 2.06$, $p = 0.046$]. Total trauma scores were positively correlated with HAM-D scores ($r = 0.42$, $p = 0.006$). The two user groups did not significantly differ on HAM-D scores. Women (n=14) scored significantly higher than men on both the total trauma score [$t(39) = 2.10$, $p = 0.042$] and the emotional trauma score [$t(39) = 2.76$, $p = 0.009$], independent of user group.
Conclusions: Early trauma exposure may chronically impact mood and severity of cannabis dependence in adulthood. Our finding of a sex difference in early trauma history is not surprising, but the impact on treatment outcome should be further explored. Clinicians need to include comprehensive screening and treatment plans that include early trauma, substance abuse, and mood symptoms. Future research might examine the effect of trauma on treatment outcome in cannabis users.
Financial Support: NIDA grants: 2P50DA009236; 5K24DA029647

648

SUBSTANCE USE, CUMULATIVE RISK AND PROMOTIVE FACTORS, PSYCHOLOGICAL DISTRESS AND DATING VIOLENCE AMONG AT-RISK YOUTH IN THE EMERGENCY DEPARTMENT.

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Aims: Previous research suggests that multiple risk and protective factors, including substance use, may contribute to dating violence among youth; however, to date much of the research has examined these factors singly. This study examines the relationship between substance use, psychological distress, peer, family, and community-level risk and promotive factors, and dating violence in a single exploratory model.
Methods: Violently injured youth (14-24) presenting to an urban ED completed a computer survey. A comparison group of youth presenting for other reasons, matched by age/gender, was recruited. Youth reporting any drug use in the past 6 months (n=600) completed a baseline interview with questions about their feelings and behaviors (e.g., drug/alcohol use), their peers, family, and community. Multi-group structural equation modeling was used to examine gender differences in the association between substance use, risk and promotive factors, psychological distress and dating violence.
Results: 59% were male (n=339), 65% were African American, and 78% received public assistance. Substantial path differences were observed for males and females. For males, past year dating victimization was associated with cumulative risk factors and psychological distress; past year dating aggression was associated with cumulative risk factors and psychological distress. For females, dating aggression was associated with substance use; dating victimization was positively associated with psychological distress and cumulative risk factors, and negatively associated with protective factors.
Conclusions: Interventions targeting dating violence should include the identification of other risk factors. For female youth, interventions should also focus on substance use and the importance of promotive factors.
Financial Support: NIDA R01 024646

649

INFLUENCE OF NALTREXONE PRETREATMENT ON THE PHARMACODYNAMIC EFFECTS OF TRAMADOL IN HUMANS.

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Aims: Tramadol is a prescription analgesic that produces its effects through mixed action in monoamine and mu opioid receptor systems. Tramadol is thought to have limited abuse potential, but laboratory data indicate that it shares some effects with prototypic mu opioid agonists. The aim of this study was to evaluate the effect of mu opioid receptor blockade on the pharmacodynamic effects of tramadol in humans.
Methods: This inpatient, double-blind, randomized, within-subject study examined the effects of oral placebo, tramadol (87.5, 175 & 350 mg) and hydromorphone (4 & 16 mg; positive control) after 1-hr pretreatment with oral placebo and naltrexone (50 mg). Ten healthy adults with recreational opioid use completed the study. Subjective, performance and physiological effects were collected before and for 6-hr after opioid administration.
Results: Hydromorphone (16 mg) produced prototypic mu opioid agonist-like effects that were blocked by naltrexone. Tramadol (350 mg) also produced significant mu opioid agonist-like effects, including increased ratings of "good effects" and "liking," respiratory depression and miosis. However, tramadol also increased ratings of "bad effects." Naltrexone largely failed to block the subjective effects of tramadol but appeared to enhance some aversive effects (e.g., "turning of stomach"). Naltrexone reversed tramadol-induced miosis and produced mydriasis.
Conclusions: These data demonstrate that naltrexone can be used to disentangle the mixed neuropharmacological actions of tramadol. Surprisingly, naltrexone blocked the mu opioid-related physiological effects of tramadol, but did little to alter the magnitude of its subjective effects. These data suggest that the non-mu opioid actions of tramadol play a critical role in its subjective profile.
Financial Support: Grant R01 DA 025649 (WWS)

650

DIFFERENCES IN RATES OF RESEARCH PARTICIPATION AMONG A COMMUNITY-BASED SAMPLE OF DRUG AND NON-DRUG USERS.

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Aims: Persons who have used illicit drugs remain underrepresented in studies in large part due to stigma. We contrast the rates of research participation between non-drug users, lifetime drug users and past-30 day drugs users and consider these rates in the context of researcher-endorsed exclusion criteria and attitudes toward drug users.
Methods: Data from a community-based sample recruited through HealthStreet (HSt) St. Louis, at Washington University (WU), were analyzed by their lifetime and past-30-day drug use and self-reported participation in research. Community Health Workers from HSt conduct health needs assessments, refer to services and link with open studies through community venues.
Results: Of the 2,562 community-recruited persons 18 – 90 years of age, 50% were non-drug users 23% had used drugs in the past 30 days, and 27% had used drugs in the past. Participation rates among non-drug users were 18%, past-30 day users 14%, and lifetime drug users 23% ($p<.01$). Older, Caucasian female lifetime drug users were most likely to have participated in research. In another R01 we are conducting, non-medical reasons for exclusions Investigators projected on drug users included lack of compliance, lack of honesty in responses, desire to participate based only on remuneration, and time and effort needed to enroll.
Conclusions: Current drug users report that they are not included in studies; lifetime drug users enroll in studies, although many barriers to their participation remain. We need to educate academic Principal Investigators on the importance of enrolling diverse samples in research.
Financial Support: UL1 RR024992, Evanoff, B, PI; HealthStreet founder Cottler, LB; R01-DA027951, Cottler, LB, PI.

651

NEUROPEPTIDE Y ATTENUATES COCAINE-PRIMED REINSTATEMENT OF A SELF-ADMINISTRATION RESPONSE IN RATS.

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Aims: Neuropeptide Y (NPY) is a neurotransmitter that acts on the neural substrates that underlie drug use and dependence. We tested the hypothesis that intracerebroventricular (ICV) NPY administration attenuates cocaine-primed reinstatement of self-administration (SA) behavior in rats with a history of cocaine SA followed by extinction training.
Methods: Male Long-Evans rats were allowed to self-administer cocaine (0.5 mg/kg, IV) for 21 3-h sessions by snout-poking. Each snout-poke into an active (cocaine-paired) hole initiated a cocaine infusion and a cued 25-sec time-out period in which no cocaine infusions were allowed. After 3 wks, snout-poking in the active hole was extinguished by exposure to the cocaine SA procedure, without cocaine infusions, for 21 sessions. After extinction, rats were tested twice for reinstatement of the snout-poking response: once after a cocaine prime (10 mg/kg, IP) and once after a saline prime (1 ml/kg, IP). NPY was administered (0, 0.1, 0.3 or 1.0 nmol, ICV) 30 min before each reinstatement test. Active and inactive snout-poking responses and number of infusions (or "sham" infusions during extinction and testing) were measured.
Results: The cocaine prime significantly increased snout-poking in the active hole compared to the response rate during the saline-primed test OR extinction whereas the cocaine prime had no effect on the snout-poking response in the inactive hole. ICV NPY (0.3 and 1.0 nmol) significantly reduced snout-poking in the active hole during the cocaine-primed test and had no effect on snout-poking during the saline-primed test.
Conclusions: These findings support the idea that central administration of NPY decreases the strength of cocaine and cocaine-associated cues to induce drug-seeking behavior.
Financial Support: Supported by NIH/NIDA Grant DA21261

652

COMPARISONS OF TREATMENT OUTCOMES FOR ADOLESCENTS WITH PROBLEM USE OF HEROIN VS. NON-HEROIN OPIOIDS.

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Aims: To compare baseline characteristics and treatment outcomes for adolescents who report problem use of heroin vs. non-heroin opioids, in addition to marijuana and/or alcohol use problems, as typically reported in clinical practice
Methods: Youth (ages 14-21) were recruited from 88 treatment sites participating in eight Centers for Substance Abuse Treatment funded grants. Youth were interviewed at intake and up to 12 months later with the Global Appraisal of Individual Needs (GAIN). Youth with opioid use disorders or weekly opioid use were divided into those with heroin problems (n=165) and those only non-heroin opioid problems (n=251). All participants had concurrent cannabis and/or alcohol problems; 43% of those with problem heroin use also used non-heroin opioids. Logistic regression was used to compare two groups in terms of both their baseline characteristics and treatment outcomes on social, substance, mental health, HIV, physical and legal domains.
Results: Those with problem heroin use were more likely than those with non-heroin opioid problem use to be older, Caucasian, and out of school. The heroin problem users reported significantly larger reductions in weekly heroin, cocaine and injection drug use; and despite 43% baseline concurrent use of non-heroin opioid use, reported significantly smaller reductions in non-heroin opioid use. Both groups combined, fewer than 3% reported receiving medications for addiction treatment while approximately one-thirds reported receiving psychiatric medications. Both groups showed statistically non-significant differences in improvements in outcomes on other domains.
Conclusions: Both heroin and non-heroin opioid problem users reported substantial improvements from largely psychosocial treatments albeit some key differences. Outcomes may be further improved with the use of specialized interventions and medications for youth with opioid problem use.
Financial Support: NIDA K12DA000357, CSAT contract 270-07-0191 and several CSAT grants and contracts.

653

FRONTO-LIMBIC CONNECTIVITY DURING ATTEMPTED AFFECT REGULATION DIFFERENTIATES COCAINE PATIENTS VS. CONTROLS.

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Aims: Stress and negative affect are recognized relapse contributors in addiction. Cocaine-dependent patients (CDs) may be poorly equipped to modulate responses to affective stimuli, given their documented frontal deficits necessary for regulating downstream limbic regions. Characterizing the modulatory dysfunction may help identify CDs at greater risk for relapse related to affect dysregulation. Toward this goal, we probed and compared the brain activity during affect regulation attempts in CDs and controls.
Methods: We used BOLD fMRI to measure brain response to aversive and neutral cues while CDs (n=10, ongoing) and controls (n=12; ongoing) attempted emotional regulation. Subjects identified and used cognitive reappraisal strategies to regulate emotions (passive-"watch"; suppression-"down"). Data were analyzed within SPM5. Task-related partial least square (PLS) and seed voxel PLS were used to contrast functional connectivity between groups and across conditions.
Results: Both groups reported significantly lower arousal level (p=<0.001) during "down." One latent variable (LV) (p<0.001) differentiated the groups in task-related activations for all conditions. Left amygdala (AMYG) was identified as a seed region. Seed PLS LV (p<0.001) revealed a main effect of "watch" and "down." CDs showed stronger positive AMYG connectivity in dorsal anterior cingulate, insula and intra-limbic region during "down" condition. Comparison group maintained stronger inverse connectivity in VMPFC during "down".
Conclusions: Though comparison group evidenced inverse ("modulatory") PFC-AMYG connectivity during attempted affect regulation, CDs failed to exhibit this pattern- instead showing positive intra-limbic connectivity. Impaired AMYG-PFC connectivity may explain CD's difficulties in regulating affect states, and may provide an important marker of relapse vulnerability and a potential treatment target in addiction.
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654

ALCOHOL PROBLEMS IN DRUNK DRIVERS IN BEIJING, CHINA, IN 2011: A PRELIMINARY SURVEY.

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Aims: Drunk drivers must be criminally punished according to the rules of the Amendment to the Criminal Law of the People's Republic of China in China (May 1, 2011). The prevalence of drunk drivers with alcohol use disorders and other psychiatric disorders in compulsory centers is unclear in China. We therefore estimated these variables from a preliminary survey conducted in compulsory centers supervised by the police in Beijing, China.
Methods: A total of 88 drunk drivers in compulsory centers in Beijing from July through November 2011 participated in the study. All of them were screened by a psychiatrist using the Social-Demographic Questionnaire and Chinese version of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, for Axis I disorders.
Results: All of the participants were men (mean age, 36 ± 9 years; mean drinking time, 14 ± 9 years). All of them were first offenders, and none had been mandated to undergo treatment. The type of alcohol consumed before the survey included liquor (58.0%) and wine or beer (42.0%). The subjects were diagnosed with the following disorders: alcohol use disorders (38.6%, including 17.0% with abuse and 21.6% with dependence), major depressive disorder (4.5%), panic disorder (1.1%), generalized anxiety disorder (1.1%), sedative-hypnotic anxiolytic drug abuse (1.1%), and stimulant, opiate, and hallucinogen polydrug abuse (1.1%).
Conclusions: Our results indicate a high prevalence of severe alcohol problems in drunk drivers and suggest that mandating the treatment of drunk drivers should be considered before sending offenders to compulsory detention centers.
Financial Support: This work was supported by the National Natural Science Foundation of China (no. 81071080) and Training Program Foundation for Excellent Talents by the Beijing Municipal Government, China (no. 2010D003034000026).

655

FRONTAL CORTEX NEUROCHEMICAL ALTERATIONS IN METHAMPHETAMINE-INJECTED RATS.

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Aims: Human methamphetamine (MA) studies employing proton magnetic resonance spectroscopy (MRS) have reported decreased levels of the neuronal marker, N-acetyl aspartate (NAA), in MA users. However, human imaging results have several innate limitations because of different levels of psychiatric co-morbidity and poly-drug use. Therefore, this translational rodent study utilized single voxel proton MRS, minimizing the possible confounds, to evaluate the consequences of MA exposure on neurochemistry, comparing in vivo brain metabolite levels between MA-injected and saline-injected rats.
Methods: Ten Sprague Dawley male rats at postnatal 77 days as well as nine saline-injected rats were scanned in a frontal cortex voxel (1.5x4.5x4 mm3) at baseline and three follow-up timepoints (1-week, 3-weeks, and 8-weeks) after an one-day, high-dose, binge MA exposure (4 injections, 2h intervals, s.c., 10 mg/kg/inj). Proton spectra were completed on a Bruker 7 Tesla scanner using point resolved spectroscopy sequence (TR/TE=2500/19 ms). MRS data were quantified using a Linear Combination of Model Spectra, and presented as ratios over unsuppressed water content.
Results: Repeated measures ANOVA showed that the MA injected rats had a significant reduction in the frontal cortex NAA levels compared to saline-injected rats (p=0.03). Also, total choline levels significantly increased following the MA injection compared to saline groups (p=0.04). Post-hoc analysis revealed that the decreased NAA and increased choline levels at 1-weeks were significantly different compared to baseline and other weeks (p<0.05).
Conclusions: These data suggests that the high-dose binge MA injection in rats produces significant neurochemical alterations at 1-week after injection, suggesting compromised neuronal integrity as well as membrane metabolism abnormalities in rat brains. This method represents suitable model of MA neurotoxicity in rats, comparable to the metabolite changes in human MRS results. The chemical changes seem to resolve after 3-weeks of MA injection.
Financial Support: NIH K24 DA015116 and USTAR

656

STREET PRICES OF PRESCRIPTION OPIOIDS DIVERTED TO THE ILLICIT MARKET.

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Aims: Prescription opioid abuse and diversion have become major public health problems in recent years, contributing to a wide range of health, social and economic consequences among affected populations. Within this context, there is an ongoing need to identify and examine new, proactive indicators to better characterize the prescription opioid abuse and diversion problem. In this regard, we implemented a national street price surveillance program with law enforcement investigators. Monitoring trends in street prices for prescription opioids may provide an indicator of drug availability, demand, and abuse potential within targeted geographic areas.
Methods: We examined street prices of diverted prescription opioids using surveillance data from a nationwide network of law enforcement officers, collected as part of the RADARS ® System. Drug diversion investigators were surveyed quarterly during 2010 and 2011 regarding the street prices of diverted prescription opioids in their areas. We computed mean and median prices per milligram for the targeted prescription opioids in order to make standardized price comparisons across drug classes. Trends in price data over time were also examined.
Results: Street prices per milligram ranked as follows: hydromorphone (mean=$5.87; med=$5.00); oxymorphone (mean=$3.00; med=$2.00); methadone (mean=$1.30; med=$1.00); oxycodone (mean=$1.14; med=$1.00); hydrocodone (mean=$1.05; med=$1.00); morphine (mean=$0.95; med=$0.96); tramadol (mean=$0.14; med=$0.10); and, tapentadol (mean=$0.13; med=$0.10).
Conclusions: Our analyses yielded substantial differences in street price by opioid class. Higher street values appear to reflect greater drug desirability/demand among abuser populations. Street price appears to be a useful indicator of drug popularity among abuser groups.
Financial Support: This research was supported by a contract from Denver Health & Hospital Authority.

657

EFFECTS OF LIPOPOLYSACCHARIDES ON THE METHAMPHETAMINE-INDUCED REWARDING EFFECTS: INVOLVEMENT OF THE REGULATION OF CYTOKINES MRNA.

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Aims: Methamphetamine is one of the most addictive psychostimulants that dramatically changes the central nerves system function. Various studies have reported to support substantial roles of mesolimbic dopaminergic pathway, which projects from the ventral tegmental area to the nucleus accumbens, in the rewarding effects of psychostimulants. It is reported that resistance to infection could be weaken in patients who are suffering from methamphetamine abuse. On the other hand, immune deficiency caused by HIV increases the rewarding effects of psychostimulants. Therefore, the activation/inhibition of immune system may affect the reinforcing/rewarding effects of psychostimulants. However, the involvement of immune system in the reinforcing/rewarding effects of psychostimulants is not demonstrated yet. The aim of the present study is to examine how lipopolysaccharides (LPS), which can activate the immune system, can affect the rewarding effects of methamphetamine in rats using behavioral and biochemical procedures.
Methods: Rewarding effects of methamphetamine were measured by conditioned place preference procedure.
Results: Here, LPS significantly and almost completely attenuated the methamphetamine-induced place preference as measured by conditioned place preference procedure, indicating that activation of immune system can regulate the rewarding effects of methamphetamine. Next, we examined the changes of cytokines in the nucleus accumbens by administration of methamphetamine and/or LPS. mRNA of IL-1β, CCR2 and glial cell-line derived neurotrophic factor (GDNF) using the PCR are significantly increased by methamphetamine, whereas, these increases induced by methamphetamine were reversed by administration of LPS.
Conclusions: Our findings suggest that regulation of cytokines like IL-1β, CCR and GDNF in the nucleus accumbens may play an important role in the acquisition of methamphetamine-induced rewarding effects.
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658

SUBSTANCE USE HISTORY, HIV TESTING, AND HIV VACCINE ACCEPTABILITY AMONG HIGH-RISK PERSONS.

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Aims: HIV transmission related to substance use remains an important route of infection in the U.S. With promising new developments in biomedical HIV prevention, interest in the possibility of an HIV vaccine may be reinvigorated. This paper examined whether: (1) HIV vaccine acceptability varied by the type of substance used; & (2) HIV/AIDS knowledge, HIV testing, or perceived risk helped to explain variation in HIV vaccine acceptability by substance used.
Methods: Subjects from Los Angeles County STD clinics, syringe/needle programs, and Latino CBOs offering HCT and health-related services were recruited using time-location sampling procedures to participate in a one-time, structured questionnaire. Eligible subjects were: ≤ 18 years old; not employed by recruitment site; & not known to be HIV+. Subjects were queried in-depth about substance use, HIV/AIDS knowledge, HIV testing, perceived HIV risk, and HIV vaccine acceptability with respect to efficacy, side effects, cost, duration of protection, dosing frequency, route of administration, and length of protection.
Results: Compared to persons with no history of hard drug use, hard drug users were significantly more likely to report: having tested for HIV (89.1% vs. 74.8%, p<.001); HIV positive test result (11.5% vs. 3.17%, p<.001); greater number of HIV tests (6.62 vs. 2.63; p<.001); higher HIV/AIDS knowledge (61.8 vs. 56.4, p<.001); higher perceived risk for HIV/AIDS (3.64 vs. 3.25, p<.001); and higher HIV vaccine acceptability (60.0 vs. 53.3, p<.05).
Conclusions: Results indicate that persons who use hard drugs are aware of their risk behaviors. In contrast, substance users who only use marijuana or alcohol, have lower perceived HIV risks and lower HIV vaccine acceptability ratings independent of their actual risks for HIV infection. Findings show segregation of HIV risk and prevention behaviors as well as HIV knowledge and vaccine acceptability by type of substance used. These findings can have a strong impact on marketing of an efficacious HIV vaccine, when ready for dissemination.
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659

ANALYSIS OF CANNABIS SEIZURES IN NSW, AUSTRALIA: CANNABINOID PROFILE AND IMPLICATIONS.

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Aims: There is concern that contemporary cannabis cultivation is biased towards plants with high THC and negligible CBD content, as it is thought to predispose users towards adverse psychiatric effects. While published potency data exist in the UK, the Netherlands and the USA, there are no equivalent data from Australia, which has one of the highest rates of cannabis use globally. This study aims to analyse the characteristics of 200 cannabis seizures obtained from New South Wales, Australia's most populous state, under the Cannabis Cautioning Scheme.
Methods: Analysis of cannabinoid content was performed using HPLC with PDA detection to quantify: THC, THCA, THCV, CBC, CBD, CBDA, CBG, CBGA, CBN. These results were cross-checked with those obtained from a GC-MS approach. Real-time RT PCR mRNA approaches were used to examine expression of the genes that encode THC-acid synthase and CBD-acid synthase. GC radioisotope analysis was used to explore similarities and differences across the 200 seized samples in terms of radioisotope (C14, N15) content.
Results: Preliminary results of HPLC analyses of the first n=105 samples revealed an average THC content (w/w%) of 12.8% (sd=5.8, range=0.5-33.5%). By comparison, CBD content was very low (median=0.04%, range=0-6.38), with 79% of samples containing less than 0.1% CBD. THC levels varied widely, although 71% contained at least 10% THC and 37% contained at least 15% THC. There were no differences in THC content between urban and rural seizures.
Conclusions: Analyses of street-level cannabis seizures from NSW, Australia confirmed international data revealing the dominance of THC compared to CBD content. Further research is required on the implications of differing cannabinoid ratios for mental health.
Financial Support: Funded by the Australian Government Department of Health and Ageing through the National Cannabis Prevention and Information Centre

660

SYNERGISTIC SUPPRESSION OF COCAINE-EVOKED ELEVATIONS IN MOTILITY AND CORTICAL SEROTONIN (5-HT) 2C RECEPTOR (5-HT_{2C}R) EXPRESSION BY COMBINED ADMINISTRATION OF A SELECTIVE 5-HT_{2A}R ANTAGONIST PLUS A 5-HT_{2C}R AGONIST.

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Aims: An excitatory role for the 5-HT_{2A}R and inhibitory role for the 5-HT_{2C}R to control the in vivo effects of cocaine are supported by the literature. In the present study, we tested the hypothesis that combined pretreatment with the selective 5-HT_{2A}R antagonist M100907 plus 5-HT_{2C}R agonist WAY163909 would synergistically suppress cocaine-evoked hyperactivity. Secondly, we evaluated this combinatorial treatment (along with controls) to block cocaine-evoked modifications of 5-HT_{2A}R and 5-HT_{2C}R expression in prefrontal cortex (PFC), a key site implicated in the modulatory roles of these receptors in the behavioral effects of cocaine.
Methods: Doses of M100907 and WAY163909 with no effects on motility alone were employed to determine whether these receptor subtypes act in concert. Male rats (n=64) were injected with M100907 or vehicle (45 min), WAY163909 or vehicle (30 min), and cocaine or vehicle (15 min; n=8/group) prior to placement in motor activity monitors. A separate group of animals underwent identical pharmacological treatments and were sacrificed 15 min after the last injection; tissue was harvested and crude membrane fractions of the PFC were analyzed using Western blot for 5-HT_{2A}R and 5-HT_{2C}R protein expression.
Results: M100907 plus WAY163909 synergistically attenuated cocaine-induced hyperlocomotion (p<0.05), but had no combined effect on basal locomotion. There was a trend toward elevated 5-HT_{2C}R protein expression in the PFC following acute cocaine administration; this effect was attenuated by M100907 plus WAY163909. No difference in 5-HT_{2A}R protein expression was observed among treatment groups.
Conclusions: Our observation that the selective 5-HT_{2A}R antagonist M100907 and 5-HT_{2C}R agonist WAY163909 synergistically suppress cocaine-induced hyperlocomotion raises the possibility that therapeutic advantage might be gained by a bifunctional selective 5-HT_{2A}R antagonist:5-HT_{2C}R agonist.
Financial Support: DA024157, DA020087

661

ALCOHOL AND DRUG USE DISORDERS AS POTENTIAL MODERATORS OF THE LINK BETWEEN AGGRESSION AND SUICIDAL BEHAVIOR.

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Aims: It is well-established that aggression confers risk for suicidal behavior. Aggression is a heterogeneous construct and it is theorized that reactive aggression (RA) in particular confers risk. However, a recent study of individuals with substance use disorders showed that proactive aggression (PA) was related to suicide attempts, raising the possibility that PA confers risk among individuals with substance use disorders in particular. To test this idea, we examined drug and alcohol use disorders as moderators of the relationships between RA and PA and suicide attempts.
Methods: Participants were 96 male and female criminal offenders, ages 18-62, in a pretrial supervision program. The sample was 52.1% African American, 29.2 % White, 18.8 % other race/ethnicity. Most (73.8%) pretrial clients invited to participate through a group announcement took part in the study.
Results: In bivariate analyses, RA was related to suicide attempt, OR (95% CI) = 1.10 (1.03-1.17), p <.01, and PA was not. After adjusting for gender, reactive aggression, and depression, symptoms of alcohol use disorder moderated the PA - suicide attempt relationship, OR (95% CI) = 1.05 (1.01-1.10), p <.05, such that among offenders with greater symptoms of alcohol use disorder, PA was associated with suicide attempts. Drug use disorder symptoms did not serve as a moderator.
Conclusions: Results suggest that alcohol use disorder is a condition under which PA is a risk factor for suicide attempts insofar as among offenders with high symptoms of alcohol use disorder the relationship between PA and suicide attempts is increased. This novel result may be due to the role of chronic- or acute alcohol use in lowering inhibitions, creating vulnerability in individuals with PA who might otherwise not be at risk.
Financial Support: This research was supported by a grant from the National Institute on Drug Abuse (K23 DA027720) to Marc T. Swogger.

662

ACTIVITY WHEEL TRAINING ALTERS THE SELF-ADMINISTRATION OF D-METHAMPHETAMINE IN MALE RATS.

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Aims: Survey evidence shows that about 66,000 Emergency department visits, and 8% of all drug/alcohol treatment admissions, involve methamphetamine (METH). Cessation studies report frequent relapses to drug taking among those that are trying to quit, thus there is an acute need for new therapies to decrease METH use. Epidemiological studies and some smoking cessation trials in humans, as well as preclinical work in rodent models of cocaine abuse, suggest physical exercise may reduce drug consumption.
Methods: Male Sprague Dawley rats were given a 6 week interval of voluntary wheel activity, ending one week prior to the opportunity to self-administer METH (0.05 mg/kg/inf) intravenously. Additional groups of rats were evaluated after 1-3 weeks of wheel access discontinued one week or one day prior to self-administration.
Results: The results show that 6 weeks of prior wheel activity decreases the amount of METH rats will self-administer, consistent with prior observations for cocaine self-administration. When 2-weeks of activity precede self-administration training, METH intake is reduced when wheel access is discontinued immediately prior, but not when access is discontinued one week prior to self-administration training.
Conclusions: The results show that escalated activity patterns may be required to produce a lasting effect on METH self-administration.
Financial Support: DA024705 and DA024105

663

A CLINICAL DECISION SUPPORT MODEL FOR SCREENING AND MANAGEMENT OF SUBSTANCE USE DISORDERS IN ELECTRONIC HEALTH RECORDS IN GENERAL MEDICAL SETTINGS.

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Aims: Preliminary and emerging research evidence for screening and brief interventions (SBI) for illicit substance use in medical settings suggests that it is feasible, leads to increased engagement in drug treatment, reduced drug use and is cost-effective. However, common data elements and consequent clinical decision support (CDS) models, for implementation of SBI in electronic health records (EHR) at practice settings taking into consideration workflow issues, are only now being considered for selection and validation. The goal is to present and capitalize on audience expertise for feedback on a recently developed CDS model.
Methods: This is NIDA Clinical Trials Network's companion effort to its initiative to develop common data elements and screening tools for SBI for substance use for incorporation in EHRs. Through an iterative process of obtaining expert research/clinician opinion and consensus building, this initiative has developed a model of CDS for SBI for substance use in primary care.
Results: NIDA will describe the content and the developmental process of the proposed CDS model. The model begins with the use of a validated one-item screener, followed by the 10-item Drug Abuse Screening Test (DAST-10) and few additional questions; responses help assign patients into none/minimal, low and high-risk categories with corresponding suggestions for interventions and monitoring. At the poster session, we also intend to obtain additional feedback on: a) content (i.e., design and rationale for the decision points and action items in the decision support algorithm) and b) feasibility (i.e., impact on workflow, staffing considerations).
Conclusions: CPDD attendees will have an opportunity to understand and provide constructive feedback on this expert and clinician consensus-based CDS model for the management of substance use disorders in general medical settings.
Financial Support: NIDA

664

SMOKING AND PSYCHOPATHOLOGY INCREASINGLY ASSOCIATED IN MORE RECENT BIRTH COHORTS: IMPLICATIONS FOR CLINICAL & GENETIC STUDIES.

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Aims: The prevalence of smoking has decreased over recent decades and become socially stigmatized, raising the question of whether current generation smokers may have a greater concentration of genetic or psychiatric vulnerability than previous generations. We examined this question by testing whether associations between smoking, psychiatric diagnoses, and personality traits, varied across six birth cohorts.
Methods: Among 4585 subjects from an NIMH Collaborative Center for Genetic Studies (55% female; 73% Caucasian/27% African-American), psychiatric symptoms and diagnoses were assessed with the Composite International Diagnostic Interview-Short Form; smoking/nicotine dependence with the Fagerström Test for Nicotine Dependence; and personality traits with the Eysenck Personality Questionnaire. Cohorts were defined by decade of birth: < 1930 (G1,N=510), 1930s (G2,689), '40s (G3,923),'50s (G4,1106),'60s (G5,735),or 1970 or later (G6,622).
Results: The proportion of lifetime smokers decreased from the earliest- to latest-born cohorts [G1-G6: 62,61,61,54,41%]. However, the magnitude of association between smoking and depression, anxiety, drug (but not alcohol) use/dependence, and neuroticism correspondingly increased [smoking x cohort x outcome interaction: p<.05(depression; p<.005(others)]. Similar findings were observed when considering nicotine dependence in place of smoking, or when using psychiatric symptoms instead of diagnoses.
Conclusions: The findings support the hypothesis that even though more current generations may smoke less, those who smoke have more psychiatric morbidity than previous generations of smokers. Selecting or stratifying by age may thus help reduce sample heterogeneity. These findings ave implications for clinical and genetic studies of nicotine dependence.
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665

AN FMRI STUDY OF SELF-REGULATORY CONTROL IN CANNABIS-USING YOUTH.

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Aims: Impaired self-regulatory control may drive and perpetuate addiction. The effects of cannabis on neural circuitry of self-regulation, especially in youth, are under-studied. The Simon Task assesses self-regulation by requiring participants to control their prepotent responses. We investigated self-regulatory control in cannabis-using youth with Simon and fMRI.
Methods: 11 Cannabis smokers (MJ) using >2 weekly and 11 healthy controls (HC) aged 16-22 were administered Simon during MRI scanning (3T, standard EPI sequence). BOLD signal during correct incongruent and congruent events was compared using Bayesian Analysis in SPM8 ($p<0.05$).
Results: Group behavior differences were not significant, however MJ participants trended towards faster reaction times at the expense of accuracy, especially on incongruent trials. HC participants showed greater activity in incongruent than congruent trials in bilateral VLPFC/OFC, caudal ACC, mPFC, right Insula, right Amygdala, Nucleus Accumbens, bilateral Hippocampus, right Precuneus, right Caudate, right motor regions, and visual cortex. Conversely, MJ participants showed greater activity in congruent than incongruent trials in a relatively constricted set of brain regions including bilateral VLPFC/OFC, left Insula, rostral ACC and mPFC.
Conclusions: Preliminary analysis suggests that in HC, conflict associated with incongruent trials manifests in engagement of a broad neural network, whereas MJ youth appear less sensitive to conflict cues and deactivate conflict-related and other brain regions. As we continue to recruit and analyze additional participants we will learn whether the behavioral trend towards faster but less accurate performance in MJ youth becomes significant and correlates with fMRI signal.
Financial Support: NIDA 2K12DA000357-11, K24DA029647

666

THE RELATIONSHIP BETWEEN PREGNANCY INTENTION AND PERINATAL ALCOHOL CONSUMPTION: AN ANALYSIS OF PRAMS DATA.

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Aims: Many women reduce or eliminate alcohol during pregnancy. Given that half of all pregnancies in the United States are unplanned, we investigated the relationship between pregnancy intention and change in perinatal alcohol consumption.
Methods: Women who self-reported any alcohol during the 3 months before pregnancy (N=94,139) were a subset of the Pregnancy Risk Assessment Monitoring System (PRAMS) cohort (N=199,917) for 2004-8 births. PRAMS is a population-based surveillance project and collects data from postpartum women on health behaviors before, during, and shortly after pregnancy. Intended pregnancy was defined by wanting pregnancy "then" or "sooner;" mistimed by "later;" and unwanted by "I didn't want to be pregnant then or any time in the future." Number of alcoholic drinks consumed before pregnancy was compared to number consumed in the last 3 months of pregnancy. Those women who reduced or quit drinking were contrasted with those who continued to drink the same amount or more. In addition, differences between heavy drinking (7 or more drinks/week) and binge drinking (5 or more drinks/sitting) groups were examined. Bivariate analysis and logistic regression were performed using the proper survey and weight functions.
Results: Most women (86.6%) reported eliminating all alcohol, whereas 7.0% reported reducing drinking, and 6.4% reported the same or more drinking in the last 3 months of pregnancy. Only 0.7% reported heavy drinking during pregnancy and 1.4% reported binge drinking. There was no relationship between pregnancy intention and reduction or elimination of alcohol consumption (adjusted odds ratio [AOR] 1.08 [95% CI: 0.94, 1.26]). However women with unwanted pregnancies were more likely to report binge drinking during pregnancy (AOR 1.56 [95% CI: 1.20, 2.02]).
Conclusions: Among women who drank alcohol prior to pregnancy, those whose pregnancies were unwanted were significantly more likely to report binge drinking during pregnancy compared to women with intended/mistimed pregnancies.
Financial Support: None

667

LET'S TALK ABOUT SEX AND THE COMPANY THAT YOU KEEP.

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Aims: The present study compared computer- and interviewer-administered responses to survey data about prenatal drug use and sexual risk behaviors. It also identified correlates of prenatal drug use in an urban sample of pregnant women.
Methods: Since disclosure of drug use and sexual activities can be embarrassing or stigmatizing, the present study compared responses to such items with the 2 administration methods. Items were drawn from the SERBAS, a validated risk behavior survey. Each participant completed the survey twice; once by each method 3 weeks apart. Order of administration was determined randomly. Novel correlates of prenatal substance use were also examined.
Results: Participants were N=123 pregnant women receiving prenatal care at an urban clinic. There were no significant differences in rates of disclosure of sensitive information by the two methods. Comparisons of women at risk for prenatal drug use (RDU) and not at risk (NRDU) found that while RDU women reported more sexual encounters and a greater number of sexual partners than NRDUs, they remained less concerned about HIV risk (all $p<.02$). One of the strongest correlates of RDU was history of incarceration (past 10 years) in primary male sexual partner. Specifically, 80% of RDU partner's had incarceration history as compared to 42% of NRDU partners ($p<.002$).
Conclusions: The latter finding warrants further study as an indirect screen to identify women at risk for prenatal drug use.
Financial Support: This research was supported by NIH grant P60 MD002256-01

668

PERFORMANCE ON THE SEXUAL DISCOUNTING TASK: A PREDICTOR OF ADOLESCENT SUBSTANCE USE AND SEXUAL ONSET?

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Aims: Adolescence is the developmental period associated with engaging in high risk behavior-sexual risk taking and substance use (Floyd, 2009).Previous research has examined the role of impulsivity as an underlying behavioral mechanism contributing to risk behavior.
For the current study, we examined performance on a novel task- the sexual discounting task (SDT)(Johnson & Bruner, 2011), as a means to measure an individual sexual impulsiveness and its relationship to adolescent reported substance use and sexual onset across the spectrum.
Methods: The present study queried individuals ages 18-25 on sexual behaviors and substance use during adolescence and young adulthood (N = 50). To add, each participant was asked to complete the SDT.
Results: Regression analyses revealed, as hypothesized, that high levels of sexual impulsiveness, significantly predicted ($p<0.05$) an earlier age of sexual onset across the spectrum- kissing (B = 0.449), touch breasts (B = 0.259), touch penis (B = 0.280), touch vagina (B = 0.314), oral sex (B = 0.453), vaginal sex (B = 0.460), and anal sex (B = 0.395); however, the SDT was not able to significantly predict alcohol (B = 0.128, p = 0.221) and marijuana (B = 0.085, p = 0.395) use.
Further regression analysis showed that age of onset for alcohol and marijuana use significantly ($p < .05$) predicted earlier sexual onset of more intimate sexual behaviors touch penis (B = 0.645, 0.739), touch vagina (B = 0.671, 0.714), oral sex (B= 0.806, 1.319), and vaginal sex (B = 1.208, 1.134), respectively.
Conclusions: The SDT has the ability to discriminate sexual impulsivity from other forms of risky behavior. The results indicate that the task can be used to differentiate adolescents who are more likely to engage in early sexual behavior, which can prompt the attention of both researchers and clinicians to examine associated high risk behaviors these adolescents may be engaging in order to decrease the negative consequences that these adolescents may experience.
Financial Support: No financial support

669

MAJOR DEPRESSION AND INITIATION OF ALCOHOL, TOBACCO, AND CANNABIS USE IN ADOLESCENCE.

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Aims: Younger age of initiation of substance use is associated with an increased risk of later substance use disorders. Major Depressive Disorder (MDD) may contribute to earlier onset on substance use initiation. This study hypothesizes that MDD is associated with earlier age of initiation.
Methods: A community sample was interviewed in adolescence (mean age 16) and in young adulthood (mean age 22). Of 1208 individuals, 57 had MDD in adolescence. Using propensity matching, we selected 114 controls without MDD by young adulthood. Survival analyses evaluated onset of each substance by group (MDD, no MDD), adjusting for sex, race and conduct disorder (CD) symptoms when significantly related to outcome.
Results: Groups did not differ significantly in initiation of alcohol (MDD=91%; no MDD=90%), tobacco (MDD=65%, no MDD=53%), or cannabis (MDD=61%, no MDD=51%) by young adulthood (all p>0.10.) Controlling for CD symptoms, a significant group by time interaction in the Cox regression models for alcohol and for tobacco indicated that prior to age 17, subjects with MDD had a higher hazard of initiating alcohol use (e.g. at age 12, HR=1.8 times (95% CI 1.03, 3.1)), and tobacco use, (e.g. at age 12, HR=3.2 times (95% CI 1.7, 5.9)). After adjusting for CD symptoms, there was no difference in initiation of cannabis use.
Conclusions: Adolescents with MDD have a greater risk of initiating alcohol and tobacco use up until age 17, at which point the risk of initiating either drug in those with and without MDD becomes equivalent. MDD had no effect on initiation of cannabis use. Those with MDD have a greater risk of initiating alcohol or tobacco use before age 17. This earlier age of initiation may increase the risk of later substance use problems.
Financial Support: P60DA011015, R01DA012845, R01DA021913

670

GENDER DIFFERENCES IN THE PREVALENCE AND CORRELATES OF ADULT ONSET SMOKING IN THE U.S.

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Aims: Little is known about gender differences in factors associated with adult onset smoking. The aim of this study is to examine the prevalence and correlates of smoking by age at smoking onset among a nationally representative sample of men and women in the United States.
Methods: Data were drawn from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Condition (NESARC), a survey of 43,093 adults between the ages of 18 and 80 residing in households in the United States. Smokers were those who reported ever smoking >100 cigarettes and were dichotomized by age at which they first smoked a cigarette (<18 and ≥18 years). Logistic regression models were used to assess gender differences by age at smoking onset in characteristics related to sociodemographics, smoking topography, and physical and mental health. Analyses were weighted to take into account the complex sampling design of the NESARC.
Results: Men (50.2%) were more likely than women (38.2%) to have reported smoking (p< 0.001). Yet of those who smoked, women (38.2%) were more likely than men (28.8%) to have started smoking in adulthood (age ≥18) (p< 0.001). Men and women adult initiators differed in a number of ways that may have implications for women's health. Compared with men adult initiators, women adult initiators were more likely to have been married (OR 2.44, CI 2.12-2.81) or parenting (OR 2.57, CI 2.20-3.00) at the age in which smoking onset occurred, to become daily smokers (OR 1.20, CI 0.99-1.44), to report fair/poor health (OR 1.28, CI 1.09-1.51), have experienced a stressful health related event (OR 1.35, CI 1.20-1.53), to develop heart disease (OR 1.56, CI 1.24-1.95), to have a lifetime diagnosis of nicotine dependence (OR 1.15, CI 1.00-1.32) or major depressive disorder (OR 2.44, CI 2.06-2.88), and to be currently divorced (OR 1.78, CI 1.50-2.10).
Conclusions: More women than men initiate smoking in adulthood and while married or parenting. Smoking initiation within this context can carry significant health risks for women and their children. Efforts to prevent smoking should target adult women, particularly women with children.
Financial Support: NIAAA OD NIDA ORWH

671

SUBSTANCE USE DISORDERS AND HOUSEHOLD POVERTY AS PREDICTORS OF FIRST-TIME HOMELESSNESS OVER 3 YEARS.

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Aims: Substance use disorders, poverty, and homelessness are important related public health concerns, but no study has prospectively examined the joint influence of substance use disorders and poverty on the occurrence of first-time adult homelessness in national data. This study used longitudinal nationally representative data to examine, among never-homeless adults, whether substance use disorders at baseline interacted with household poverty to predict first-time homelessness over a 3-year follow-up period.
Methods: Participants were interviewed in Wave 1 (2001-2002) and 2 (2004-2005; N=39,653) of the NESARC. Wave 1 DSM-IV substance use disorders were measured by the AUDADIS. Household poverty was calculated using 2001 federal poverty guidelines, adjusted for household size, income, and state. First-time homelessness, assessed at Wave 2, was defined as having no place to live for ≥1 month since Wave 1 (3.68%; N=1,222). The attributable proportion (AP) of homelessness due to interaction of substance use disorders with household poverty was estimated and tested with logistic regression, adjusted for demographics, psychiatric disorders, and state cost-of-living.
Results: Significant interactions were found between household poverty and any substance use disorder (AP=0.39; CI=0.18,0.61), drug and alcohol use disorders (AP=0.36; CI=0.09,0.62), and nicotine dependence (AP=0.45; CI=0.21,0.69), differentially increasing the risk of first-time homelessness.
Conclusions: This is the first study to prospectively examine the joint influences of substance use disorders and household poverty on subsequent adult first-time homelessness in national data. The combination of substance use disorders and household poverty created significantly greater risk for the first-time incidence of homelessness than either factor alone. Given the economic climate in the United States at this time, this study reinforces the importance of prevention and treatment of substance use disorders, and can serve as a benchmark for future studies on the etiology of homelessness.
Financial Support: K23DA032323, U01AA018111, K05AA014223.

672

ACUTE TOPOGRAPHY CHARACTERISTICS OF VERY LOW NICOTINE CIGARETTES WITH AND WITHOUT NICOTINE REPLACEMENT VS. USUAL-BRAND CIGARETTES IN SMOKERS WITH SCHIZOPHRENIA AND CONTROLS.

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Aims: Smoking very low nicotine content (VLNC) cigarettes acutely increases total puff volume and CO boost relative to higher-nicotine content research cigarettes, indicative of compensatory smoking. As nicotine may have unique benefits for smokers with schizophrenia (SWS), we hypothesized that compensatory smoking would be exacerbated among SWS and that combining VLNC with high-dose nicotine replacement would reduce compensatory smoking in SWS and controls.
Methods: SWS (n = 26) and non-psychiatric controls (n = 23) underwent 3 conditions in counterbalanced order: VLNC cigarettes (Quest 3; 0.05 mg nicotine) + 42 mg transdermal nicotine replacement (NRT), VLNC + placebo patches (PLA), and usual brand cigarettes. In each 5-hr session, cigarettes were cued according to participants' typical smoking rate. Cigarettes were smoked through CReSS topography systems (Borgwaldt KC) and carbon monoxide (CO) boosts were calculated (post-session minus pre-session CO).
Results: ANOVA results indicate that SWS smoked more total puffs and had shorter inter-puff intervals, as previously reported. There was also a significant main effect of Condition; overall, participants took larger puffs (p=.08), longer puffs (p<.05) and had shorter inter-puff intervals (p<.001) in the VLNC+PLA condition vs. the usual-brand condition; puff characteristics in the VLNC+NRT condition were intermediate. However, participants took fewer puffs (p<.01) and had less total puff volume (p<.001) in both VLNC conditions compared to the usual-brand condition. CO boost did not differ by Condition and there were no significant Group x Condition interactions.
Conclusions: These findings suggest that: (1) acute smoking of VLNC cigarettes increases measures of puff intensity, which are reduced by combining VLNC with NRT; (2) acute smoking of VLNC with or without NRT does not increase total smoke exposure compared to usual brand cigarettes. These findings support the continued investigation of VLNC cigarettes as a potential reduced exposure product.
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673

THE ASSESSMENT OF PAIN IN A METHADONE-MAINTAINED POPULATION: DOES READING LEVEL MATTER?

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Aims: Pain is common in methadone maintenance (MM) patients, who also have a wide range of educational achievement. Few studies have investigated optimal pain assessment in this population.
Methods: Treatment-seeking volunteers with DSM-IV cocaine and opioid dependence who qualified for MM were enrolled in an outpatient clinical trial of concurrent MM and topiramate (or placebo) for cocaine dependence; 115 participants who completed at least 20 weeks of the study were analyzed. The FACES scale and a 0-100 pain visual analog scale (VAS) were measured at baseline and weekly thereafter. Reading grade level was assessed with the Wide Range Achievement Test (WRAT). The cohort was divided into quintiles based on WRAT grade level. Spearman's rank correlation was used to measure agreement between the scales at baseline. Pain ratings on both scales were transformed to a z-standardized score; the standardized FACES score was subtracted from the standardized VAS score to give a "scale variance measure." 1-factor ANOVA was used to investigate differences in this measure amongst the 5 reading groups. Test-retest reliability was measured with intraclass correlation coefficients (ICC) in weeks 13-20 when methadone and study medication were at stable doses.
Results: Volunteers were 65% African American, 47% female; mean age was 42.3 years. Median reading level was 8th grade. 47% of the sample had at least mild self-reported pain (VAS>4) at baseline. The overall Spearman's correlation coefficient (r) between the two scales at study baseline was 0.87 ($p<0.001$). When restricted to those with at least mild pain, there was still high correlation ($r=0.77$, $p<0.001$). ANOVA did not show significant variability between the pain scales across the 5 reading groups ($F=0.8$, $p=0.53$). Reliability over 8 weeks was moderate (ICC=0.44 and 0.47 for FACES and VAS, respectively), and did differ across reading groups.
Conclusions: The FACES and VAS pain scales are highly correlated. Either scale may be used to assess pain with proper instructions in a MM population, regardless of reading ability.
Financial Support: DA021808, DA07209, DA023186

674

NICOTINE EXPOSURE AND SUICIDE: DOES ROUTE OF ADMINISTRATION MATTER?"

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Aims: A growing body of epidemiological evidence suggests an excess risk of suicide among smokers compared to nonsmokers. Although the causality of this association is still debated, many suggest the nicotine in cigarettes affects suicide risk. However, to our knowledge no study has tested the consistency of this association by asking if smokeless tobacco use also associated with suicide.
Methods: We used a nationally representative sample of persons 18+ using data from the 2008-2009 National Surveys on Drug Use and Health with computer assisted assessment of both smokeless tobacco and cigarette use as well as past year suicide related behaviors (suicidal ideation, plans and attempts) (n=75,206). The tobacco use exposure was categorized as follows: never users, former users (quit >3 years prior to assessment), recent former users (quit 1-3 years prior to assessment), and past year users. Using a logistic regression, we tested the effects of recency of tobacco use on past year suicide related behaviors.
Results: There was trend between cigarette smoking status and suicide related behaviors. For example, relative to never users, current users and recent former users were at an increased odds of suicide attempt (OR =2.9 95%CI[2.0,4.4]) and OR=1.7 95%CI[2.0,4.4] respectively). Similar trends were found for ideation and attempts. This was consistent with smokeless tobacco use: current users and recent former users were at an increased odds of suicide attempt relative to never users (OR=2.1 95%CI[1.4,3.1] and OR=1.7 95%CI[0.8,3.4] respectively) while former users and never users did not differ. After covariate adjustment, smokeless tobacco use only predicted suicide attempts while cigarette use predicted all three outcomes.
Conclusions: This study suggests that smokeless tobacco use may be a predictor of suicide related behaviors although it appears to be a weaker predictor than cigarette smoking. Future studies might consider the differences in levels of nicotine exposure and the speed at which nicotine reaches the brain in testing the nicotine and suicide association across routes of administration.
Financial Support: NIDA support: T32DA021129; K05DA15799

675

ASSOCIATIONS BETWEEN DIMENSIONS OF DISTRESS TOLERANCE AND TOBACCO DEPENDENCE CHARACTERISTICS: INCREMENTAL RELATIONS OVER AND ABOVE ANXIETY AND DEPRESSIVE SYMPTOMS.

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Aims: Poor distress tolerance is a putatively important risk factor for tobacco dependence. However, it remains unclear whether different dimensions of distress tolerance have disparate relations to tobacco dependence, whether relations extend to a wider variety of dependence markers, and if these associations are incremental to or amplified by comorbid depressive and anxiety symptoms. This cross-sectional study examined the relationship between four dimensions of subjective emotional distress tolerance (Tolerance, Appraisal, Absorption, and Regulation) and tobacco dependence characteristics.
Methods: Current cigarette smokers (N=212; > 5 cig/day, M age = 24.6, 53% female, 64% Caucasian) were administered questionnaires assessing distress tolerance, anxiety, depression, and tobacco dependence characteristics (i.e., dependence severity and cigarette craving).
Results: Overall distress tolerance and all four dimensions were significantly associated with a wide variety of tobacco dependence characteristics. After controlling for affective symptomatology, the Total Distress Tolerance score and Appraisal subscale retained the majority of their significant associations with overall levels of dependence, craving, and markers of negative reinforcement smoking. By contrast, the relation of the other distress tolerance scales with these characteristics exhibited less robust and fewer statistically significant findings after controlling for affective symptomatology.
Conclusions: The current study highlights the importance of distinguishing subdimensions of distress tolerance when investigating relations to tobacco dependence and also addresses the importance of distress tolerance as a separate target for treatment on top of symptoms of anxiety and depression.
Financial Support: NIH grants DA026831 and DA025041

676

PAIN IS ASSOCIATED WITH ILLICIT DRUG USE IN HIV-INFECTED RUSSIAN DRINKERS.

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Aims: This study examined the association between pain and substance use in a cohort of HIV-infected problem drinkers in Russia.
Methods: We analyzed baseline data from 699 HIV-infected Russians in the HERMITAGE study, who had a history of past 6 month risky drinking (NIAAA criteria) and unprotected sex. The main predictor was pain that at least moderately interfered with daily living, based on a single question from SF-12 ("During the past month, how much did pain interfere with your normal work?"). Primary outcomes were past month use of: 1) any illicit drugs and 2) risky amounts of alcohol. Secondary outcomes were use of each of the following drugs: heroin; stimulants (amphetamines, ephedrine or cocaine); and cannabis. Multivariable logistic regression models assessed associations between pain and each outcome adjusting for age, marital status, education and gender.
Results: Participants had a mean age 31(SD±5) years, were 41% female, 22% < 9th grade education and 36% married. In the past month, 47% reported use of illicit drugs and 81% risky drinking. Heroin was the drug most often used (38%), followed by cannabis (21%) and stimulants (12%). Nearly half (46%) had pain that at least moderately interfered with daily living. After adjustment for covariates, pain was associated with greater odds of using any illicit drugs in the past month (AOR=1.44, 95% CI: 1.06-1.95). The association between pain and risky drinking was not significant (AOR=1.30, 95%CI: 0.87-1.92). In the secondary analysis, pain was significantly associated with heroin use (AOR=1.66, 95% CI: 1.21-2.27), but not use of other drugs (stimulant AOR=1.50, 95% CI: 0.94-2.39; cannabis AOR=1.23, 95% CI: 0.84-1.80).
Conclusions: Among HIV-infected Russian drinkers, pain that at least moderately interfered with daily living was associated with higher odds of using any illicit drugs and specifically heroin use. Pain may be an under-recognized risk factor for illicit drug use in this population.
Financial Support: Supported by NIH: R01AA13216, K24AA015674, and K23DA027367

677

MORE IMPULSIVE SMOKERS EXHIBIT EARLIER PREFERENCE REVERSALS IN LABORATORY TASK.

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Aims: Cigarette smoking is the most preventable cause of morbidity and mortality in the US. About 45% of smokers make a quit attempt each year yet smoking cessation failure rates remain high. There is a clear need for research on the variables associated with smoking relapse.
Temporal discounting (TD) refers to the reduction in the subjective value of a delayed reward as a function of the delay to that reward. Research indicates that elevated TD is associated with greater rate of cigarette smoking, shorter duration of abstinence attempts and lower rates of treatment-seeking. Importantly, elevated TD predicts higher likelihood of preference reversals (PR), thought to be a behavioral analog of smoking relapse.
The current study sought to test the predictive relationship between TD and PR. We hypothesized that impulsive choice (i.e., higher discount rates) would be associated with greater likelihood of exhibiting a PR.
Methods: Participants were 40 adult smokers recruited from the Washington, D.C. area. Participants completed a computerized measure of TD and a novel PR task for reward magnitudes of $50 and $1000. The PR choice task required participants to choose between a series of two hypothetical choices: a smaller, sooner (SS) option, and a larger, later (LL) option. The value of the LL option was fixed ($50, $1000), as was the delay between the SS and LL choices (1 week, 1 month). The delay to the SS was varied across trials, making the choices more temporally remote.
Results: Results revealed a significant association of TD and PR in the $50, 1 month condition, $F(2,35) = 5.33$, $p<.01$ and the $1000, 1 month condition, $F(2,38) = 6.69$, $p<.01$, such that greater TD was associated with greater likelihood of preference reversal. The relationship between impulsive choice and preference reversal was not significant for either of the 1 week delays, $p's>.6$.
Conclusions: Smokers with elevated TD are more likely to exhibit PR. This finding supports the conceptualization of hyperbolic discounting as a behavioral mechanism of smoking relapse. Findings will be discussed in terms of implications for intervention.
Financial Support: R01 DA011692

678

DOES CANNABIS USE IMPACT HIV DRUG AND SEX RISK BEHAVIORS?: A RUSSIAN PERSPECTIVE.

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Aims: Aims: To examine the association between cannabis use and risk behaviors among HIV-infected Russians.
Methods: Methods: We analyzed data from 700 HIV-infected Russians in the HERMITAGE study, who had a history of past 6 months risky drinking (NIAAA criteria) and unprotected sex. The primary independent variable was cannabis use (recent [past month]; non-recent [past year but not past month]; no use past year). Primary outcomes were needle sharing past 3 months (recent) and number of unprotected sexual episodes past 3 months. Secondary outcomes were any drug injection past month, number of injections past month, and multiple sex partners in the past 3 months. Regression analyses controlled for the following potential confounders: age, gender, marital status, education, CD4 count, ART use, recent alcohol use, other drug use and depressive symptoms.
Results: Results: Participants were 41% female with a median age of 29 years. Cannabis use was common: recent 20% (n=143), non-recent 26% (n=183), and no past year use 54% (n=374). Recent cannabis use was significantly associated with number of unprotected sex episodes (adjusted IRR 1.58, 95% C.I: 1.09, 2.29) and with multiple sex partners (AOR 1.79, 95%CI: 1.10, 2.92). Stratified analyses found an association for recent cannabis use (AOR 3.07, 95%CI: 1.28, 7.34) and non-recent use (AOR 3.24, 95%CI: 1.48, 7.07) with multiple sex partners among women, but not men. No significant associations were identified between drug risk behaviors and cannabis use.
Conclusions: Conclusion: Cannabis use was associated with sex risk behaviors among Russian HIV-infected risky drinkers; this association was particularly notable for multiple sex partners among women. Cannabis use was not significantly associated with drug risk behaviors.
Financial Support: Supported by: National Institute on Alcohol Abuse and Alcoholism (R01-AA016059)

679

PREVENTION OF ILLICIT DRUG USE DURING THE POSTPARTUM PERIOD.

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Aims: While most women who use illicit drugs either quit or cut down during pregnancy, survey data from both the Substance Abuse and Mental Health Services Administration (SAMHSA) and the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) reveal that 6% of postpartum women report using illicit drugs, with many resuming their use once they give birth. Illicit drug use during this period has been associated with a number of risks and negative consequences for both infant and mother, including compromises in the safety and health of the infant. Further, postpartum women who become pregnant while using drugs are at risk for preterm labor and delivery, birth defects, neonatal withdrawal and neurobehavioral deficits. While research has identified several risk factors associated with drug use during postpartum, surprisingly few preventive interventions have been developed to target use during this period in a woman's life. A critical review of the literature was conducted to identify and examine preventive intervention studies for illicit drug use during postpartum. Studies included pregnant or postpartum women who either had or were at risk for illicit drug use. Preventive strategies that were evaluated include community-based, home-visitation interventions, as well as a brief, computer-delivered intervention.
Conclusions: Overall, methodological limitations may have restricted the effect of home-visitation intervention on drug reduction. The computer-based intervention demonstrated positive effects and suggests an encouraging approach in identifying and intervening with women at risk for drug use during the postpartum period. Given the small number of studies included in this review, it is recommended that additional controlled trials be conducted.
Financial Support: Supported by T32 AA007459

680

EVALUATING THE EFFECTS OF GUANFACINE ON STRESS-PRECIPITATED SMOKING LAPSE BY GENDER.

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Aims: Guanfacine, an alpha-2 adrenergic receptor antagonist, has been shown to attenuate stress-induced drug reinstatement in rats, but its effects on stress-precipitated drug use in human are unknown. Women have been found particularly vulnerable to stress-related smoking, suggesting the importance of evaluating medication effects by gender and developing gender-sensitive treatment strategies. The present study aimed to examine gender differences in the effects of guanfacine on stress-precipitated smoking behaviors. It was hypothesized that guanfacine attenuated stress-precipitated smoking more strongly in women than men.
Methods: Thirty-three daily smokers (40% women; age = 35.9±12.0, cigarettes per day = 18.1±7.7) were randomly assigned to guanfacine (n = 17; 35% women) or placebo (n = 16; 44% women). After a 3-week medication pretreatment period (3mg/day), participants completed two laboratory studies (stress vs. neutral conditions), during which they completed personalized guided imagery procedure, followed by a 1-hr ad-lib smoking period. Both sessions were completed after 15-hr nicotine deprivation. Multivariate repeated measures ANOVA was used to examine the effects of medication condition, gender, and their interaction on smoking behaviors and related variables.
Results: Guanfacine significantly improved the ability to resist smoking, reduced the number of cigarettes smoked, and attenuated tobacco craving after stress in women. Guanfacine did not affect stress-induced smoking behaviors or craving in men, but attenuated the self-reported reinforcement effects of smoking.
Conclusions: Consistent with pre-clinical studies, guanfacine attenuates stress-precipitated smoking lapse in human. However, stress reactivity was only reduced in women. In men, guanfacine was effective in attenuating reinforcing effects of smoking. The observed gender differences have important implication for the possible development of gender-specific pharmacological smoking cessation strategies, using alpha-2 adrenergic agents.
Financial Support: NIDA RL1DA024857 and K12DA031050

681

TOPIRAMATE AND CONTINGENCY MANAGEMENT IN THE TREATMENT OF COCAINE DEPENDENCE: A RANDOMIZED CONTROLLED TRIAL.

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Aims: Topiramate (TOP) has shown promise in the treatment of cocaine dependence in pilot studies. This stage II double-blind trial evaluated the efficacy of TOP and contingency management (CM) alone and in combination for the treatment of cocaine dependence. Thus, the efficacy of topiramate for cocaine dependence was assessed under two levels of motivation for drug abstinence.
Methods: After a 5-week baseline period cocaine dependent methadone patients (N = 171) were randomly assigned to one of 4 groups: TOP/CM, TOP/No-CM, Placebo/CM and Placebo/No-CM. Participants were inducted onto TOP or placebo over 7 weeks, stabilized for 8 weeks at 300 mg/day, then given a 3-week dose taper. CM groups received monetary vouchers when urinalysis indicated recent cocaine abstinence. The CM intervention was in place during the last 4 weeks of induction and for the entire stabilization period. The primary outcome measure was cocaine use (Y/N) as measured by 3x weekly urinalysis and analyzed using GEE. Samples were considered positive if they met the new use criteria of Preston et al. (1998). A secondary outcome, treatment retention, was analyzed with a Cox regression model. All analyses were intent-to-treat and included the period of active CM intervention.
Results: There were no significant differences in demographic characteristics between the 4 groups. There was no significant difference in cocaine use in any TOP vs placebo comparison. Participants who received the CM intervention were less likely to use cocaine than participants who did not receive the CM intervention when missing samples were treated as positive (P = 0.040, OR = 2.52, 95%CI = 1.05 – 6.01), but not when they were ignored (P = 0.056). Neither TOP nor CM significantly affected participant retention. There were no significant TOP x CM interactions.
Conclusions: TOP did not decrease cocaine use relative to placebo and did not interact with the CM intervention.
Financial Support: R01DA021808, K24DA023186 & T32DA07209

682

MEASURING INTEGRATION OF BEHAVIORAL HEALTH SERVICES IN PRIMARY CARE SETTINGS.

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Aims: Due to health care reform, integration of behavioral health services into primary care settings has taken on increased urgency. Our aims are to:
1) Assess the feasibility of using the Dual Diagnosis Capability in Health Care Settings (DDCHCS) and surveys to measure integration and staff perceptions in federally qualified health centers (FQHCs).
2) Examine baseline data from multiple FQHCs.
3) Assess whether these measures are useful in guiding and measuring improvements.
Methods: In 2010-2011, SAMHSA and HRSA supported a pilot study of the DDCHCS to evaluate the efforts of two FQHCs to integrate behavioral health services at two time points. SAMHSA also provided funding to conduct baseline DDCHCS data collection at 11 additional FQHCs across six states: In California, UCLA conducted DDCHCS and surveys of staff perceptions of integration.
Results: The majority of FQHCs scored just below the "partially integrated" behavioral health services at baseline. In the case of the two FQHCs with both baseline and followup data, gains were made within one year such that partial integration status was achieved. These gains were intentional and measurable using the DDCHCS. The DDCHCS and survey scores reflected a wide range of strengths and opportunities for improvement across the FQHCs in different domains.
Conclusions: 1) DDCHCS and staff surveys can provide practical and useful measures of integration and staff perceptions in FQHCs;
2) DDCHCS can document and provide objective, standardized information about integration across FQHCs;
3) DDCHCS data are useful in guiding improvements, and the measure is sensitive to changes made; and
4) FQHC leadership had a favorable experience and welcomed a second visit for follow-up data collection.
Financial Support: SAMHSA, HRSA

683

EFFECTS OF SMOKED COCAINE AND LEVODOPA-CARBIDOPA-ENTACAPONE ADMINISTRATION ON COCAINE-RELATED ATTENTIONAL BIAS IN COCAINE ABUSERS.

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Aims: Dopaminergic medications may have benefit for cocaine users by impacting the cognitive mechanisms of cocaine dependence. The purpose of this study was to assess the individual and combined effects of Levodopa-Carbidopa-Entacapone (LCE) and smoked cocaine administration on cocaine-related attentional bias in cocaine users, under controlled laboratory conditions.
Methods: Eight healthy nontreatment-seeking cocaine smokers (7 male) who reported using cocaine approximately 3 (SD=2.2) times weekly ($202/week; SD=166.8), participated in this 10-day inpatient within-subjects study. Volunteers completed two 5-day phases during which they were maintained on LCE (400mg/100mg/200mg) or placebo; the order of medication condition was counterbalanced. Volunteers underwent cognitive testing without cocaine on day 4 of each phase and again after smoking repeated doses of cocaine on day 5 of each phase. Attentional bias was measured by a Drug Stroop task that assessed attentional performance in the presence and absence of cocaine-related stimuli.
Results: There was a main effect of cocaine condition ($p<0.05$), with volunteers experiencing greater interference from cocaine-related stimuli after cocaine smoking compared to the no-smoking condition. No significant main effect of LCE or interaction between cocaine and LCE was observed ($p>0.05$).
Conclusions: In regular cocaine users, attentional bias towards cocaine cues increased after cocaine smoking, consistent with the notion that cocaine intoxication increases the salience of cocaine cues. This may represent a novel cognitive mechanism that contributes to the prolonging of cocaine use once it is initiated.
Financial Support: This research was supported by NIDA grant 09236.

684

FUNCTIONAL GENETIC EVOLUTION OF ADDICTION: A NEW APPROACH USING COMPARATIVE GENETICS FOR UNDERSTANDING DRUG DEPENDENCE.

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Aims: Addiction pathologies evolve from conserved natural behaviors and environmental interactions. Understanding the functional genetic evolution of addiction, the evolutionary origins of addiction and the molecular evolution of the genes which underlie it, can help modern researchers better understand the biology of addiction and create better treatments.
Methods: Functionally parallel genetic sources of behavioral variation, such as the promoter polymorphisms of *SERT* and *MAOA*, are observed across numerous, though not all, species. Adaptation in species can also be informative, whether alcohol metabolism in fruit flies or cocaine and caffeine as natural insecticides. By comparing genetic divergence and polymorphism across species, we can better understand both the processes and vulnerabilities leading to addiction.
Results: We show that the mu opioid receptor gene (*OPRM1*) is an example of how the functional genetic evolution of addiction can lead to better models and treatments. Polymorphisms in humans that associate with dependence are found outside of Africa (A118G, N40D) and within African populations (T17C, V6A). We identified a polymorphism in rhesus macaques (C77G, P26R) that demonstrates similar functional effects and phenotypic associations, as well as polymorphisms in the same region and at similar frequencies in marmoset (A111T, L37F) and squirrel monkey (C55T, P19S). Our in vivo and in vitro functional studies demonstrate that these variants show similar effects on alcohol drinking behaviors and therapeutic responsivity to naltrexone in non-human primates as they do in humans. Evolutionary pressures have seemingly led to parallel phenotypes.
Conclusions: Through understanding the evolutionary history of genes between species and populations we can better understand the genetic factors leading to addiction. These differences offer insight into developing interventions and have important implications for complex association studies across populations. These in turn may help to better predict vulnerabilities and target treatment options.
Financial Support: AA019688, DA025697 and RR000168

685

GATEWAY BEHAVIOR VS. "GATEWAY" SEQUENCE IN THE RISK FOR ADDICTION.

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Aims: To test whether non-normative socialization mediates the association between transmissible liability to addiction measured in childhood and cannabis use disorder manifested by young adulthood, and whether the sequence of drug use initiation ("gateway", consuming legal drugs before cannabis, or the reverse) contributes to accuracy of prediction of cannabis use disorder beyond deviant socialization.
Methods: Sons of fathers with or without substance use disorders (SUD) related to illicit drugs were tracked from 10-12 to 22 years of age to model the association between a quantitative measure of the risk for SUD (Transmissible Liability Index, TLI), socialization (a peer deviance measure), order of drug use initiation ("gateway" or reverse sequence), and development of cannabis use disorder. Path analysis was used to evaluate relationships among the variables.
Results: Non-normative socialization mediates the association between transmissible risk measured during childhood and cannabis use disorder manifest by young adulthood. The sequence of drug use initiation did not contribute additional explanatory information to the model.
Conclusions: The order of drug use initiation does not play a substantial role in the etiology of cannabis use disorder, whereas deviant socialization represents a potential mechanism of realization of the risk for addiction.
Financial Support: National Institute on Drug Abuse grant P50DA005605

686

FIRST STEPS IN REDUCING HEALTH DISPARITIES IN INFANT MORTALITY AND MORBIDITY: DEVELOPMENT OF A SCREENING TOOL TO IDENTIFY WOMEN LIKELY TO BENEFIT FROM HEALTH SYSTEM NAVIGATION.

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Aims: African American (AA) women are more likely to deliver LBW or preterm infants than Caucasians. To reduce disparities, some have focused on improving prenatal care attendance. Two promising strategies are Health System Navigation (HSN) and Behavioral Incentives (BI). As part of an ongoing study, we created a screening tool to focus on risk factors and identify pregnant AA women most likely to benefit from HSN and BI. The present study examined relationships among risk factors and their contributions to study eligibility and willingness of women to receive HSN and BI.
Methods: N=907 Pregnant AA women completed an anonymous 23-item screener at their first prenatal visit. Screener domains included demographics, substance use, depression, etc. Summary scores ranged from 0 to 21, with study eligibility defined by cut-off scores > 4. Chi-squares and t-tests were used to identify associations between risk factors and 3 screening outcomes: Not eligible; Eligible but not interested; and Eligible, interested and either consented or unable to contact for enrollment.
Results: Mean age of the sample was 24.9; nearly half were unemployed (48.5%) and nearly one-fifth (17.7%) had contact with legal system. Chi-square analyses found both groups of eligible subjects different from ineligible women, with higher rates of unemployment (62.3; 62.7 and 42.8%, respectively; $p<.001$), lower education (29.9%, 39.8% and 21.0% < high school; $p<.001$) and a greater contact with legal system (36.5%; 24.5%; 11.4%; $p<.001$). They were also twice as likely to have an open or recent CPS case, and rates of depression > 2 times higher.
Conclusions: Preliminary analyses affirm study eligible women differed from ineligible women, regardless of whether those eligible consented to the study. The consistency of this pattern across domains suggests the majority of items are contributing to the identification of group differences.
Financial Support: CDC 5U58DP000983

687

MATERNAL COCAINE USE AND CHILD BEHAVIOR PROBLEMS: ROLE OF PARENTING AND CHILD EXPOSURE TO VIOLENCE.

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Aims: This study examined the association between prenatal cocaine exposure(PCE)and child behavior problems(BPs)in kindergarten. Child gender was also assessed as a moderator of this association while maternal harshness and sensitivity were evaluated as moderators of the relation between exposure to violence(EV)and BPs.
Methods: The sample consisted of 161(85 cocaine-exposed(CE),76 non-cocaine exposed(NE))mother-child dyads participating in an ongoing longitudinal study of PCE. Prenatal cocaine status was determined by a combination of self-report, chart review, and maternal hair analysis. Maternal reports of child's EV were obtained at kindergarten using the Survey of Exposure to Community Violence, and child BPs obtained from Child Behavior Checklist Scale. Maternal harshness and sensitivity were coded from observations of mother-child interactions in the infant-toddler period.
Results: We first examined the association between PCE and BPs using ANCOVA with maternal alcohol,cigarette,and marijuana use during pregnancy as covariates and child gender as a potential moderator. Results indicated no main effect of group, but a significant group by gender interaction($F(1, 154)=3.80, p<.05$)with CE girls revealing significantly greater BPs($M=31.37$, $SE=3.58$)compared to the NE girls ($M=24.38$, $SE=3.88$). Results from hierarchical regression analyses indicated that EV among children with sensitive mothers was associated with lower BPs in kindergarten. Among children who were exposed to violence, higher maternal harshness was associated with more BPs.
Conclusions: These findings suggest an association between PCE and child BPs for cocaine-exposed girls but not for boys. Contrary to expectations, EV did not mediate the association between PCE and child BPs. However, results did support the hypothesis that maternal sensitivity across the first two years of life would have a protective effect among children with EV while maternal harshness would exacerbate the impact of EV on BPs.
Financial Support: National Institute on Drug Abuse grant#1R01 DA13190

688

THE IMPACT OF MARIJUANA USE ON HIGH AND DESIRE FOR COCAINE IN COCAINE-DEPENDENT INDIVIDUALS.

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Aims: The primary aim of this study was to evaluate whether marijuana use affects the "desire" for, and/or the "high" associated with cocaine in cocaine-dependent individuals.
Methods: We administered the multi-drug use questionnaire (MDUQ) to non-treatment seeking cocaine-dependent volunteers (n=144, to date), focusing on two main questions: 1) Does marijuana use affect the "high" that you experience from cocaine, and 2) Does marijuana use affect your "desire" for cocaine?
Results: All participants met DSM criteria for cocaine dependence, and they were primarily male (81%) and African American (86%). Participants used cocaine for 16.8 ± 7.3 (mean ± S.D.) years and 18.8 ± 8.3 days in the last 30 days.
The majority of cocaine-dependent participants were also current users of marijuana (63.8%), alcohol (89%) and nicotine (90%). No difference was reported in total years of cocaine use among marijuana users (19.1 ± 8.0) vs. non-marijuana users (18.4 ± 8.7, $p=0.65$). Similarly, no difference was reported in recent use of cocaine (last 30 days) among marijuana users (16.3 ± 7.4) vs. non-marijuana users (17.6 ± 7.2, $p=0.32$). Interestingly however, the data from the MDUQ suggests that marijuana use does not alter the high or desire produced by cocaine.
Conclusions: On the basis of self-reports, the current findings indicate that the use of marijuana does not alter the high or desire for cocaine among cocaine-dependent individuals. Interestingly, and as reported by others, although the cocaine-dependent respondents in the present study were more likely to also use marijuana than non-cocaine users, it remains to be determined why cocaine-dependent individuals are more likely to also use marijuana. Nonetheless, it will be interesting to see whether treatments that work for cocaine-dependence alone will be similarly effective in individuals who co-abuse other drugs, like marijuana.
Financial Support: This study is sponsored by NIH via support to RDLG (DA023624, DA023588, DA028387) and TFN (DA017705, DA018197).

689

SELF-ADMINISTRATION OF PRESCRIPTION OPIOIDS IN OPIOID ABUSERS WITH AND WITHOUT CHRONIC PAIN.

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Aims: To examine whether self-administration of prescription opioids differed between opioid (OP) abusers with (w/) and without (w/o) pain.
Methods: OP abusers w/ and w/o moderate chronic pain (at least 6 months in duration, non-malignant, non-neuropathic) were admitted to a research unit for a 4-week, randomized, double-blind, placebo-controlled study. Participants were maintained on a fixed dose of 8 mg Subutex™. Three laboratory sample sessions were completed, each separated by 24 h. Sample sessions consisted of PO administration of randomized, over-encapsulated placebo (PBO), morphine 180 mg (M180) or oxycodone 60 mg (O60); drugs were identified as A, B or C. Participants then completed 5 choice sessions, during which they chose whether to self-administer drug A, B, or C.
Results: Seven participants (5 OP abusers w/o pain; 2 OP abusers w/pain) have completed the study to date. OP abusers w/o pain were 43 (±10) years old, white/hispanic (80%) males (80%), using 8 (±1) bags of heroin per day. OP abusers w/pain were 51 (±10) years old, white (100%), males and females (50% each) using heroin (2 bags per day) or oxycodone (405 ±488 mg per day), for back (100%) or knee (50%) pain. Mean number of choices ranged from 0-5: PBO = .29 (±.49), M180 = 2.3 (±2.6), and O60 = 2.4 (±2.4). The combined sample chose more O60 than PBO ($p < .05$), yet number of choices did not differ between M180 and PBO, or between M180 and O60. O60 was chosen because it was liked more than the other drugs (53% of choices), or to relieve pain (29%). M180 was chosen because the other drugs (O60 and PBO) were liked less (31%), M180 was liked more than the other drugs (25%), or to get high (25%).
Conclusions: Conclusions should be tempered due to the small number of OP abusers w/pain, however, these preliminary analyses revealed that self-administration of prescription opioids is similar between OP abusers w/ and w/o pain.
Financial Support: This research was supported by DA-016759-06A1.

690

EFFECTS OF MU AND KAPPA OPIOID RECEPTOR LIGANDS ON THE EXPRESSION AND EXTINCTION OF CONDITIONED FEAR IN C57BL/6J MICE.

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Aims: Posttraumatic Stress Disorder (PTSD) is an anxiety disorder that affects over 7.7 million adults and is insufficiently treated with typically prescribed medications. Prophylaxis against developing PTSD with opioid analgesics has been suggested, but comorbidity for opiate abuse and PTSD after its development has also been noted. Anti-stress effects of kappa opioid receptor antagonists have been reported by several laboratories. Thus, it is important to resolve the potential importance of administering mu and kappa opioid receptor agents in the treatment and prevention of PTSD.
Methods: Mice were subjected to Pavlovian fear conditioning, a procedure thought predictive of some aspects of PTSD. Conditioning was conducted over three days: a conditioning day; an exposure day; and an extinction test day. Doses of test compounds were administered 20 min prior to Day 2 exposure sessions to separate groups of 8 mice each (morphine 1, 3, & 10 mg/kg; buprenorphine 0.3, 1, 3 mg/kg; naloxone 0.1, 1, 10 mg/kg; enadoline 0.0001, 0.001, 0.01, 0.1 mg/kg; norbinaltorphimine 1, 10, 30 mg/kg). Drug treated groups were compared to vehicle controls with two-way ANOVAs and Dunnett's post hoc tests for each drug ($p<0.05$ considered significant).
Results: Morphine reduced acute contextual freezing and facilitated extinction of contextual freezing. Buprenorphine reduced acute contextual freezing but did not affect extinction. Naloxone did not affect acute contextual freezing or its extinction. Enadoline exacerbated acute contextual freezing but facilitated its extinction. Norbinaltorphimine reduced acute contextual freezing and also facilitated its extinction.
Conclusions: These results support the use of opioid analgesics and kappa opioid antagonists when associated with trauma for preventing and treating PTSD. These results also suggest self-medication as a possible determinant involved in the comorbidity of opioid abuse in PTSD patient populations.
Financial Support: NIDA training grant T32DA007027

691

PARENT SUPPLY, PARENT FACTORS AND ADOLESCENT ALCOHOL USE: FIRST RESULTS FROM A LONGITUDINAL AUSTRALIAN COHORT.

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Aims: Parents are the largest supplier of alcohol to adolescents. Despite the public health burden of adolescent alcohol use, the effects of parental alcohol supply are unknown. It is hypothesised: 1) Parent alcohol use and alcohol initiation age are related to parental alcohol supply and child alcohol initiation; and 2) Parent income, religiosity, employment and education are related to parental alcohol supply.
Methods: Parent-child dyads were recruited via schools. In total, 1808 dyads completed baseline surveys. Descriptive analyses and significance tests using Chi-Square and ANOVA were conducted in SPSS.
Results: Sixty eight percent of children (M=12yrs) had tried alcohol. Parents drinking in the presence of their child were more likely to have children who had tried alcohol (χ^2=34.74, p<.005). Fifty four percent of parents had given a sip of alcohol to their child. Parents who did supply alcohol, drank alcohol more frequently (χ^2=13.28, p=.04). Parents with younger alcohol initiation were more likely to supply alcohol (F=19.28, p<0.005) and their child more likely to have tried alcohol (F=22.79, p<0.005). Higher income (χ^2=9.95, p=.02) and less religious parents (χ^2=14.03, p=.003) were more likely to supply alcohol. Parent employment (χ^2=2.15, p=.14) and education (χ^2=2.72, p=.61) were not related to supply.
Conclusions: Parent alcohol use, religiosity, income and age of first alcohol use are significantly related to parental supply of alcohol and adolescent alcohol use.
Financial Support: This research is funded by: Australian Research Council Discovery Project (DP1096668), Australian Rotary Health Mental Health Research Grant and Whitcroft Family Scholarship, and Foundation for Alcohol Research & Education Project Grant.

692

ACUTE ALCOHOL INTOXICATION AND NON-SUICIDAL SELF-INJURY.

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Aims: Over one-million people die by suicide each year, and research suggests that as many as one-half of these deaths involve acute alcohol intoxication. The present study examined a possible mechanism which might underlie the connection between acute alcohol intoxication and non-suicidal self-injury (NSSI) in a controlled, laboratory setting. Specifically, we examined how alcohol might worsen the impact of a suicide risk factor (viz., thwarted belongingness—the failure to form meaningful relationships) and lead to an increase in NSSI.
Methods: 40 problem-free, moderate drinkers with no history of suicide or self-injurious behavior completed a series of questionnaires, including personality inventories. Participants received one of two types of bogus feedback alleged to reflect their personality. "Thwarted belongingness" feedback forecasted a lonesome future lacking relationships. "Misfortune control" feedback forecasted a future filled with injury and accident, but with no mention of belongingness. Participants then consumed alcoholic (BrAC: 0.08) or non-alcoholic beverages in a room devoid of distraction which was intended to facilitate the "crying-in-one's-beer" effect and thus worsen the impact of the distressing feedback. NSSI was then measured via a cold pressor.
Results: As predicted, a significant Feedback x Beverage interaction was found ($p < 0.001$), and a large effect size was observed ($p\eta^2 = 0.19$) such that those who experienced thwarted belongingness and then consumed alcohol engaged in significantly greater NSSI (i.e., submerging one's hand in a cold pressor) than participants in all other groups.
Conclusions: This study identified a mechanism linking acute alcohol intoxication and non-suicidal self-injury. Specifically, individuals whose belongingness was "thwarted" and subsequently consumed alcoholic beverages engaged in more serious self-injurious behavior. Given research identifying thwarted belongingness as a key risk factor for suicide, and the frequency with which individuals consume alcohol as a means to cope with distress, results from this study are especially worrying.
Financial Support: Funded by the Florida State University Alcohol Studies Laboratory

693

ARIPIPRAZOLE DOES NOT ALTER METHAMPHETAMINE SELF-ADMINISTRATION.

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Aims: Methamphetamine use disorders remain a significant public health concern. Medications development efforts have sought a pharmacotherapy to treat methamphetamine dependence. A methamphetamine antagonist pharmacotherapy might reduce drug taking through extinction processes. This study sought to determine the effects of a potential methamphetamine antagonist, aripiprazole, on methamphetamine self-administration.
Methods: Seven subjects with histories of recreational stimulant use completed a placebo-controlled, crossover, double-blind protocol in which they first sampled doses of oral methamphetamine (0, 4, 8 or 16 mg) following pretreatment with aripiprazole (0 and 15 mg). During each sampling session, subjects also completed a battery of subject-rated and physiological measures. In subsequent self-administration sessions, subjects were provided the opportunity to earn the previously sampled methamphetamine dose on a progressive ratio procedure. Data were analyzed using repeated-measures ANOVA.
Results: Methamphetamine functioned as a reinforcer and produced prototypical stimulant-like subject-rated and physiological effects (e.g., increased ratings of Good Effects; elevated blood pressure). Aripiprazole alone was generally devoid of effects. When combined with methamphetamine, aripiprazole failed to alter methamphetamine self-administration but did attenuate some positive subject-rated effects of methamphetamine (e.g., ratings of Stimulated).
Conclusions: As has been demonstrated previously, a potential pharmacotherapy produced divergent effects on subject-rated and reinforcing effects of a drug of abuse. The self-administration outcomes are concordant with clinical trial data suggesting that aripiprazole is not an effective pharmacotherapy for managing methamphetamine use.
Financial Support: Supported by a grant from NIDA (R01 DA 017711) to CRR

694

HORMONE MODULATION OF MOTORIC BUT NOT ANTINOCICEPTIVE EFFECTS OF I.C.V. THC IN OVARIECTOMIZED FEMALE RATS.

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Aims: Supraspinally administered Δ-9-tetrahydrocannabinol (THC) produces greater antinociception in proestrous-estrous female rats compared to estrous females and males. The aim of this study was to examine which ovarian hormone modulates the antinociceptive effects of supraspinally administered THC.
Methods: Adult female Sprague-Dawley rats were ovariectomized; vehicle or ovarian hormones (2 μg estradiol, or 500 μg progesterone, or both) were administered on Days 3 and 7 after surgery. On the morning or late afternoon of Day 8, or on the morning of Day 9, vehicle (1:1:8 ethanol:cremaphor:saline) or THC (100 μg) was administered into the right lateral ventricle (i.c.v.) (N=4-12/day/hormone condition/dose). Antinociception was measured using paw pressure and warm water tail withdrawal tests at 5-180 min post-injection. Horizontal locomotion was examined in 5-min periods at 15-180 min post-injection, and catalepsy was measured at 15 and 30 min post-injection.
Results: THC produced peak antinociception at 15-30 min post-injection on both tests, with response latencies returning to baseline at 120-180 min post-injection (paw pressure: THC x time, $P<0.001$; tail withdrawal: THC x time, $P<0.001$). THC also reduced locomotor activity, which recovered to baseline levels by 120-180 min post-injection (THC x time, $P<0.001$). THC produced significant catalepsy (THC, $P<0.001$). THC's effects did not differ among the various hormone-treated groups on either nociceptive test or on the catalepsy test, and also did not significantly differ across test days. However, estradiol lengthened the duration of THC-induced suppression of locomotor activity (time x estradiol, $P=0.013$).
Conclusions: These results suggest that estrous stage modulation of the antinociceptive effects of i.c.v. THC is not simply due to estradiol or progesterone, with 75% of subjects tested thus far. Estradiol does appear to sustain i.c.v. THC-induced suppression of locomotor activity over the time course examined.
Financial Support: This research was supported in part by funds provided for medical and biological research by the State of Washington Initiative Measure No. 171.

695

DRUG AND ALCOHOL ABUSE IN NEW YORK STATE CLINICS: PROGNOSTIC PREDICTORS.

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Aims: Understanding relationships between substance abuse treatment outcome and prognostic factors from an epidemiological view may lead to greater insight relative to that provided by studying an individual clinic. We describe a random sample of New York State chemical dependency outpatient programs and client demographics, treatment utilization, and goal achievement as a function of drug abuse, alcohol abuse, and their combined abuse. We hypothesized that clients with combined abuse would have a worse prognostic picture.
Methods: In 2006, New York State listed 321 licensed outpatient rehabilitation programs. The New York State Office of Substance Abuse Services made data available to us regarding admissions and discharges at a randomly selected 198 clinics. Each clinic contributed admissions from a 6-month retrospective window, resulting in a total of 115,993 clients. This sample of outpatient clients was 28% female, averaged 34.3 years old (SD = 12.5), with an average of 12.7 years of education (SD = 3.1).
50% of clients reported abuse of both alcohol and drugs (i.e., the "mixed" group); 25% reported abuse of alcohol only; and 25% reported abuse of drugs only. T-tests and chi-square tests compared the alcohol-only and the drug-only group with the mixed group.
Results: Comparison of alcohol-only with mixed clients indicated that the alcohol-only clients were older (39.9 v 33.2 years), were less likely to have a comorbid psychiatric disorder (21.4% v 34.1%), had a longer treatment stay (135.4 v 119.7 days), and were more likely to "achieve" alcohol treatment goals (60.0% v 40.6%) and have a "complete" treatment (52.0% versus 28.9%).
Comparison of drug-only with mixed clients indicated that the drug-only clients were more likely to be female (33.8% v 26.8%), had fewer treatment sessions (29.8 v 32.4 sessions), were less likely to have a comorbid psychiatric disorder (29.2% v 34.1%), and were less likely to "achieve" drug treatment goals (34.4% v 38.0%).
Conclusions: In sum, mixed clients fared worse than alcohol-only clients and slightly better than drug-only clients.
Financial Support: National Institute on Alcohol Abuse and Alcoholism

696

NO EVIDENCE OF INCREASED HEROIN USE OR DECREASED DETOXIFICATION TREATMENT AFTER OVERDOSE EDUCATION AND NALOXONE DISTRIBUTION.

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Aims: Providing naloxone to reverse opioid-related overdoses to opioid users may increase substance use or reduce entry into substance abuse treatment by reducing the perception of consequences and decreasing interactions with emergency services. To determine whether heroin use and inpatient detoxification (detox) changed after receiving naloxone rescue kits, we conducted a cohort study among active substance users who provided information about 30-day substance use and detox during enrollment in the Massachusetts overdose education and naloxone distribution (OEND) program from 2006 to 2010.
Methods: At OEND enrollment, demographics, substance use and detox history were collected. Among OEND participants who enrolled twice, we used paired t-tests to compare the mean number of days of heroin use at the 1st and 2nd enrollments. We used McNemar's test to compare the proportions with past year detox treatment.
Results: Among 4918 individuals enrolled in OEND who reported 30-day substance use, 325 were enrolled twice. Characteristics were similar in demographics and drug use, though twice enrollers more often reported a history of overdose and detox in the last year. The mean age of the twice enrollers was 33 years, 63% were male, and 63% had a previous overdose. The mean number of days using heroin in the last 30 days at the first enrollment was 14.5 and at the second enrollment was 13.9 ($p=0.54$). Past year detox treatment was reported by 57% at the first enrollment and 62% at the second enrollment ($p=0.29$).
Conclusions: Among OEND program participants with active substance use, we found no evidence that heroin use increased or detox treatment decreased after OEND enrollment. Concern about increased drug use or decreased treatment access should not impede the expansion of overdose education and naloxone distribution programs.
Financial Support: CDC National Center for Injury Prevention and Control 1R21CE001602-01

697

ATOMOXETINE FOR THE TREATMENT OF COCAINE DEPENDENCE: A PILOT DOUBLE-BLIND, RANDOMIZED OUTPATIENT TRIAL.

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Aims: Atomoxetine (ATMX), a norepinephrine reuptake inhibitor, is marketed for the treatment of ADHD. Preclinical data suggest it may reduce cocaine cue-induced drug seeking and relapse. This 12-week, placebo-controlled, double blind, randomized, outpatient study sought to examine the potential efficacy of ATMX to reduce cocaine use.
Methods: Cocaine dependent individuals (n=148) were screened carefully over a two-week period and stratified by age, sex and frequency of recent cocaine use before urn randomization (n=25/group) to either placebo or ATMX (80 mg/day with an initial 4-day dose run-up). Clinic visits occurred thrice weekly (MWF); subjects presented for pill counts and supervised dosing and provided urine and breath samples for drug and alcohol testing, respectively. Attendance and study procedure adherence were reinforced with an escalating contingency payment schedule. Once weekly manual-guided cognitive behavior therapy was offered throughout the trial. A broad array of outcome measures was collected repeatedly over the 12 weeks.
Results: Groups did not differ on key demographic characteristics. Survival analysis revealed no significant group differences in study completion rates (64% placebo) and (48% ATMX). With GEE analysis, counting missing urines as cocaine positive, results revealed that 67% and 74% of all samples were cocaine positive for the placebo and ATMX groups, respectively (p>.05). Similarly, counting missing urines as missing, 66% and 73% of urines were cocaine positive for the placebo and ATMX groups, respectively (p>.05).
Conclusions: These findings do not support the pursuit of atomoxetine for the treatment of cocaine dependence.
Financial Support: Supported by NIDA (R01DA22191, T32 DA 016176).

698

GETTING TO IT LATER: CANNABIS USE AND PROCRASTINATION.

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Aims: Clinical lore and patient report converge to identify procrastination as a notable component of cannabis use. However, the empirical literature bearing on this relationship is scant, and is largely comprised of self-reported procrastination among treatment seeking samples. The present study combines self-report and behavioural indicators of procrastination to assess associations with regular cannabis use.
Methods: Participants were 1184 university students. The primary procrastination outcome was time in days to completion of a survey for course credit. Behavioural assessment of procrastination was supplemented by self-report for 609 participants. Cannabis use was assessed using the Cannabis Use Disorders Identification Test (CUDIT).
Results: Cannabis use was associated with behavioural and self-report indices of procrastination. Relative to those who used cannabis less than monthly (n = 971), participants who reported using cannabis monthly or more (n = 213) waited longer to complete the behavioural task, $F(1, 1182) = 9.12$, $p < .01$, and scored higher on self-reported procrastination, $F(1, 607) = 15.26$, $p < .01$. Results were consistent using more stringent cannabis use criteria (i.e. weekly use versus no use). Supplementary analyses indicated that results were not attributable to trait conscientiousness.
Conclusions: These results present preliminary empirical evidence for an association between procrastination and cannabis use. From a clinical perspective, the prominence of procrastination among negative cannabis use outcomes identify it as a potential target for increasing motivation to change use patterns among frequent cannabis users. The relative tardiness of cannabis users with regard to research participation may be of interest to researchers studying cannabis use among university populations.
Financial Support: This research was supported by a grant to from the Social Sciences and Humanities Research Council of Canada to Zach Walsh.

699

AN INVESTIGATION OF COGNITIVE FUNCTION IN METHADONE-SUBSTITUTED OPIATE USERS.

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Aims: Methadone maintenance treatment (MMT) has been used to treat opiate dependence since the mid-1960s. Previous studies have investigated the effects of methadone on cognitive function however the findings have been inconsistent. Some report a complete absence of deficits while others report different types of cognitive impairment. Our research aimed to investigate the effect of MMT on cognitive function by comparing the performance of patients currently enrolled in MMT (N= 32) with opiate-dependent subjects (N=17) and healthy controls (N=24).
Methods: Subjects were evaluated using a battery of self-administered computerized neuropsychological tests (IntegNeuroTM, Brain Resource Company, Australia), to determine pre-morbid IQ and six cognitive domains: memory, specifically speed of processing and motor function, attention, executive function, verbal function and emotion identification. Group comparisons were made using Analyses of variance (ANOVA) with group as a fixed factor and age and education as covariates. .
Results: Analysis revealed significant differences between each group using the Continuous Performance (sustained attention, $F = 9.095$, $p = 0.000$], Motor Tapping (motor function, $F = 4.779$, $p = 0.012$) and Maze task (executive function, $F = 5.562$, $p = 0.006$). Post hoc comparisons using the Tukey HSD test showed that those currently opiate dependent performed significantly worse than healthy controls on all three tasks. However the performance of those currently undertaking MMT was not significantly different from healthy controls.
Conclusions: Our findings indicate that MMT does not significantly affect an individuals' cognitive Function. Consequently the deficits induced by opiate dependence may recover when engaged in MMT. In contrast those who are currently opiate dependent and not engaged in treatment may suffer from difficulties with concentration, fine motor movement (e.g. hand), planning, organizing and strategizing.
Financial Support: School of Pharmacy, The University of Auckland

700

A NEW METHOD FOR DETERMINING THE CONCENTRATION OF BUPROPION AND ITS THREE METABOLITES IN UMBILICAL CORD PLASMA USING LC-ESI-MS/MS.

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Aims: Bupropion (BUP) has not been approved for smoking cessation during pregnancy because of the lack of information on its safety and efficacy in this patient population. Ex vivo and in vitro data obtained in our laboratory revealed that BUP crosses the placenta and it is metabolized by trophoblast tissue to two major metabolites threo-(TB) and erythrohydrobupropion (EB) and to a lesser extent to hydroxybupropion (OH-BUP). This data suggested that fetal exposure to BUP and its pharmacologically active metabolites is possible. Therefore, the aim of this investigation was to develop an analytical method for quantitative determination of BUP and its metabolites in umbilical cord plasma.
Methods: Plasma proteins were precipitated by the addition of acetonitrile. The chromatographic separation was achieved by using a C18 column (150 x 4.6mm, 5um), with an isocratic aqueous solution made of methanol and 0.04% formic acid (v/v) at a flow rate of 1.0 mL/min. Detection was carried out by mass spectrometry using positive turbo-ion spray ionization mode and monitoring the compounds by a multiple reactions monitoring (MRM) method. Deuterium-labeled compounds were used as internal standards. All calibration curves showed good linearity ($r2 > 0.99$) within the ranges tested.
Results: The relative deviation of this method was less than 12% for intra- and inter-day assays, and the accuracy ranged between 88 & 102%. Recovery of the four analytes and internal standards ranged between 88 & 96%.
Conclusions: A high performance liquid chromatography in tandem with electrospray mass spectrometry (LC-ESI-MS/MS) method have been developed and validated for the quantitative determination of BUP and its three metabolistes (OH-BUP, TB and EB) in human umbilical cord plasma.
Financial Support: This work was supported by NIDA DA030998.

701

PREVALENCE AND PREDICTORS OF SEXUAL DYSFUNCTION IN ALCOHOLICS: RESULTS FROM AN OUTPATIENT TREATMENT CENTER.

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Aims: Little is known about the prevalence and impact of sexual dysfunction in alcohol dependent individuals. We expect this to play a major role regarding quality of life and drinking behavior as well as comorbid disorders like major depression.
Methods: We collected questionnaires from patients, being currently treated in our outpatient unit. These included duration and severity of alcohol dependence, comorbid nicotine dependence, affective symptoms, psychoactive medication and any form of sexual dysfunction following ICD-10 and DSM-IV-TR criteria.
Prevalence and predictors are calculated in using logistic regression models.
Results: Our first results in 33 patients revealed a high prevalence of 79 % with a lifetime history of sexual dysfunction in this sample. Furthermore 53% experienced this in the last 4 weeks, indicating a major phenomenon in the course of alcohol dependence.
Conclusions: Preliminary Data showed high rates of sexual dysfunction in alcoholics in an outpatient treatment center, questioning for additional therapeutic options in maintaining abstinence.
Financial Support: This work did not receive any financial support.

702

CARRIERS OF THE A1 ALLELE OF THE D2 DOPAMINE RECEPTOR GENE HAVE BETTER OUTCOMES IN AN INCENTIVE-BASED INTERVENTION FOR PREGNANT SMOKERS.

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Aims: The present study was conducted to examine associations between the D2 dopamine receptor (DRD2) A1 allele and response to an incentive-based intervention for smoking cessation among pregnant women.
Methods: All participants (n = 136) were enrolled in clinical trials evaluating the efficacy of financial incentives for smoking cessation, consented to participate in the genetic component of the study, and provided a blood sample. Women were assigned to either an intervention condition wherein they earned vouchers by smoking abstinence or a control condition wherein they received vouchers despite smoking status.
Results: Carrier status was a significant predictor of smoking abstinence after controlling for potential confounds ($\chi 2$ (1) = 4.6, p = .03; OR = 2.8, 95% CI: 1.1-6.9), which was largely attributable to greater abstinence among carriers of the A1 allele in the intervention (56.5 vs. 29.8, $\chi 2$ (1) = 4.7, p = .03) than the control condition (12.5 vs. 14.7, $\chi 2$ (1) = 0.1, p = .79), although the interaction of carrier status and treatment condition was not significant ($\chi 2$ (1) = 2.1, p = .14). Carriers and non-carriers alike had superior outcomes in the intervention compared to the control condition (carriers: 56.5% vs. 12.5%; non-carriers: 29.8% vs. 14.7%).
Conclusions: Pregnant smokers who are carriers of the DRD2 A1 allele may be especially responsive to incentive-based interventions.
Financial Support: This research was supported by research (R01 DA14028) and training (T32 DA07242) grants from the National Institute on Drug Abuse and GCRC MO1RR109 from the National Institutes of Health.

703

REINFORCING AND ICSS THRESHOLD-LOWERING EFFECTS OF THE "BATH SALTS" DRUG MDPV.

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Aims: In recent years, there has been a rapid increase in the use of synthetic cathinones, often called "bath salts", in the western world. Despite widespread use, very little scientific information exists regarding the abuse potential of these compounds. The purpose of the present study was to evaluate the abuse potential of methylenedioxypyrovalerone (MDPV), a common "bath salts" compound.
Methods: In experiment 1, three groups of rats (MDPV doses of 0.05, 0.1, and 0.2 mg/kg/infusion) were placed into 2 hr daily self-administration (SA) sessions for 10 days followed by a single 16 hr overnight progressive ratio (PR) session. Next, rat groups were split into 2 hr short access (ShA) or 6 hr long access (LgA) daily sessions for 10 days. In experiment 2, rats were implanted with electrodes into the medial forebrain bundle and trained to respond for intracranial self-stimulation (ICSS). All rats were then tested for changes in threshold ICSS values following MDPV treatment (within-subject, vehicle, 0.1, 0.5, 1.0, and 2.0 mg/kg i.p.).
Results: SA experiments revealed successful discrimination of active and inactive levers by day 5 for each dose as well as clear dose effects for total number of infusions obtained per session. The PR test revealed a significant dose effect for breakpoints indicating a greater reinforcing efficacy at higher doses. Additionally, LgA rats exhibited an escalated intake of 0.1 and 0.2 mg/kg MDPV infusions across the final 10 days of SA. A dose-dependent reduction in ICSS thresholds was observed with significant decreases at the 1.0 and 2.0 mg/kg doses of MDPV versus vehicle.
Conclusions: Together, these results reveal that MDPV is a potent reinforcer and activates the brain reward circuitry, suggesting a significant potential for abuse. Furthermore, these findings have significant implications for researchers and policy makers regarding synthetic cathinone abuse and addiction.
Financial Support: This work was supported by NIH grant DA025606.

704

DRUG USE AND PROBLEM SEVERITY OF PRISONERS PAROLING TO RURAL ADJACENT COUNTIES.

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Aims: Although research has examined drug use in prisoners from rural and urban areas, viewing rural areas as homogenous may mask differences between rural and urban areas, as well as variability within rural areas. One important characteristic of rural areas to consider is whether they are in close proximity to urban areas. These rural adjacent areas maintain a rural identity, yet are not remote enough to be considered isolated from urban influences. The objective of this research was to examine drug use and problem severity of prisoners who were paroling to urban, rural adjacent to urban, and rural nonadjacent to urban counties.
Methods: The TCU Drug Screen was administered to 349 prisoners in 4 Kentucky state prisons who were approaching parole and consented to be participants in CJ-DATS protocols. The instrument measures the use of several drugs and contains items based on DSM drug dependence criteria, which are consequences associated with problem severity. Beale codes were used to create the three parole county groups: urban (n=215), rural adjacent (RA; n=55), and rural nonadjacent (RN; n=79).
Results: The drug use profile was similar for prisoners paroling to RA and RN counties, characterized by statistically significant higher rates of opiate (59%/62%) and methamphetamine (37%/36%) use than those paroling to urban counties (36% & 18%). However, prisoners paroling to RA counties were similar to those paroling to urban counties and statistically different from RN parolees with respect to several of their drug-related problems: spending less time at work, school, or with friends (54%/54% vs. 68%), drug-related physical (37%/44% vs. 58%) and psychological (48%/53% vs. 74%) problems.
Conclusions: Findings suggest that proximity to urban areas may contribute to the types of drug-related problems individuals experience, irrespective of the types of drug used and that rural areas may not be homogenous with respect to drug-related problems. Implications for treatment planning and defining rurality are discussed.
Financial Support: This research is funded by NIDA (U01-DA016205, PI: Leukefeld).

705

VARENICLINE EFFECTS ON ALCOHOL SEEKING AND SELF-ADMINISTRATION IN BABOONS.

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Aims: Varenicline, an α4β2 nicotinic receptor partial agonist, is an FDA-approved treatment for smoking cessation and is currently under investigation for the treatment of alcohol dependence. Ideally, treatments for alcohol dependence would reduce craving and motivation to drink as well as alcohol consumption. In laboratory animals, behaviors directed towards obtaining alcohol access (seeking) and drinking alcohol (self-administration) can be used as indices of the incentive-motivational processes involved in the maintenance of drinking. The aim of the current study was to examine the effects of chronic administration of varenicline on alcohol seeking and self-administration.
Methods: Alcohol self-administration was maintained under a chained schedule of reinforcement (CSR) in baboons (n=4). The CSR consisted of 3 separate linked components, each associated with distinct stimuli (cue) and different behavioral contingencies (schedule requirements) leading to the opportunity to self-administer alcohol (4% w/v). Fulfilling the schedule requirements in the 2nd component was necessary to progress to the 3rd component where alcohol was available for 2 hrs under a fixed ratio schedule per drink. Failure to complete the response schedule in the 2nd component ended the session with no alcohol access for the day. Each dose of varenicline (0.032-0.32 mg/kg) and vehicle (saline) was administered 30 min before the session for 5 consecutive days.
Results: Under baseline conditions, baboons self-administered 1 g/kg alcohol, which we have shown previously results in BAL of >80 mg/dL. ANOVA indicated varenicline significantly reduced alcohol seeking response latency resulting in later access to alcohol ($p<0.0001$) and reduced alcohol self-administration ($p<0.0136$). Post-hoc tests indicated effects were significant at 0.32 mg/kg (both $p<0.05$).
Conclusions: These results indicate that varenicline may be a useful treatment to reduce alcohol drinking, but the specificity of this effect will need to be determined.
Financial Support: Supported by NIAAA R01AA015971

706

MEDIAL PREFRONTAL CORTEX ACTIVATION CORRELATES WITH IMPULSIVITY AND MEDIATES DOPAMINERGIC REWARD NETWORK RESPONSE.

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Aims: The neural substrates of impulsivity, a trait associated with harmful drug use, include striatal, limbic and prefrontal regions. This multi-modal study utilized the monetary incentive delay (MID) task during positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) to elicit mesolimbic reward response and link those responses with impulsivity.
Methods: Methods: Twelve healthy female subjects completed the NEO Personality Inventory, Revised (NEO-R) and performed the MID during [11C] raclopride PET and fMRI scans. Linear regression was performed using nucleus accumbens (NAcc) dopaminergic reward response and fMRI Reward-Neutral anticipation contrast images. Regions of interest were extracted for statistical and mediation analyses.
Results: Behaviorally induced left NAcc dopamine release correlated with BOLD anticipatory reward response in the left angular gyrus, substantia nigra/ventral tegmental area (SN/VTA), left medial prefrontal cortex (mPFC), middle frontal gyrus and right prefrontal cortex ($p\leq0.001$ uncorrected). NEO-R Impulsivity, associated with inability to resist urges, negatively correlated with left mPFC ($p=0.01$) BOLD response. mPFC response mediated the relationship between SN/VTA BOLD response and left NAcc dopaminergic reward neurotransmission (confidence interval: 0.07-5.5).
Conclusions: NAcc dopamine reward transmission was associated with increased neural activation in the brainstem, its dopaminergic source, and the mPFC, a region linked with introspective activity and differential processing of unfavorable outcomes. The negative relationship between mPFC function and impulsivity may represent cognitive influence on reward processing through regulation of mesolimbic dopaminergic projections. mPFC influence may be protective against psychopathologies such as substance abuse where dopaminergic responses and dysfunction are critically involved.
Financial Support: NIH grants: BW, K01 DA031755; MH, K01 DA020088; RZ, R01 AA12217, R37 AA07065; JZ, R01 DA022520 and Phil Jenkins Foundation Award.

707

RELIABILITY OF NONMEDICAL PRESCRIPTION DRUG USE ITEMS DESIGNED FOR THE YOUTH RISK BEHAVIOR SURVEY.

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Aims: Nonmedical prescription drug use (NMPDU) by youth remains a major public health concern in the United States. NSDUH and MTF provide important prevalence estimates about NMPDU, but they are involved and their sampling renders them unsuitable to conducting community needs assessments. To address this problem, 18 self-report items designed to measure: the prevalence of NMPDU among adolescents; age of initiation; where prescription drugs were obtained; and motivations for use were developed and pilot tested. Items were developed for each of the major classes of prescription drugs. Results from an initial pilot study (Howard, et al., 2009) suggested the items were reliable. That study was conducted with a small, homogeneous sample. Therefore, the main aim of this study was to test the reliability of the items using a larger and more geographically, racially, and ethnically diverse sample.
Methods: Data were collected twice in a 2-week period from a sample of 3,445 9th – 12th grade students enrolled in five high schools in five states (CA, FL, IL, NJ, WV). Responses from Time 1 and Time 2 were matched using a protocol designed to ensure anonymity. Kappa statistics were used to calculate the item reliability using SAS. Strength of agreement was interpreted using the benchmarks established by Landis and Koch (1977).
Results: Kappas ranged between .26 and .61 (M=.42) for lifetime and 30-day prevalence; .54 and .60 (M= .56) for age of initiation; .54 and .57 (M= .55) for where adolescents obtained prescription drugs; and .48 and .57 (M =.52) for motives for use. Of the 18 items, the majority (66%) demonstrated moderate reliability.
Conclusions: Generally, students appeared to report behavior related to NMPDU reliably over time. While some items appear to be measured reliably, further examination is needed for some items to determine if they should be revised or deleted for future applications.
Financial Support: Grant from Purdue Pharma L.P.

708

THE IMPACT OF DEPRESSIVE DISORDERS AND GENDER ON TRANSITIONS IN SMOKING IN THE U.S. POPULATION.

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Aims: This study examined the impact of gender and depression diagnosis on smoking transitions using two waves of data from the NIAAA's National Epidemiologic Survey on Alcohol and Related Conditions (Wave 1, 2001-2002; Wave 2, 2004-2005).
Methods: Analyses were conducted on 14,576 adults (50.7% female) classified as Current or Former Smokers at Wave 1 who provided data on their smoking status at Wave 2. Multinomial logistic regression analyses were used to test the main and interactive effects of gender and each depressive disorder (Current and Lifetime Major Depressive Disorder (MDD), Current and Lifetime Dysthymia, and Lifetime Minor Depression) on likelihood of being classified to one of four smoking transition groups (Stable Current Smokers, Quitters, Relapsers, or Stable Former Smokers).
Results: Depression and gender were both significantly associated with smoking transition classifications. Each of the 5 depression diagnoses and female gender was associated with continued smoking and difficult quitting smoking. There were no significant interactions of depressive disorder and gender.
Conclusions: This study was the first to use longitudinal data epidemiological to show a relationship between a range of depression diagnoses and smoking transitions in a representative sample of the U.S. population. While the magnitude of the impact of depression was similar for women and men, gender differences in the rates of depression suggest a greater overall impact of depression on smoking transitions for women. Smokers with both current and past depression may benefit from more intensive smoking cessation interventions and on-going monitoring of abstinence.
Financial Support: The National Institutes on Health (R03-DA027052 to AHW, K12-DA000167 to AHW, and P50-AA015632-109002 to SAM), Women's Health Research at Yale, and the State of Connecticut, Department of Mental Health and Addiction Services.

709

QUALITY OF LIFE OVER TIME IN THE MULTI-SITE CTN PRESCRIPTION OPIOID ADDICTION TREATMENT STUDY.

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Aims: The 10-site Prescription Opioid Addiction Treatment Study, conducted as part of the NIDA Clinical Trials Network, examined different lengths of buprenorphine-naloxone (bup-nx) treatment with different intensities of counseling for patients dependent upon prescription opioids. The aim of the current study is to examine change in quality of life in this patient population.
Methods: A 2-phase adaptive treatment research design examined outcomes 1) during a brief taper and 2) while maintained on bup-nx for 12 weeks. Successful opioid outcome was defined as abstinence in week 12 of Phase 2 (the last week of bup-nx stabilization) and ≥2 of the previous 3 weeks (weeks 9-11). Quality of life was measured with the SF-36, a 36-item self-administered questionnaire using Likert scales, at 4 times from baseline to end of follow-up.
Results: Mixed models, adjusted for counseling intensity, showed that the Physical Component Summary measure improved significantly over time. Physical quality of life was better among patients who were married, younger, employed full-time, and reported more years of education; but was not related to counseling intensity, white race, gender, prior heroin use, self-help attendance, and opioid outcome at the end of treatment or follow-up (i.e., 24 week follow-up in phase 2). Similarly, the Mental Component Summary measure improved significantly over time. Better mental quality of life was associated with higher education, being male, no self-help attendance, and good outcomes at the end of treatment and follow-up, but was not related to counseling intensity, white race, marital status, employment, age, and prior heroin use.
Conclusions: Among patients with prescription opioid dependence, both mental and physical measures for quality of life improved during treatment and remained stable at follow-up.
Financial Support: NIDA grants U10DA015831, K24DA022288, U10DA020024, K23DA022297

710

EXTRACELLULAR SIGNAL-RELATED KINASE IN THE BASOLATERAL AMYGDALA, BUT NOT THE NUCLEUS ACCUMBENS CORE, IS CRITICAL FOR THE RECONSOLIDATION OF COCAINE MEMORIES THAT UNDERLIE INSTRUMENTAL COCAINE SEEKING IN RATS.

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Aims: The ability of drug-paired contexts to elicit cocaine seeking depends on the reconsolidation of cocaine memories into long-term storage following retrieval. The basolateral amygdala (BLA) and nucleus accumbens core (NACc) mediate the reconsolidation of associations that underlie motivated behaviors, but the molecular mechanisms that contribute to this phenomenon are not well understood. Extracellular signal-related kinase (ERK) is required for the reconsolidation of memories that control cocaine-conditioned place preference. Thus, we hypothesized that ERK in the BLA and NACc would similarly be required for the reconsolidation of memories that elicit instrumental cocaine seeking.
Methods: To test this hypothesis, rats were trained to self-administer cocaine in a distinct context followed by extinction training in a different context. They were then briefly re-exposed to the cocaine-paired context to destabilize cocaine memories and trigger memory reconsolidation. Next, rats received bilateral microinfusions of VEH or the MEK inhibitor, U0126 (1.0 μg/0.5 μl/side), to prevent ERK phosphorylation, into the BLA or NACc. The effects of these manipulations on drug context-induced cocaine seeking (non-reinforced active lever presses) were assessed after additional extinction training.
Results: Re-exposure to the cocaine-paired context during the test session elicited robust cocaine seeking in previously VEH-treated rats. Post-reactivation infusions of U0126 into the BLA, but not the NACc, attenuated subsequent cocaine seeking, relative to VEH. Similar to U0126, post-reactivation neural inactivation of the NACc with baclofen + muscimol (1.0/0.01 mM/0.5 μl/side) failed to alter cocaine seeking in a follow-up experiment.
Conclusions: These findings suggest that ERK in the BLA, but not the NACc, is required for the reconsolidation of cocaine memories that control instrumental cocaine seeking.
Financial Support: NIDA R01 DA17673, NIDA R01 DA025646, NIDA T32 DA007244, and NIDA F31 DA028051.

711

ALTERED BEHAVIOR AND BRAIN ACTIVITY AS A FUNCTION OF INCREASING WORKING MEMORY LOAD IN ALCOHOL-DEPENDENT HEAVY DRINKERS.

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Aims: Heavy alcohol use is associated with many cognitive deficits, including impairments in working memory (WM). Of the 41% of heavy drinkers who have an alcohol use disorder, only 24% meet criteria for dependence (Chen et al., 2006). Identifying characteristics unique to this subset of heavy drinkers is imperative for strategies to reduce alcohol dependence. This study examined behavior and brain activity, as a function of increasing WM load, in dependent and nondependent heavy drinkers and normal controls.
Methods: Controls (Control: n=11) and heavy alcohol drinkers who met criteria (Alc-Dep; n=13) or did not meet criteria (Alc-NonDep; n=11) for dependence (based on the SCID) performed the N-Back WM task in an fMRI scanner. Behavior and brain activity was isolated during low (0- vs. 1-Back) and higher (1- vs. 2-Back) load conditions. Errors associated with low and higher loads were calculated and correlated with increases and decreases in brain activity for each condition, in each group.
Results: During low load, behavior and brain activity did not differ among the groups (mean ±S.D. accuracy: Control =.892±.07, Alc-NonDep =.925±.05, and Alc-Dep =.869±.07). During higher load, however, accuracy in the Alc-Dep (.587±.16) group was significantly lower than the Control (.763±.14) and Alc-NonDep (.767±.20) groups. During this time, the Alc-Dep group lacked functional decreases in the medial prefrontal cortex (mPFC), compared to the Control group and functional increases in the superior parietal lobe, compared to the Alc-NonDep group. Finally, commission errors were significantly correlated with increased cerebellar activity and decreased insular and hippocampal activity in Alc-Dep during the higher load condition.
Conclusions: Heavy drinkers who meet criteria for dependence perform poorly at higher WM loads, compared to controls and nondependent heavy drinkers. The lack of functional decreases and increases at high WM loads, suggest impaired functional flexibility and cognitive reserve in these individuals.
Financial Support: NIDA grants DA007246, DA020074, and DA06634

712

THE EFFECTS OF ADOLESCENT EXPOSURE TO METHYLPHENIDATE ON THE AVERSIVE PROPERTIES OF COCAINE IN ADULTHOOD.

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Aims: Methylphenidate (MPH) is the most prescribed treatment for adolescent ADHD in the US. Animals chronically exposed to MPH in adolescence acquire stable cocaine (COC) self-administration (SA) more quickly as adults than vehicle-exposed controls, yet exhibit attenuated place preferences conditioned by COC. These findings can be interpreted as MPH-induced suppression of reward, but increases in adult SA may indicate attenuation of the aversive effects of COC, which are believed to interact with reward to limit drug intake. To test this possibility, adolescent male rats were chronically exposed to MPH in two experiments and then conditioned for taste aversions to COC as adults.
Methods: Experiment 1: 84 adolescent male S-D rats were injected with a clinically relevant dose of MPH (2 mg/kg, 2x/day for 15 days) or saline vehicle (VEH) and then underwent COC-induced taste aversion conditioning with three doses [10, 18 and 32 mg/kg, compared to controls with the emetic LiCl (0.6 mEq/kg) or VEH]. Experiment 2: 48 rats were tested for taste aversions as adults to COC (18 mg/kg) and MPH (30 mg/kg) after adolescent exposure to MPH (10 mg/kg, 1x/day for 15 days). Body weight (during preexposure) and MPH-locomotor activation (in adulthood) were also assessed.
Results: Experiment 1: COC induced robust dose-dependent taste aversions, such that saccharin consumption was inversely related to dose, while VEH groups increased consumption across trials. LiCl groups suppressed intake in a manner similar to the highest dose of COC. There was no effect of MPH preexposure. Body weights did not differ among groups, although there was a trend toward enhanced locomotor activation to low and mid challenge doses of COC. Experiment 2: COC and MPH induced similar suppression of intake, as opposed to increases in VEH groups. Again, there was no effect of MPH preexposure, although MPH blunted growth and enhanced motor activation by COC.
Conclusions: Elevations in adulthood SA of COC following chronic adolescent exposure to MPH are not likely mediated by changes in COC's aversive effects.
Financial Support: Mellon Foundation to ALR, BW

713

A COMPARISON OF PHYSICAL AND MENTAL HEALTH FUNCTIONING DEFICITS IN ALCOHOL-DEPENDENT ADULTS IN EIGHT COUNTRIES.

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Aims: Compare (1) the burden of alcoholism relative to a non-diseased population; (2) the added physical and mental health burden associated with alcoholism when added to physical chronic conditions only, mental chronic conditions only, and combined with physical and mental conditions; and (3) the burden of alcoholism across countries compared to a normative sample.
Methods: Data from a population survey, the 2010 National Health and Wellness Survey (N=177,759; US, UK, Japan, China, France, Germany, Italy, and Spain), were used. For aims 1 and 2, respondents were categorized as healthy, mental condition only, physical condition only, or both mental and physical condition. Each group was further divided by self-reported lifetime alcoholism. Differences across groups were assessed using linear models with SF-12v2 Physical and Mental Component Summary measures (PCS and MCS) as outcomes, controlling for age and gender. For aim 3, a subgroup of those who self-reported alcoholism (N=4,866; 2.7%) were used to compare country differences in PCS and MCS scores using the US population as the norm.
Results: Collapsing countries and relative to healthy respondents, being an alcoholic (but otherwise healthy) was associated with a 2.1 and 3.1 mean decrement PCS and MCS respectively (p<.0001). The presence of alcoholism in conjunction with a mental condition was associated with a mean decrement in the MCS score of 3 points as compared to a mental condition alone (p<.0001). The presence of alcoholism in conjunction with a physical condition, or mental and physical conditions was statistically significant but small. There was striking variation in the relative differences between the US norm mean and country means for MCS scores of alcoholics (range -6.7 to -13.0). PCS scores showed less variation among countries (range -.03 to-5.4).
Conclusions: Alcoholism adds significant physical and mental health burden, to varying degrees, compared to non-alcoholics, and the amount of burden varies among countries.
Financial Support: Internal funding from QualityMetric Inc.

714

IN VITRO CRUSH AND EXTRACTION TESTING OF OXYMORPHONE EXTENDED-RELEASE TABLETS DESIGNED TO BE CRUSH RESISTANT.

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Aims: To evaluate the resistance of a new formulation of oxymorphone ER (Oxy-CRF) to crushing or extraction in liquid media. Opioid abusers frequently tamper with extended-release (ER) tablets via crushing or extraction to accelerate opioid release; resistance to crushing and extraction may present an obstacle to abuse.
Methods: Oxymorphone hydrochloride (HCl) 5, 7.5, 10, 15, 20, 30, and 40 mg was embedded in a matrix (INTAC™, Grünenthal GmbH, Aachen, Germany) of polyethylene oxide (Polyox WSR-303), polyethylene glycol (Macrogol 6000), hypromellose, citric acid, and α-tocopherol. Tablets were formed using a novel process consisting of hot melt extrusion and compression. The 5-mg and 40-mg tablets were investigated because they are the lowest and highest doses of this formulation.
Results: The tablets could not be pulverized using spoons, professional pill crushers, a pharmacopeial breaking force tester (forces up to 1000 N, even after freezing at −20°C), or hammers (forces of 5–10 kN). Attempts at crushing increased in vitro extraction of oxymorphone from the Oxy-CRF tablet by <10%. Attempts at extraction by intensive shaking (15 min) of Oxy-CRF tablets in simulated alcoholic beverages (5%, 12%, and 40% ethanol; 6.2%–12.3% extraction) or water or simulated soda (0.001 N HCl; 9.4%–16.7% extraction) resulted in little or no increases in extraction compared with the dissolution of intact tablets in buffer (9%–14%). Testing in 10 types of acidic, basic, and organic solvents did not increase extraction.
Conclusions: These results suggest that Oxy-CRF successfully resists crushing and extraction in liquid but still releases oxymorphone from the tablet at a rate suitable for 12-hour dosing. Mechanical barriers to tampering may present an obstacle to abuse and also protect against accidental misuse.
Financial Support: Support: Supported by Grünenthal GmbH and Endo Pharmaceuticals Inc.

715

FAILURE TO LOOK BEFORE LEAPING: THE BARRATT IMPULSIVENESS SCALE PREDICTS TREATMENT COMPLETION IN COCAINE- AND METHAMPHETAMINE-DEPENDENT PATIENTS.

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Aims: Greater impulsivity as assessed by the Barratt Impulsiveness Scale-11 (BIS-11) and the Stroop has been associated with treatment outcomes in patients with stimulant use disorders. The present study evaluated the relationships among impulsivity, baseline stimulant use status, and treatment outcomes in methamphetamine- and/or cocaine-dependent participants.
Methods: Six sites participating in a multi-site clinical trial evaluating 12-step facilitation for stimulant abusers (STAGE-12) obtained the Stroop and BIS-11 from 183 methamphetamine- and/or cocaine-dependent participants. The relationships of the BIS-11 and Stroop to baseline stimulant use and treatment outcomes through 6-month follow-up were evaluated.
Results: Methamphetamine-dependent, relative to cocaine-dependent, participants evidenced greater impulsivity as measured by BIS-11 Total score ($X2=6.6$; $p=0.01$). There was a trend for poorer response inhibition, as measured by the Stroop, in cocaine-dependent, relative to methamphetamine-dependent, participants ($X2=3.5$; $p=0.06$). When accounting for other factors related to treatment completion, the BIS-11 Motor Impulsiveness score, which assesses the tendency to act without thinking, was predictive of treatment completion status ($d=0.52$, $p=0.001$). No relationship greater than $r=0.2$ was observed between impulsivity and stimulant use during either baseline or treatment/ follow-up.
Conclusions: BIS-11 Motor Impulsiveness was a significant predictor of treatment retention. Treatment-seeking methamphetamine and cocaine-dependent patients may have different impulsivity profiles.
Financial Support: National Institute on Drug Abuse, Center for Clinical Trials Network.

716

BRIEF INTERVENTION FOR DRUG-ABUSING ADOLESCENTS: ONE YEAR OUTCOMES.

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Aims: To evaluate 1-year outcome, as well as mediators and moderators, of a brief intervention to address moderate drug abuse among adolescents.
Methods: We present the 1-year evaluation results of a randomized controlled trial to examine the efficacy of a manualized brief intervention for moderate drug abusing adolescents. Student/parents (N = 315) were randomly assigned to receive one of these three conditions: 2-session adolescent only (BI-A), 2-session adolescent and additional parent session (BI-AP), or assessment only control. Self-reported drug use behaviors and related variables were collected at intake and 6- and 12-months post-intervention.
Results: Follow-up assessments at 6- and 12-months post-intervention on showed significant improvement on drug use variables for adolescents in both the BI-A and BI-AP conditions compared to the assessment only group. Also, youth in the BI-AP group had consistently better outcomes compared to adolescents receiving BI-A. The most significant mediators of positive effects at 6-months were improved adolescent problem solving and use of community services after the intervention. At 12-months outcome, improved problem solving continued to show a mediation effect.
Conclusions: Three major significant findings were observed from the study: (1) both brief intervention conditions were associated with reduced drug use behaviors at 6- and 12-months follow-up, and these improvements exceeded the changes in the assessment-only control group; (2) the intervention group that included a parent session (BI-AP) exhibited greater and more consistent beneficial effects compared to the condition in which only the adolescent client received services (BI-A); and (3) improvements in problem solving by the adolescent mediated positive outcomes.
Financial Support: This study was supported by grants K02 DA015347 and R01 DA017492 from the National Institute on Drug Abuse, and AA14866 from the National Institute on Alcohol Abuse and Alcoholism.

717

TRANSITIONS IN SUBSTANCE USE, ABUSE, AND DEPENDENCE STATUS OVER TIME IN CONDUCT-DISORDERED ADOLESCENTS.

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Aims: Adolescents with conduct disorder and substance abuse often use multiple substances and have elevated risk for adult substance dependence, but studies rarely examine integrated, developmental shifts between stages of polysubstance use. We examined transitions in use, abuse, and dependence for multiple substances over time in high-risk youth.
Methods: Individuals with at least one DSM-IV criteria of substance abuse and conduct disorder in adolescence (N = 306, mean age=16.1, 71% male) completed follow up measures at ages 18 and 21. Latent substance status was indicated by any use, frequency of use, and number of abuse and dependence criteria for alcohol, marijuana and hard drugs. Latent transition analyses estimated latent status classes and the probabilities of status transitions over time.
Results: A three-class model was a good fit to the data (Entropy = 0.88, BIC = 14,769). The three statuses were alcohol abuse only (8% at baseline), alcohol & marijuana dependent (58%), and tri-dependent (34%). Alcohol abuse at age 18 was more likely (ps<.001) for those previously in alcohol abuse (69%) compared to alcohol & marijuana dependent (26%) or tri-dependent (23%). Alcohol & marijuana dependence at age 18 was most likely (ps<.001) after adolescent alcohol & marijuana dependence (54%), and more likely (p<.05) for adolescent tri-dependence (31%) than alcohol abuse only (15%). However, transitioning to age 21 alcohol & marijuana dependence was more likely (p<.001) for age 18 alcohol abuse (20%) compared to age 18 tri-dependence (11%). Tri-dependence in adolescence was as likely (p=.17) to shift into alcohol abuse (31%) as tri-dependence (46%) at age 18, but tri-dependence at age 18 was more likely (p<.05) to remain tri-dependence (61%) than to shift to alcohol abuse (28%) or alcohol & marijuana dependence (11%) by age 21.
Conclusions: Stage-dependent differences in transitions between substance use statuses may explain heterogeneity in adult clinical outcomes.
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718

RECRUITMENT AND RETENTION STRATEGIES FOR DRUG ADDICTION RESEARCH BASED IN MEDICAL EDS.

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Aims: Recruitment and retention are a challenging task in the most ideal of environments and difficulties in recruitment and retention can lead to a drain on resources and threaten study success. Recruiting substance users from a medical Emergency Department (ED) setting poses many unique challenges as does tracking these participants for follow-up assessment. We describe the recruitment and retention procedures used in a NIDA Clinical Trials Network protocol designed to test the impact of a brief intervention on individuals presenting in medical EDs who screen positive for problematic drug use.
Methods: Recruitment and the initial baseline assessment for this study take place at six different EDs in the United States. The population recruited in this study are high risk drug users with problems in many life domains including acute medical concerns, homelessness, legal troubles, and other problems that make tracking and retention difficult. We present recruitment and retention strategies that are helping us achieve our recruitment goals and maintain impressive follow-up rates for a difficult population from the protocol that is currently underway.
Results: We have found that two factors are key to successful recruitment in this study: 1) Appropriate selection of ED sites that promote successful recruitment by having available adequate patient volume of drug users, past research experience, and available space and staff to conduct research. 2) Thorough staff training occurring pre and post-recruitment commencement to ensure that staff are prepared and continually educated in proper recruitment techniques. We have found that numerous strategies and ongoing development of techniques are integral to retention success, which can be grouped under the following headings:1) Ongoing training and collaboration among sites. 2) Use of techniques gleaned from past research. 3) Awareness of new trends emerging in the field such as texting and social networking.
Conclusions: Successfully addressing recruitment and retention issues are core to our research success.
Financial Support: U01DA015833

719

SMOKE EXPOSURE AND CARDIOVASCULAR RISK: CAN THE RISKS OF SMOKING EVER BE MODIFIED?

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Aims: A leading cause of death from cigarette smoking is cardiovascular disease (CVD). Among the thousands of potentially harmful constituents in smoke, the toxicity of smoke particles is often overlooked. We examine smoke exposure and CVD risk in relationship to "modified risk" combusted products.
Methods: Medline was searched for references discussing smoke and smoking-related terms. References were circularly searched and primary reports of smoke exposure data and risk estimates were selected. Secondhand smoke (SHS) and smoking risk papers were limited to recent larger studies. Data were standardized into common units and analyzed to estimate exposure to respirable fine particulate matter (PM2.5), and relative risks (RR) of such exposure for CVD.
Results: PM2.5 exposure is greatest from cigarette smoking (12,000 mcg/m3), followed by open fires (2,099 mcg/m3), and SHS in a closed automobile (1,521 mcg/m3). In comparison, exposure to PM2.5 from polluted outdoor air is 87 mcg/m3. The RR for CVD is elevated in occupations involving exposure to PM2.5, such as asbestos work (RR=1.3-3.1) and chimney sweeping (RR=1.2-2.2). The RR for CVD in smokers is over 2.0, and from 1.19-1.52 for SHS. Numerous studies have reported that smoke exposure is related to elevations of inflammatory markers of increased CVD risk, such as C-reactive protein, interleukins, and fibrinogen.
Conclusions: A strong association exists between fine respirable particulates and elevated CVD risk. Smokers are exposed to very high levels of fine particulates, and exposure to PM2.5 results in elevations of biomarkers of endovascular inflammation that are related to CVD. The dose-response relationship is reported as log-linear: reductions in risk require very large reductions in exposure. While reductions in toxic constituents may well reduce the risk of cancer, small reductions in smoke content or alterations in smoke composition are unlikely to significantly reduce CVD risk. Modifying the risk of CVD from combusted products poses a significant challenge.
Financial Support: This work was funded by Rock Creek Pharmaceuticals, Inc., Gloucester, MA.

720

CHRONIC ETHANOL CONSUMPTION ALTERS CHANGES IN RESPONSE TIME DISTRIBUTION IN RHESUS MACAQUES.

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Aims: Response times, which can be altered by a variety of drugs, do not lend themselves to parametric analysis because they tend to lack normal distribution and display unequal variances. To better quantify ethanol-induced changes in response times, data from a 5-choice serial response time (5CSRT) task were fit to an ExGaussian probability distribution function (ExGau-PDF) and analyzed with separate 2-way repeated measures ANOVAs.
Methods: Adolescent male rhesus macaques were trained to respond on touch sensitive panels controlled by CANTAB ® software (Lafayette Instruments, Lafayette, IN, USA). Performance in the 5CSRT task was determined at the onset of chronic ethanol consumption (D1) and then again after 120 ethanol drinking sessions (D120). Ethanol was added to a flavorant (6% TANG ® solution or similar) to facilitate consumption.
Results: In the chronic ethanol consumption group (N=5), mean daily alcohol consumption varied between 1.25 and 1.75 g/kg across the treatment period. Monkeys in the vehicle control group (N=5) drank a solution containing only the flavorant (VEH). During test sessions, consumption was limited to either the VEH or a maximum ethanol dose of 1.5 g/kg. Alcohol-induced changes in the mu and sigma components of ExGau-PDF were dependent upon whether the monkey chronically consumed alcohol ($p < 0.05$ for both). Mu and sigma are respectively defined as the mean and standard deviation of the Gaussian component of the PDF. When tested at D120, mu values were reliably higher and sigma values were reliably lower than they were at D1 for the VEH-treated group. In contrast, these parameters were indistinguishable in the EtOH-treated group. Further, mu and sigma values reliably differed between the groups at D120, regardless of whether ethanol was consumed before the session.
Conclusions: These data suggest that chronic ethanol consumption alters the evolving response time patterns that are observed under baseline conditions, even in the absence of the drug.
Financial Support: USPHS R13-AA20766,R01-AA16807,T32-AA07456

721

POLYDRUG USE AMONG METHADONE MAINTENANCE TREATMENT PATIENTS IN SHANGHAI, CHINA: EFFECTS OF A MOTIVATIONAL INCENTIVES INTERVENTION.

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Aims: China has recently adopted Methadone Maintenance Treatment (MMT) nationally to prevent the spread of HIV among drug users. This study explores poly drug use among MMT patients and investigates the effect of a motivational incentives intervention on poly drug use.
Methods: 159 participants were recruited in 2009-2010 from 3 Shanghai MMT clinics. They were randomly assigned to usual care (n=79) or usual care with incentives (n=80) for a 12-week trial. Patients in the incentives group received accumulative prizes based on either consecutive negative urine results or consecutive attendance to treatment. Urine tests of 4 popular illicit drugs in China, opiate, methamphetamine, ecstasy, and ketamine, were conducted at baseline, 1 month, 3 month, and 6 month follow ups.
Results: Poly drug use rate was 36.3% at baseline and was reduced to 6.9% 6 months later. However, there was no significant difference between study conditions at any of the 4 test times. Attrition rate was 27.7% and poly drug use was not associated with attrition. Besides the primary use of opiate (93.7%), ketamine and methamphetamine were the most often used drugs (34% and 17%) among this sample at baseline, followed by ecstasy (3.8%). While the use of opiate (11.4% at 1month, 8% at both 3 and 6 month), methamphetamine (1.5% at 1 month, 0 at 3 month, 1.8% at 6 month), and ecstasy (0 at 1 month and 3 month, 1% at 6 month) significantly reduced, ketamine usage showed an increase over time, 40.3%, 46%, and 66% respectively. This trend was consistent across the two study conditions.
Conclusions: Although poly drug use reduced along the course of MMT for study participants, it is not associated with the motivational incentives intervention. Future endeavor is needed to study ketamine use among this population.
Financial Support: This work is funded by NIDA Grants # R21DA025385, P30DA016383, and K05DA017648 (PI: Hser).

722

NICOTINIC ACETYLCHOLINE RECEPTOR STIMULATION IS CRITICAL FOR THE ABILITY OF COCAINE-PAIRED CONTEXTUAL STIMULI TO CONTROL IMPULSIVE DECISION MAKING IN RATS.

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Aims: Chronic cocaine exposure produces an unconditioned enhancement in impulsive decision making. However, little is known about the effects of cocaine-paired conditioned stimuli on this behavior. Thus, this study explored the effects of cocaine-paired contextual stimuli on impulsive decision making and a putative neuropharmacological mechanism of this phenomenon.
Methods: Rats were trained in a standard operant conditioning chamber (neutral context) to achieve stable performance on a delay discounting task, which involved lever press-based choice between a single food pellet (small reward) available immediately and three food pellets (large reward) available after a 10, 20, 40, or 60s delay. Rats then received Pavlovian context-cocaine and context-saline pairings in two other contexts. On subsequent test days, rats' delay discounting task performance was assessed in the previously cocaine-paired or saline-paired context following pretreatment with cocaine (15 mg/kg) or saline (Experiment 1) or with the nicotinic acetylcholine receptor (nAChR)antagonist, mecamylamine (0.2, 2 mg/kg) or saline (Experiment 2). The pretreatments and testing contexts were counterbalanced across subjects using a full within-subjects design.
Results: Independent of cocaine pretreatment, rats exhibited a greater decrease in preference for the large reward as a function of delay duration when tested in the previously cocaine-paired context, relative to the saline-paired context. Systemic mecamylamine pretreatment dose-dependently increased the preference for the large reward in the previously cocaine-paired context, but not in the saline-paired context, relative to vehicle.
Conclusions: These findings indicate that cocaine-paired contextual stimuli evoke an increased state of impulsive decision making, which depends on the stimulation of nAChRs. Such drug context-induced impulsivity may increase the propensity for drug relapse in cocaine users, making the nAChRs an interesting target for relapse prevention.
Financial Support: NIDA DA017673 and DA025646

723

A PROMOTER VARIANT IN OPRK1 MODULATES STRESS-INDUCED CRAVING, BRAIN ACTIVITY AND RELAPSE IN COCAINE DEPENDENCE.

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Aims: Kappa opioid receptor regulates human emotion and stress response via the activation of hypothalamic (the hypothalamic-pituitary-adrenal: HPA axis) and limbic brain circuits. Here, we investigated the relationship between a potential functional variant in OPRK1 and individual cortisol level in response to stress, craving and the time of relapse. To understand whether or not OPRK1 modulates stress neuronal circuitry, we further studied the effect of a promoter variant on neural response to stress in cocaine dependent individuals
Methods: Seventy-nine treatment-seeking cocaine dependent subjects were recruited for the study. One promoter variant, rs6980250 C>G was genotyped. We measured subjective craving and serum cortisol level following a laboratory imagery paradigm in neutral, stress and drug cue conditions. Using functional MRI, we scanned the genotype and demographically matched subjects to measure brain function in three conditions. All subjects were followed prospectively for 90 days to assess the treatment outcome. Liner Mixed Effect (LME) models were applied for data analysis to test main effects and interactive effects among different variables.
Results: Rs6989250 modulated craving severity, cortisol levels, and neural responses to stress. Compare to G allele at rs6989250, the C allele that abolishes a transcription binding site in OPRK1 was linked to greater craving, higher cortisol level and hyperactivity of hypothalamus and midbrain regions in stress versus neutral conditions. Subjects carrying C allele relapsed more rapidly within 30 days after treatment, suggesting the importance of early intervention for these subjects.
Conclusions: The results suggest that a promoter variant in OPRK1 alters HPA activity possibly via hyperactivation of the hypothalamic and midbrain regions. It is associated with increased stress-induced craving, cortisol responses and relapse in cocaine dependent individuals in African Americans
Financial Support: R01-AA013892 (RS), R01-AG022982 (RLH), R01-MH074697 (RLH), T32-MH019961, R25-MH071584.

724

NEWLY INCIDENT TOBACCO CIGARETTE SMOKING AND TIME TO FIRST CIGARETTE AFTER WAKING.

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Aims: Time to first cigarette (TTFC) after waking is a highly regarded and readily measured manifestation of a tobacco dependence process. We aim to estimate short TTFC as it occurs very soon after onset of cigarette smoking (CS) in a community sample of newly incident smokers, all 12-21 years of age, and to study risk variation in relation to age of CS onset.
Methods: Data are from the 2004-9 United States National Surveys on Drug Use and Health, which yield a nationally representative sample of community residents aged 12-21 years (n=166,399), for whom exact age and age of first cigarette values are available. The Fagerstrom TTFC construct and related variables are assessed via computer-assisted self-interviews. The 3741 newly incident smokers in this sample are those assessed within 6 months after first cigarette. Estimated age-specific cumulative incidence proportions (CIP) are estimated and compared, with due attention to complex survey design and weights.
Results: For the very recent onset and newly incident smokers age 12-17 years, an estimated 5% already had developed a short and clinically significant TTFC within 6 months after CS onset (95% CI = 4%, 6%). The corresponding estimate for 18-21 year old newly incident smokers is just below 4% (95% CI = 3%, 5%). A trend test is consistent with the null hypothesis of no excess risk for newly incident smokers with onset age of 12-13-14 years. The peak CIP value was observed for those age 16 years at smoking onset.
Conclusions: For every 20-30 newly incident cigarette smokers in the study population, there is one who develops a short and clinically significant TTFC very soon after first cigarette (within 6 months). The predicted probability of short TTFC does not vary appreciably by age of CS onset. Our long-term goal is to identify malleable gene-environment interactions and other mechanisms for accelerated tobacco dependence processes.
Financial Support: T32DA021129 (JT); K05DA15799 (JCA). WX and JT are 1st & 3rd year predoctoral fellows in MSU's Drug Dependence Epidemiology Training Program.

725

NICOTINE-RELATED BRAIN ACTIVITY: INFLUENCES OF SMOKING HISTORY AND BLOOD NICOTINE LEVEL.

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Aims: Cigarette smoking and nicotine administration are associated with activity in many brain regions. PhMRI has been effectively used to explore BOLD neural responses to nicotine under a variety of paradigms. However, no phMRI studies were found that examined the relationships among smoking history, blood nicotine levels and nicotine related neural activity. In this exploratory analysis, we aimed to assess brain activity in response to nicotine (1.5 mg/70 kg), taking into account serum nicotine levels and smoking history.
Methods: 5 nicotine dependent men were imaged twice in a within-subject design. They received nicotine or saline, IV, on separate visits following a period of abstinence. Blood was sampled prior to and following nicotine or saline infusion. Smoking history was calculated as pack years. The subjects' individual serum nicotine measures were used to assess neural activity relating to nicotine. Peak nicotine was added into the model to explore its impact on nicotine related neural activity.
Results: Smoking history correlated positively with peak serum nicotine levels ($r=0.84$, $p<0.05$). Subjects with greater lifetime exposure to nicotine had higher peak levels of nicotine in their blood. BOLD activations to the nicotine infusion were consistent with previous reports. However, peak nicotine, assessed separately, accounted for a significant proportion of the variability in the model. Inclusion of peak nicotine levels resulted in significant negative BOLD activity, potentially indicating a relative decrease in neural activity corresponding to increased smoking history. Caution is urged when considering these results due to the low number of subjects in the study. In addition, using the fixed effects model does not allow for generalization to a broader population.
Conclusions: Even so, these results raise questions regarding studying nicotine's, or other drugs', effects on neural activity; suggesting exposure history and differences in processing the drug should be taken into account.
Financial Support: R01DA025065

726

PREGNANCY EXPOSURE TO METHADONE: A POPULATION-BASED RETROSPECTIVE STUDY ON INFANT HEALTH OUTCOME.

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Aims: In this study, we compared the occurrence of an array of health outcomes in infants born to mothers enrolled in methadone maintenance program in Taiwan.
Methods: Building upon the National Methadone Maintenance Treatment (MMT) database and the National Birth Notification Database in Taiwan, we identified 1584 women who had delivery history through the period of 2001-2009. The number of neonates born prior to and after the MMT enrollment was 1712 and 396 (294 remained in MMT and 96 were methadone-free during pregnancy), and a total of 21202 neonates born to the methadone non-exposed women with matching on delivery age and residential region.
Results: Women in MMT were more likely to give births at younger ages, at places other than medical institution, and by caesarean section. Compared with neonates born to the women in general population, neonates born to women who had ever enrolled in the MMT generally had higher risk of adverse health outcomes, including stillbirth, low Apgar score at 1 minute, and low birth weight (Odds Ratio [OR]=4~5). Further analyses indicated that low birth weight was especially higher among those deliveries by women remaining in the MMT throughout pregnancy (OR=4.8), followed by those methadone-free after the MMT enrollment (OR=4.3), and those delivered prior to the MMT enrollment (OR=3.8). Having delivery at the places other than clinics and hospitals and caesarean section were also associated with neonatal unfavorable health outcomes.
Conclusions: Special attention is needed to neonates born to women treated by methadone. Improving overall prenatal healthcare may help reduce unfavorable health outcome in the offspring of drug-using women.
Financial Support: Funding for this study was provided by grant NHRI PH-100-PP-45 to Dr. Chuan-Yu Chen from the National Health Research Institutes.

727

CHARACTERIZING A PROFILE OF ACUTE COCAINE EXPOSURE IN THE LABORATORY USING REMOTE PHYSIOLOGICAL MONITORING.

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Aims: A critical limitation of current cocaine treatments is the inability to objectively monitor cocaine use in real-time. The purpose of the current, ongoing study is to utilize BioHarness to identify a physiological profile consistent with recent cocaine exposure under controlled, laboratory conditions.
Methods: Participants include non-treatment-seeking, cocaine-dependent volunteers enrolled in an inpatient, clinical trial examining the effects of Rivastigmine and Huperizine A on the positive subjective and reinforcing effects produced by cocaine. In addition to standard hospital equipment, physiological measures are being assessed with BioHarness (hear rate, respiration, activity, etc.). As part of the main protocol, participants are administered cocaine (0 and 40 mg, IV) on study days 1 and 9. Currently, 13 participants have completed the study and we predict a final N=37 by June, 2012. To date, participants are predominately male (85%), African-American (62%), primarily crack-cocaine users (92%), and cigarette smokers (92%).
Results: Repeated-measures ANOVA for heart rate revealed a significant effect of DRUG ($F1,24=28.6$, $p<.0001$), TIME ($F27,648=4.6$, $p<.0001$), and DRUG X TIME interaction ($F27,648=4.5$, $p<.0001$). For respiration, only a significant effect of DRUG was observed ($F1,24=28.6$, $p=.02$). No significant effects were observed for activity. Simple linear regression revealed a strong, positive correlation between heart rate obtained using BioHarness as compared to standard hospital equipment ($r2=.88$, $p<.001$).
Conclusions: These data suggest that BioHarness can accurately detect physiological changes consistent with recent cocaine exposure. In the final analysis, the effects produced by the study medications on responses to acute cocaine administration will be discussed. The implications of this research are that this device, or others like it, can be used in the future to monitor illicit drug use in in drug treatment programs or research protocols.
Financial Support: This study is sponsored by NIH via support to RDLG (DA023624, DA023624-03S1).

728

"BABY SCHEMA" RESPONSE AS A PROBE OF CAREGIVING DEFICITS IN DRUG-USING MOTHERS.

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Aims: Addicted mothers show significant deficits in caring for their children, yet the neural mechanisms involved have remained largely unexplored. Our studies in healthy women indicate that a set of infantile features, termed "baby schema" by Konrad Lorenz (1943), acts as a natural reinforcer and elicits caregiving motivation through activation of brain reward circuits (Glocker et al., 2009, PNAS; Glocker et al., 2009, Ethology). In this ongoing study, we hypothesize that behavioral and brain reward responses to baby schema are impaired in drug-using mothers (DM) as compared to mothers without a history of drug use (control mothers; CM).
Methods: Responses to infant faces parametrically manipulated for baby schema content (i.e., low, unmanipulated and high) were collected on two behavioral measures (i.e., cuteness perception and caretaking motivation) in DM (current N=18) and CM (current N=33).
Results: We found a robust effect of baby schema on cuteness perception ($p<0.001$) and caretaking motivation ($p<0.01$), with high baby schema infants rated as cuter and eliciting higher levels of caretaking motivation than low baby schema infants, consistent with our previous findings. We also found an interaction of baby schema and group on cuteness perception ($p<0.01$), driven by DM providing lower scores in response to low and unmanipulated, but not high, baby schema infants. Finally, there was a group effect on caretaking motivation ($p<0.03$) with DM scoring lower on this measure than CM.
Conclusions: These preliminary findings suggest that the baby schema response may serve as a valuable probe of reduced sensitivity to infant cuteness and motivation for caretaking in DM—behavioral alterations that could underlie caregiving deficits in this population. This work forms a foundation for our ongoing fMRI study examining group differences in the brain response to baby schema and the link between this response and caretaking motivation.
Financial Support: Supported by NIH/NIDA T32 DA028874 and CURE Addiction Center.

729

PARTNERSHIPS THAT IMPROVE OUTCOMES FOR FAMILIES AFFECTED BY SUBSTANCE USE DISORDERS.

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Aims: 1) To inform participants of the collaborative program strategies Regional Partnership Grantees are implementing to improve outcomes for families in the child welfare system affected by substance use disorders
2) To present performance indicator data on over 19,000 children and 13,000 adults participating in services
3) To inform participants of the lessons learned in implementing a large-scale program
Methods: The Child and Family Services Improvement Act of 2006 enacted the broadest Federal program ever launched to assist States, Tribes and communities to improve the well-being, permanency and safety outcomes of children who are in out-of-home placement, or are at risk of placement as a result of a parent's or caregiver's methamphetamine or other substance abuse by creating the Regional Partnership Grant (PRG) program. A web-based RPG Data Collection and Reporting System was developed to compile case-level child/youth, adult and family functioning performance indicator data across 53 grantees.
Results: The programs have greatly advanced cross-systems collaboration and are closing the gaps in their local systems of care with 70 percent of grantees reporting ten or more local partners in their service array. Children in the RPG program are less likely than comparison children to experience repeat child maltreatment. RPG children at risk of removal from the home are significantly more likely to remain in their parent's custody, while children placed in protective custody are reunified more quickly and less likely to re-enter foster care after being reunified. RPG adults are accessing substance abuse treatment more quickly, staying in treatment longer and showing greater reductions in substance use than comparison adults.
Conclusions: Deepening the knowledge base about child, adult and family services and outcomes will help address the sustainability challenge and promote the dissemination of best practices that can inform other related Federal program opportunities and policy changes.
Financial Support: Financial support for this project is provided by the Substance Abuse and Mental Health Services Administration and the Administration on Children, Youth and Families.

730

DEVELOPING A COMPETENCY MAPPING METHODOLOGY USING MULTIDIMENSIONAL SCALING (MDS) FOR ITS APPLICATION IN SUBSTANCE ABUSE RESEARCH.

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Aims: This demonstrates a novel and innovative methodology using multidimensional scaling (MDS). This method can be applied in developing competencies for global substance abuse research to inform curriculum planning.
Methods: In July 2009, 22 Mailman faculty members were invited to participate. Participants were asked to suggest around 10 competencies that reflect global health knowledge and substance abuse expertise of Mailman public health graduates. Statements were mounted on cards and sorted into thematic groupings by 10 recent master's level graduates and doctoral students. Analysis utilized MDS software and consisted of graphical plots of aggregate statement groupings.
Results: The following four clusters resulted from the analysis: global professional skills, engaging global contexts, global approaches and global environmental awareness. Graphical plots were stratified by the number of student raters, departmental appointment of faculty members and primary geographical region of faculty's research focus. Faculty members in environmental health were more likely to propose competencies in the global environmental awareness cluster than faculty in other departments.
Conclusions: This innovative method can be applied to the substance abuse field to identify common ground where various decision makers (e.g. policy makers, researchers, clinicians) use consensus judgment as a means to identify commonalities and priorities.
Financial Support: The author was supported as a predoctoral fellow in the Behavioral Sciences Training in Drug Abuse Research program sponsored by Public Health Solutions and National Development and Research Institutes with funding from the National Institute on Drug Abuse (5T32 DA007233). Points of view, opinions, and conclusions in this paper do not necessarily represent the official position of the U.S. Government, Public Health Solutions or National Development and Research Institutes.

731

LEGAL AND ILLEGAL SUBSTANCE CONSUMPTION AMONG AUSTRIAN STUDENTS.

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Aims: Consumption of legal and illegal substances among students constitutes a sociopolitical, controversially discussed issue. The aim of this study was to explore the prevalences of legal and illegal substance use among students in Vienna with a focus on sex differences.
Methods: 1036 students from the Medical University of Vienna and the University of Vienna (different faculties; mean age 21.03), 386 (37.3%) male and 650 (62.7%) female, were asked to complete questionnaires regarding their substance consumption.
Results: Alcohol was the most commonly consumed substance among all students, 88.6% reported drinking alcohol at least monthly. Concerning the weekly and daily consumption, men showed a more frequent use than women ($p < .001$); 28.2% of the students showed relevant problems with alcohol drinking. Regarding nicotine consumption, 40.2% of the students reported smoking in the past six months; 19% were daily smokers, with insignificant sex differences. At least monthly use of pain medications was reported by 37.6% (47.5% women and 20.8% men; $p < .001$). Sleeping medications and tranquilizers were used by 7.5% with a significant higher use in females (8.6%) than in males (5.8%; $p = .020$). Regarding the last half-year 22.6% indicated the consumption of at least one illegal substance, with a significantly higher prevalence in men than women ($p = .001$). The most commonly consumed illicit substance was cannabis (21.1%), followed by mushrooms/biogenic drugs (2.3%), cocaine (1.5%) and ecstasy (1.3%).
Conclusions: The considerable amount of substance use deserves special awareness. Prevention and intervention strategies should be implemented at universities with a special attention to gender aspects and the students' disciplines.
Financial Support: No financial support.

732

QUANTITATIVE ANALYSES OF TIME AND DOSE RELATIONSHIPS FOR FLUMAZENIL TO ANTAGONIZE MIDAZOLAM IN RHESUS MONKEYS.

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Aims: Drugs are studied across a range of conditions on the assumption that their interaction is not qualitatively impacted by changes in dose or time after administration, yet seldom is this hypothesis tested directly. This study examined how changing the dose of the benzodiazepine antagonist flumazenil as well as the time between administration of flumazenil and the benzodiazepine midazolam altered the nature of their interaction.
Methods: Four monkeys discriminated 0.178 mg/kg of midazolam while responding under fixed-ratio 10 schedule of stimulus-shock termination; Schild plots were constructed for flumazenil at several time points by constraining the slope to unity.
Results: When given 15 min before midazolam, 0.1 mg/kg of flumazenil shifted the midazolam dose-effect curve 8-fold rightward. There was a time-related decrease in the magnitude of shift of the midazolam dose-effect curve as the interval between administration of flumazenil and midazolam increased; flumazenil did not significantly shift the midazolam dose-effect curve when given 120 min earlier. The potency of flumazenil, estimated by apparent pA2 values (95% CI), was 7.33 (7.08, 7.59), 7.13 (6.70, 7.56), 6.99 (6.39, 7.59), 6.64 (6.27, 7.01) at 15, 30, 60 and 120 min after flumazenil administration, respectively. Increasing the dose of flumazenil to 0.32 mg/kg shifted the midazolam dose-effect curve further to the right, as compared with the shift produced by 0.1 mg/kg given at the same time before midazolam; when added to Schild plots, these results did not differ from those predicted by lines defined by the point obtained with 0.1 mg/kg of flumazenil and a slope equal to unity.
Conclusions: Thus, increasing the interval between administration of flumazenil and midazolam causes orderly decreases in potency; however, across a range of doses and pretreatment times, the qualitative nature of the interaction does not change.
Financial Support: Supported by USPHS grants R01DA09157 and K05DA017918 (CPF)

733

DOES PROVISION OF ADDITIONAL NICOTINE REPLACEMENT THERAPY FOLLOWING SMOKING CESSATION IMPROVE LONGTERM ABSTINENCE?

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Aims: Even though pharmacotherapies for smoking cessation are effective in initiating abstinence, maintaining abstinence can be a challenge with most clinical trials showing high rates of relapse at 6-months post-treatment. The aim of this study was to examine whether additional nicotine replacement therapy (NRT), in smokers who achieved short-term abstinence using NRT, would improve abstinence rates at 6-months.
Methods: Participants (n=3,366)in a smoking cessation program consisting of 5-weeks of NRT (patch, inhaler, gum or lozenge) and self-help materials provided free of charge were contacted at end-of-treatment. Those reporting being abstinent (n=670) were assigned to either be offered additional NRT (gum and lozenge) to be used prn for relapse prevention (n=212), or not (n=458).
Results: At 6-month follow-up, those who were not offered or rejected additional NRT (noNRT group) (n=321) had a self-reported abstinence rate of 63.6% (7 day point prevalent abstinence, 56.2%). Those who accepted the additional NRT (NRT group) (n=115) had a self-reported abstinence rate of 61.6% (7 day point prevalent abstinence, 49.2%) (OR 1.3; 95%CI, 0.87-2.01). This lack of a significant between group difference may be explained by significantly higher ratings of confidence (p=0.013) and importance (p=0.005) for remaining abstinent in the noNRT group compared to the NRT group.
Conclusions: Providing additional nicotine gum or lozenge in order to prevent relapse in smokers who have quit using NRT was not effective. However, high self-ratings of confidence and importance for remaining abstinent was associated with longer-term abstinence. Therefore, enhancing self-efficacy should be a focus of cessation treatment in order to increase long-term abstinence.
Financial Support: This study was supported by the Ontario Ministry of Health Promotion and Sport.

734

CORRELATES OF HCV INFECTION AMONG MMT PATIENTS IN SHANGHAI, CHINA.

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Aims: To identify correlates of and potential risk factors for Hepatitis C (HCV) infection among opioid dependent patients at a methadone maintenance treatment (MMT) clinic in Shanghai, China.
Methods: We collected and analyzed self-report data on behavioral risks for HCV transmission, including lifetime histories of illicit drug use, injection drug use (IDU), equipment sharing, involuntary drug rehabilitation (compulsory treatment lasting 3-6 months or drug rehabilitation through labor camp (DRTLC) lasting > 1 year), as well as demographic information and HCV test results from a sample of 120 patients active in MMT in November 2008.
Results: 75% of the study participants were male, with the mean (SD) age of 40 (9); 92% were unemployed; 42% were married. They reported 12 (4) years of heroin use history, 83% reported lifetime IDU, and 13.3% reported lifetime needle sharing. The average duration of their current MMT was 374 days. 76/120 (63.3%) in the study sample were HCV positive. We found that HCV seropositive status was significantly associated with a history of IDU ($p<0.01$), duration (years) of drug use ($p<0.01$), the lifetime DRTLC history and the number of times in DRTLC ($p<0.01$ for both). Lifetime history of needle sharing was also significantly associated with a history of any involuntary drug treatment, including both the short term compulsory treatment and DRTLC ($p<0.05$).
Conclusions: The significant association between DRTLC participation, lifetime needle sharing, and HCV raises troubling questions about the potential adverse impact of DRTLC. Further studies with larger samples and more detailed information regarding the onset of IDU or needle sharing and timing of involuntary treatments would be needed to investigate whether this reflects causality or more results from greater likelihood of DRTLC or compulsory treatment for individuals with more severe drug use or HCV risk factors.
Financial Support: Shanghai Health Fund for Young Physicians (2007Y15), NIDA INVEST Fellowship and IAS-NIDA Fellowship

735

DEVELOPMENT OF TETRAHYDROISOQUINOLINE-BASED OREXIN-1 RECEPTOR ANTAGONISTS.

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Aims: Emerging evidence indicates that the orexin system, OX1 receptor in particular, plays an important role in drug reward and reinstatement of drug seeking, and antagonism of the OX1 receptor may be of value for the treatment of drug addiction. Ligand studies suggest that tetrahydroisoquinoline, a common structural moiety present in the potent dual OX1/OX2 receptor antagonist ACT-078573 and the OX2 selective antagonist TCS- OX2-29, is important for activity at these receptors. This study further explores the structural requirements of the tetrahydroisoquinoline containing ligands, with the aim to develop potent and selective OX1 antagonists.
Methods: Target compounds were fully characterized and evaluated in a calcium-dependent functional assay using a FlexStation II384 and the calcium-4 dye kit in RD-HGA16 (Molecular Devices) cell lines stably expressing either the OX1 or OX2 receptor.
Results: A series of analogs with modifications at various positions have been synthesized and evaluated and a number of them showed low nanomolar potency at the OX1 receptor. Structural features identified that are important for OX1 activity include high sensitivity of certain positions to steric and electronic modifications. For instance, while the 1-benzyl group was favorable, groups such as substituted phenyl, alkyl or phenylalkyl at the 1-position all resulted in significantly decreased potency at the OX1 receptor.
Conclusions: We have developed a series of compounds, several of which showed excellent potency at the OX1 receptor and identified the structural requirements at several positions. These results will facilitate the development of potent and selective antagonists for the OX1 receptors.
Financial Support: Grant DA026582 and Research Triangle Institute

736

CHRONIC NICOTINE EXPOSURE AFFECTS THE SURVIVAL AND REPRODUCTIVE CAPACITY OF ADULT ZEBRAFISH.

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Aims: Although recent evidence indicates that zebrafish are a powerful model for studying various aspects of complex behavior, studies on nicotine effects in the species are limited. Furthermore, almost all reported studies concentrated on the acute effects. The aim of this study was to determine how chronic nicotine exposure affects the survival and reproductive capacity of zebrafish.
Methods: Various nicotine concentrations — 0 μM, 1 μM, 2.5 μM, 5 μM, 10 μM, 15 μM, 20 μM, 25 μM, and 30 μM — were examined. Each experimental group consisted of 7 fish, which were examined individually. The survival rate of each group was determined by counting the number that survived 3 months of nicotine treatment. The reproductive capacity of each group was determined by counting the number of eggs laid by each fish weekly.
Results: After 3 months, the number of zebrafish in the 15 μM and 20 μM nicotine-treated groups had dropped to 5 from 7, and all animals receiving 25 μM and 30 μM had died. There were no deaths in other groups. The reproductive capacity of the nicotine-treated fish decreased as the nicotine concentration increased.
Conclusions: Chronic nicotine exposure at a concentration of 15 μM or higher has toxic effects on both survival and reproductive capacity of zebrafish. The appropriate nicotine concentration for acute treatment should be 10 μM or less.
Financial Support: This study was in part supported by the Basic Research Funds from both Zhejiang University and The First Affiliated Hospital.

737

RISK FACTORS FOR HCV SEROCONVERSION IN MMT PROGRAMS IN WUHAN, CHINA.

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Aims: Methadone maintenance treatment (MMT) programs in China are expanding and offer important treatment services to an increasing number of opiate dependent individuals. However, behavioral risks associated with infectious diseases transmission continue to be prevalent among MMT patients in China after they initiate drug treatment.
Methods: To identify the risk factors for HepC (HCV) seroconversion after admission to MMT, we collected repeated serological tests for HCV and self-report data on risk behaviors at treatment entry and at six-month intervals on 3,465 patients enrolled in MMT clinics in Wuhan, China between 2006 and 2010 who were seronegative for HCV antibodies at MMT entry.
Results: 73% of the participants were male; their mean age was 42.6 years; 18 patients were HIV positive; and 52 patients had a positive syphilis VDRL test. We recorded 449 HCV seroconversions in this cohort, corresponding to an incidence rate of 11.47 per 100 person-years. The average time to HCV seroconvension was 16.11 months. Injection drug use in the past 30 days (OR=17.96; 95%CI=11.39-28.37), frequency of current contacts with other drug users in the past 30 days (OR=4.0; 95%CI=3.39-4.72), and having good relationships with the family (OR=0.17; 95%CI=0.12-0.22) were found to be significant predictors of HCV seroconversion.
Conclusions: We found a high rate of HCV seroconversion among MMT patients in Wuhan, China. This finding suggests that MMT patients continue to engage in behaviors that increase their exposure and vulnerability to infectious diseases. Prevention efforts should attempt to add specific interventions to MMT programs to reduce risk behaviors and to reduce seroconversions for these high-risk groups.
Financial Support: Supported by NIDA DA026797 & CMHC/DMHAS/State of Connecticut

738

INVOLVEMENT OF DYNORPHIN AND KAPPA OPIOID RECEPTOR (KOP-R) IN STRESS-PRECIPITATED HEROIN SEEKING IN RATS.

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Aims: Although KOP-r antagonists reduce stress-induced reinstatement of cocaine, alcohol and nicotine seeking behavior, the role of KOP-r in mediating stress-induced reinstatement of heroin-seeking has not been investigated. Previous studies showed that stress responsive prodynorphin (pDYN) gene is activated during opiate withdrawal. These studies were undertaken to determine: 1) whether yohimbine stress (Yoh, inducing heroin craving in humans) alters heroin seeking and HPA hormones in rats withdrawn from heroin self-administration (SA); 2) if pretreatment with selective KOP-r antagonist norBNI prevents heroin seeking and HPA responses; 3) in which mesolimbic brain regions, pDYN or KOP-r mRNA level was altered by Yoh in heroin SA rats.
Methods: Heroin SA for 12 days (3h/d, 0.05mg/kg/inf) in Sprague-Dawley rats was followed by 8-day extinctions. Yoh (1.25mg/kg) induced lever press was tested in Reinstatement (REIN) Test 1 on 9th day withdrawal. Pretreatment with norBNI (20mg/kg) was given 1 day before 2nd Yoh and REIN Test 2 on 11th day withdrawal. After Test 2, rat brains and plasma were collected. pDyn and KOP-r mRNA levels were quantitatively measured in nucleus accumbens (NAc) shell and core, caudate-putamen, CeA and Me/BLA. HPA hormones were measured in plasma.
Results: Yoh stress reinstated lever press associated with heroin, and norBNI pretreatment reduced the stress-induced reinstatement. Yoh elevated HPA hormones in heroin SA rats and the effect was blunted by norBNI. Neither pDYN mRNA nor HPA hormonal level was altered after heroin withdrawal without stress. However, Yoh increased pDYN mRNA level in NAc shell of rats withdrawn from heroin SA with no change in NAc core. No change of KOP-r mRNA levels in these two regions.
Conclusions: These data suggest that pDYN/KOP-r system (including the NAc shell) is a critical component of neural circuitry underlying the effect of negative emotional states on drug seeking and HPA activation by stress.
Financial Support: NIDA Center Grant DA-P60-05130 (MJK) and NSERC (FL). NIH-NIDA Division of Drug Supply and Analytical Services

739

COMBINED BEHAVIORAL TREATMENT (WHEEL RUNNING) AND MEDICATION (PROGESTERONE) DECREASE STRESS- AND CUE-INDUCED COCAINE SEEKING IN FEMALE RATS.

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Aims: Individually, both treatment with progesterone (PROG) and concurrent access to an exercise wheel have been shown to reduce cocaine self-administration under long-access conditions and to suppress cocaine-primed reinstatement in female rats. Treatment with the PROG metabolite allopregnanolone also decreased reinstatement to cocaine seeking by the pharmacological stressor yohimbine (YOH). In the present study, the combined effect of wheel running and PROG on YOH-induced cocaine seeking was assessed.
Methods: Twenty adult female rats were allowed to acquire wheel running and establish a baseline over 3 days. Rats then were catheterized and allowed to self-administer cocaine (0.4 mg/kg, iv) during 6-hr sessions for 10 days without access to the running wheel. Subsequently, auditory and visual stimuli that signaled drug delivery were unplugged, and rats were allowed to extinguish lever pressing for 14 additional sessions. During this period, rats were divided into 2 groups and given access to either a locked or unlocked running wheel. Next, both groups were tested in a within-subjects design for reinstatement of cocaine seeking precipitated by YOH (2.5 mg/kg, ip) alone or YOH + cocaine-paired stimuli in the presence of concurrent wheel access, PROG (0.5 mg/kg, sc), or both.
Results: In agreement with prior work, preliminary results indicate that concurrent unlocked wheel access decreased responding during extinction of cocaine seeking. Further, in both groups, concurrent wheel running and PROG, separately and combined, decreased YOH-primed and YOH+cue-primed reinstatement of cocaine-seeking behavior. However, the combination of wheel access and PROG may have been most effective.
Conclusions: Combined, concurrent wheel running and PROG seem to be the most effective at reducing stress-induced cocaine seeking. Thus, combined behavioral (i.e., exercise) and pharmacological (i.e., PROG) interventions are highly successful, possibly more so than either intervention alone.
Financial Support: Research supported by R01 DA003240 and K05 DA015267 (MEC).

740

TEMPERAMENT, CHILDHOOD TRAUMA, GENDER, AND ALCOHOL CONSEQUENCES: A STUDY OF PERSON/ENVIRONMENT INTERACTIONS ACROSS THE TRANSITION TO COLLEGE.

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Aims: There is a robust relationship between temperament and problem alcohol use. Few studies, however, have examined whether environmental factors interact with temperament to predict problem alcohol use. Such moderation studies are critically important in that they (1) highlight the degree to which environmental risk factors for alcohol misuse can be exacerbated or mitigated by personality traits and (2) help to identify high-risk groups that might be most in need of prevention and intervention efforts. The present study sought to address this issue by examining the extent to which temperament (disinhibition and neuroticism) interacted with early childhood trauma to predict alcohol consequences across the transition to college. Additional exploratory analyses were conducted to determine whether these interactions differed by gender and/or types of trauma.
Methods: Participants were 623 incoming freshmen at a large, urban university (43% male, 46% Caucasian). Participants were surveyed at their new student orientation and were re-contacted during the fall of their freshman year and invited to complete an online follow-up survey.
Results: Results indicated that childhood trauma predicted time 2 alcohol consequences above and beyond the effects of temperament, gender, and baseline alcohol consequences. Additionally, there was a three-way interaction between conscientiousness, trauma and gender such that, for males, the relationship between trauma and time 2 alcohol consequences was stronger for those low versus high in conscientiousness. The type of trauma most predictive of alcohol consequences was sexual abuse, and this was particularly true for males.
Conclusions: The present study reveals an interaction between childhood trauma and disinhibition, in the prediction of problem alcohol use and suggests that personality and trauma exposure may be used as early indicators of high-risk drinking behaviors, even among healthy college students with low rates of alcohol use.
Financial Support: This study was supported by a grant from the Alcohol Beverage Medical Research Foundation to Emily R. Grekin, Ph.D.

741

GENDER DIFFERENCES IN FAMILY FACTORS ASSOCIATED WITH BINGE DRINKING.

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Aims: Verify gender differences in family factors associated with binge drinking by adolescents.
Methods: The sample was made of high school students from all Brazilian capitals (N=17261). We used weighted multinomial logistic regression to analyze factors associated with binge drinking. Drinking patterns were assessed by a questionnaire based on a instrument suggested by WHO and parenting styles by the Scale of Parenting Styles. Variables related to family structure and parents' drinking patterns perceived by adolescents were investigated.
Results: The sample was composed by 9551 boys and 7710. Compared to non-drinkers, older adolescents were more likely to have engaged in binge drinking (boys (B) RRR:1.55[1.41–1.71]; girls (G) RRR:1,16[1,05 – 1,27]). Studying at private school increased the likelihood of binge drinking (B RRR:1,46[1,17–1.82]; G RRR:1.41[1.16–1.72]). Not being punished if found drunk increased the likelihood, for both girls and boys (B RRR: 2.08[1.55–2.81]; G RRR:3.08[1.89–5.00]). Boys and girls were less likely to have strict parents (B RRR:0.9[0.86–0.94]; G RRR:0.85[0.81–0.88]). Living only with the mother increased the rink of binge for girls (RRR: 1.29[1.05–1.60]). Mother drinking (B RRR:1.7[1.34–2.15], G RRR:2.4[1.89–3.04]) and father drinking (B RRR:1.79[1.47–2.03]; G RRR:1.65[1.30–2.10]) increased the likelihood for both genders, but boys were more likely to perceive mothers' drunkenness (RRR:1.73[1.08 – 2.76]) while girls were more likely to perceive the fathers' (RRR: 1.4[1.08–1.82]).
Conclusions: The results showed some gender differences in the factors associated to binge drinking, concerning family structure and role model of drinking by both parents.
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742

SUBSTANCE ABUSE TREATMENT COMPLETION AMONG HOMELESS ADULTS IN MARYLAND: WHO BENEFITS FROM MEDICAID?

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Aims: Failure to complete substance abuse treatment is a common phenomenon in homeless individuals and one factor often associated with treatment completion is insurance coverage. Given that a significant portion of currently uninsured homeless adults will be newly eligible for Medicaid in 2014 as part of the Affordable Care Act, there is a strong need to determine how the policy change may impact treatment success in this group. Therefore, the present study sought to demonstrate the impact of Medicaid coverage on treatment completion among homeless substance abusers and to determine what factors modify this relationship.
Methods: Data from this study came from the Treatment Episode Data Set (TEDS) 2008 discharge data. Bivariate and multivariate logistic regressions were used to assess the relationship between Medicaid coverage (yes or no) and treatment completion (yes or no), and interaction terms were created with Medicaid and a number of socio-demographic variables.
Results: Those with Medicaid were 1.76 times more likely to complete treatment than were those without insurance. Significant interactions with Medicaid coverage were observed for gender and treatment modality. Stratified analyses revealed that among males, Medicaid was associated with a 2.17 increased odds of completion, but no significant relationship was observed between Medicaid coverage and treatment completion among females. Similarly, for those in inpatient treatment, Medicaid was associated with a 1.78 increased odds of completion, while no significant relationship was observed for those in outpatient treatment.
Conclusions: The present study suggests that while Medicaid coverage is a significant predictor of substance abuse treatment completion, only some subsets of homeless adults benefit from this coverage. Our findings shed light on groups that may be most impacted by the expansion of Medicaid, as well as groups that may be in need of other types of interventions.
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