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FREE VS PAID SERVICES: A COMPARATIVE ANALYSIS IN A HARM-REDUCTION-ORIENTED OUTPATIENT METHADONE MAINTENANCE CENTER.

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Aims: Since the opening of our center in June 2007 we where supposed to offer 60 free services for IDU's that where HIV positive, for pregnant women and mothers with children under 2 year old, or disabled and homeless patients. Another 150 places are offered for ~160 $ a month. Already after the first 6 month we have seen how disrupting and problem generating for the therapeutic alliance is the tax collection, but now we have done an objective analyze between the two groups.
Methods: We compare different aspects as retention, frequency of positive urine tests and attrition between our patients who benefit of free treatment and the ones that are paying for services we present the preliminary results from the first 150 enrolled patients; the full 658 sample will be presented at the meeting.
Results: We had 78% male patients, 59% where roma (gypsies), 2% where foreign citizens, the median heroine use was 9, 6 years, 2 of them where heavy opiate smokers. The majority of them where multiple drug users (57% alcohol, 34% hypnotics and sedatives, 29% marijuana and 98% smokers). The two groups where comparable with the exception of the women proportion which was greater in the free treatment group.
Conclusions: As expected the retention was better in the free treatment group, but not impressive. The attrition was greater in the paid services group and the positive urine test where not significantly different between the groups.
Financial Support: This work did not receive any financial support.

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MALE-FEMALE DIFFERENCES IN THE ESTIMATED INFLUENCE OF CAREGIVER, SIBLING, AND PEER SMOKING ON THE FIRST CHANCE TO TRY TOBACCO DURING THE PRE-ADOLESCENT YEARS.

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Aims: To examine male-female differences in the first chance to try tobacco during the pre-adolescent years and to estimate the relative effects of exposure to caregiver smoking (CS), smoking by at least one sibling (SS), and smoking by peers (PS) on initial tobacco opportunity.
Methods: Data were collected in the context of the longitudinal Miami Prenatal Cocaine Study (MPCS). 390 African American pre-adolescents (196 females and 194 males), enrolled in the MPCS at birth, were assessed at a 12-year follow-up study visit. A modified Communities That Care Youth Survey was administered to assess age at first chance to try tobacco, SS and PS. Caregiver smoking status was obtained via the Addiction Severity Index. Crosstabulation analyses followed by regression modeling were used to estimate the relative effects of CS, SS, and PS, and to contrast the estimates for girls and boys, separately.
Results: Estimates indicated stronger CS, SS, and PS effects on the girls' first chance to try tobacco (all $p<0.05$), and weaker (and statistically null) relationships for boys (all $p>0.05$). Regression modeling confirmed these results and indicated that these exposure effects were statistically independent from one another for the girls (all $p<0.05$) in a model with chance to try tobacco by age 12 regressed upon covariate terms for CS, SS, and PS. Relationships did not vary across subgroups defined by prenatal cocaine exposure.
Conclusions: These data suggest exposure to social role models for smoking may have more influence on the earliest stages of tobacco involvement for girls during the pre-adolescent years, and may be less important for boys.
Financial Support: K01 DA 016720; P50 DA 024584; R01 DA 006556

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DEVELOPMENT OF A WEB-BASED PSYCHOSOCIAL INTERVENTION FOR ADOLESCENTS WITH SUBSTANCE USE DISORDERS.

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Aims: Adolescent substance use disorders (SUD) are a significant public health issue. While some interventions have been shown to be effective, significant barriers prevent their delivery in community systems. We describe our iterative development and evaluation of a unique web-based intervention for adolescents with SUDs, the first program of its kind.
Methods: The intervention consists of 12 sessions for youth (4 for caregivers) and is based on the Adolescent Community Reinforcement Approach, an effective and cost-effective intervention. It is provided via an interactive delivery system that employs informational technologies effective in promoting relevant knowledge and skills. With input from expert consultants, we developed text, video, audio and animation content for the program. We then conducted focus groups with adolescents in treatment for SUDs (n=17) and caregivers of these adolescents (n=3). Once the beta-version of the program is completed, we will conduct a series of sessions in which adolescents (n=30) and their caregivers (n=10) will be asked to provide feedback regarding the program's acceptability, ease of use, likeability, helpfulness, relevance to the experience of adolescents with SUDs, ability to promote learning and anticipated effect on behavior.
Results: Focus groups revealed that the proposed approach would be widely acceptable. Themes included the need for authenticity of the narrator and videos, relevance of the content, ability to track goals, and desire for ongoing support. Data from the feedback sessions will be analyzed prior to the presentation.
Conclusions: This presentation of our methodology for systematically developing technology-based interventions may inform others in the development of novel tools that are science-based, cost-effective, acceptable, and delivered in a way that ensures intervention fidelity and allows for widespread dissemination.
Financial Support: NIDA/NIH R01DA025072-01

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EFFECTS OF ACUTE ALCOHOL CONSUMPTION ON RESPONSE INHIBITION: EVIDENCE OF A TASK-DEPENDENT EFFECT.

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Aims: Neuropsychological tasks that probe response inhibition have been used interchangeably, despite fMRI evidence that neural basis of behavioral control is task dependent. The aim of the present study was therefore to investigate (1) the effects of alcohol on response inhibition (2) the similarity of any effects of across three measures of response inhibition.
Methods: Healthy, social alcohol users (n=72) were examined in a double-blind placebo-controlled design. Participants received either an acute dose of alcohol at 0.40 g/kg or 0.60 g/kg or placebo (0.00 g/kg) in a between-subjects design. Response inhibition was measured using Go/No-Go, Stop-Signal and Color Stroop tasks. Analyses were performed for omission error, commission error and correct response reaction time data.
Results: Color Stroop data indicated a significant difference in number of colour naming errors between challenge condition groups ($F [2, 66] = 4.57$, $p = 0.014$), such that following an acute moderate dose of alcohol (0.40 g/kg) participants made more errors relative to placebo and a high dose of alcohol (0.60 g/kg). Go/No-Go data indicated a significant difference in number of commission errors between challenge condition groups $F [2, 67] = 3.45$, $p = 0.034$). Post-hoc comparisons indicated that following a moderate acute dose of alcohol (0.40 g/kg) participants made more errors of commission, relative to participants receiving placebo. Stop-Signal data indicated a significant difference in omission error rate between challenge conditions, such that following an acute moderate dose of alcohol (0.40 g/kg) participants made more errors relative to placebo ($p = 0.048$).
Conclusions: Data indicate that the nature of alcohol impaired behavioral control in social drinkers may operate in mechanisms associated with both cognitive and behavioral disinhibtion and response activation. Additionally, our data suggest alcohol's disinhibitng effects are restricted to acute moderate alcohol consumption in contrast to previous evidence of dose-dependent effects.
Financial Support: University of Bristol Scholarship

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EMERGENCE OF CLINICAL FEATURES OF DEPENDENCE SOON AFTER ONSET OF EXTRA-MEDICAL USE OF OPIOID-ANALGESIC COMPOUNDS.

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Aims: In prior research on extra-medical users of opioid analgesics (EMUAs), we found that 3-4% developed an opioid dependence syndrome within 24 months after onset of use, with females at excess risk. In this project, we estimate risk of individual clinical features of opioid dependence soon after extra-medical use of opioid analgesics (EMUA) onset, also with a focus on male-female variation in risk.
Methods: Data are from 222,221 participants in the National Surveys on Drug Use and Health (NSDUH), 2004-2007, with confidential computer-based self-interviewing to assess drug involvement, including recent onset EMUA and seven clinical features of DSM-IV-TR dependence. A generalized estimating equations (GEE) approach is used to estimate variation in risk of experiencing each feature.
Results: There were 6,365 recent onset EMUAs, and about 20% had experienced at least one of the clinical features. Tolerance and salience had been experienced by 10% or more; the other clinical features were seen less often (<4%). For 6 of the 7 clinical features, female EMUAs were at excess risk ($p<0.05$). Inability to cut down use was the clinical feature with no male-female variation in risk.
Conclusions: Once extra-medical use of opioid analgesics has occurred, an estimated 1 in 30 develop a dependence syndrome soon after onset, and one in five of these users experience at least one clinical feature associated with dependence, of which tolerance and salience are most likely. The male-female variation in risk offers an intriguing lead for future studies.
Financial Support: NIDA award K05DA015799 & T32DA021129

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INCREASED STRIATAL ACTIVATION IN COMPULSIVE INDOOR TANNERS UPON EXPOSURE TO ULTRAVIOLET LIGHT COMPARED TO SHAM LIGHT.

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Aims: Many tanners exhibit behaviors consistent with an addictive disorder. The neural response mechanisms underlying compulsive tanning remains unexplored. This study was designed to explore changes in neural functioning induced by ultraviolet (UV) vs. sham (UV filtered) radiation in subjects who met criteria consistent with an addictive tanning disorder.
Methods: Seven [4 women; 29.3±7.3 years old (mean±SD)] frequent indoor tanners were studied. All subjects met our modified criteria for a "tanning addiction," consistent with DSM-IV criteria for substance dependence. On two separate days, subjects were exposed in a pseudo-randomized, single-blind design to a UV-light emitting and sham tanning bed while undergoing brain single photon emission tomography (SPECT). The radioligand was administered immediately upon subject placement in the tanning bed.
Results: SPECT imaging revealed increased ($p<0.01$) regional cerebral blood flow in the caudate and putamen during UV radiation exposure compared to the sham light. During UV exposure, subjects exposed to UV light reported a decreased desire to tan ($p<0.002$) whereas subjects exposed to sham light maintained a high desire to tan. Of the six subjects expressing a preference for a tanning bed, five chose the active condition.
Conclusions: These findings demonstrate that UV radiation exhibits centrally rewarding properties in frequent tanners.
Financial Support: This study was funded, in part, by the James N. Gilliam, MD, Chair in Dermatology Endowment.

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CANNABIS INVOLVEMENT AND THE COURSE AND MEASUREMENT OF BIPOLAR DISORDER.

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Aims: Rates of cannabis use and cannabis use disorders are considerably elevated in those with Bipolar disorder (BD). We use the NIMH Bipolar Disorder Genetics Sample to examine the association between BD and aspects of cannabis involvement. Using psychometric methods, we also examine whether cannabis involvement is related to differential functioning of DSM-IV criteria for mania and depression.
Methods: Logistic regression was used to examine the association BD and aspects of cannabis involvement. Item response modeling, using multiple groups, was used to determine whether individual criteria had varying difficulty and/or discrimination in those who never used cannabis, cannabis users without symptoms and those with cannabis abuse/dependence.
Results: Compared with the control population, individuals with BD were 6.8 times more likely to report a lifetime history of cannabis use. Rates of DSM-IV cannabis use disorders in those with BD was 29.4%, considerably higher than population estimates. Individuals meeting criteria for DSM-IV cannabis use disorders were significantly more likely to report increased suicide attempts, experience mixed episodes and disability attributable to BD. All associations were independent of presence or absence of psychotic features. Thresholds for certain criteria used to assess manic episodes varied considerably across levels of cannabis involvement.
Conclusions: The comorbidity between cannabis involvement and BD indexes increased illness severity and is not attributable to presence of psychotic features.
Financial Support: DA23668 (to A.A.) and DA18660 and DA18267 (to M.T.L.).Funding support for the Whole Genome Association Study of Bipolar Disorder was provided by the National Institute of Mental Health and genotyping of samples was provided through the Genetic Association Information Network (GAIN). The datasets used in this study were obtained from the database of Genotype and Phenotype (dbGAP) found at http://www.ncbi.nlm.nih.gov/gap through dbGAP accession number phs000017.v3.p1.

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EFFECTS OF ALCOHOL ON SEROTONIN RECEPTORS AND HISTONE DEACETYLASE 2.

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Aims: Previous Studies have demonstrated that alcohol abuse is a complex addiction regulated by multiple mechanisms such as neurotransmitter, hormones, and intracellular networks. Serotonin may contribute to alcohol effects, and serotonin receptors including 5-HT3 appear to play an important role in alcohol abuse. Recent studies have also implicated regulation of gene expression by histone deacetylases (HDACs) in drug addiction. Furthermore, HDAC inhibitors have been known to modulate other genes involved in drug addiction such as the mu-opioid receptor gene. Therefore, we hypothesized that HDACs may play an important role in alcohol dependence and modulation of 5-HT3 receptor expression. The main aim is to study the effects of alcohol on serotonin receptor, 5-HT3, and histone deacetylase, HDAC2.
Methods: To test the effects of alcohol on 5-HT3 and HDAC 2, the human neuroblastoma cell line, SK-N-MC, was treated with different concentrations of EtOH, and the gene and protein expression of 5-HT3 and HDAC2 were assessed at different time points. Furthermore, cells were also treated with the HDAC 2 receptor inhibitor, Trichostatin A (TSA), and the effects on gene expression were evaluated by quantitative PCR and protein expression by western blot and flow cytometry.
Results: Our results show a dose dependent increase in 5-HT3 and Histone Deacetylase 2 gene expression after acute ethanol treatment at 48 hrs. Studies blocking the HDAC 2 receptor with the inhibitor Trichostatin A (TSA) show modulation of ethanol effects on 5-HT3 gene expression and downregulation of HDAC2 expression.
Conclusions: These results suggest that alcohol affects 5-HT3 receptors through mechanisms involving histone deacetylases and used of HDAC inhibitors may be of therapeutic significance for the treatment of alcohol dependence.
Financial Support: This work was supported in part by National Institute on drug Abuse grants R37DA025576, R01DA01DA2366, and R01DA021537.

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TECHNOLOGICALLY-ENHANCED INTERVENTION TO REDUCE NIDU IN HIV PRIMARY CARE PATIENTS.

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Aims: Non-injecting drug use (NIDU) is increasingly associated with HIV transmission and HAART non-adherence, so interventions to reduce NIDU in HIV-infected individuals are an important priority. HIV primary care clinics should be good settings for NIDU-reduction interventions if they are brief and acceptable to patients, while demanding little in time and resources from busy staff. We conducted a feasibility and preliminary efficacy study of such an intervention.
Methods: Patients with ≥4 days of NIDU (cocaine/crack, heroin, methamphetamine) in the prior 30 days were recruited from a large urban HIV primary care clinic. Two counselors were trained in MI. Patients were randomly assigned to two conditions, both including brief (30 min) Motivational Interviewing (MI) at baseline. (1) Baseline MI-only. (2) Baseline MI+daily patient calls (2-3 min) to an interactive voice response (IVR) system to report past-24 hour drug use, HAART, and other variables. IVR calls provided regular, externally-structured self-monitoring. Patients calling the IVR returned to their MI counselor at 30 and 60 days for brief (10-min) graphed feedback on their drug use produced from the IVR database. Patients were compensated for evaluation but not for IVR calls. Drug use over the prior 30 days was assessed with the Timeline Follow-Back at baseline, 30 and 60 days.
Results: Of all patients approached, only one refused participation; of the 33 eligible and randomized, retention to 60 days was 78.8%. At 60 days, effect size (ES) results factored MI+IVR over MI-only for number of days used primary drug in prior 30 days (ES=0.62), amount ($) of primary drug used on days used (ES=0.52) and days missed HAART meds (ES=0.79). Qualitative patient feedback suggested that IVR calls and the feedback graphs were helpful.
Conclusions: MI+IVR to reduce NIDU (1) is acceptable to HIV primary care patients, (2) feasible in a large HIV primary care clinic, and (3) shows preliminary evidence of efficacy, warranting further study.
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HOW RESILIENCE AND ITS FACTORS CONTRIBUTE TO DRUG USE IN ADOLESCENTS.

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Aims: Assess how resilience and its factors contribute to drug use in adolescents. We hypothesized resilience and its factors decrease the odds of drug use.
Methods: Private school students from São Paulo (Brazil) were selected by a representative, stratified and cluster sample. It was applied a self-report questionnaire measuring alcohol, binge drinking, tobacco, marijuana, cocaine and inhalants 30-day use and the Resilience Scale, which in Brazilian validation, is composed by three factors: "impetuosity", "capacity to act based on ones values" and "persistence and self-sufficiency". Weighted data were analyzed by descriptive, bivariate (GLM) and logistic regression statistics. Significance level was set at 5%.
Results: The sample was comprised of 2691 students, between 14 and 20 years. 52% were female and 95% were from upper economic classes. Prevalence of 30-day alcohol use was 50%, binge drinking 35%, tobacco 14%, marijuana 6%, cocaine 1% and inhalants 4%. There was no relation between resilience score and drug use, however resilience factors were associated with them. The higher the factor "impetuosity" the higher the odds of alcohol(OR=1.151), tobacco(OR=1.044), marijuana(OR=1.086) and cocaine(OR=1.164). It was the inverse for "capacity to act based on ones values", which the higher the score the lower the odds of binge drinking(OR=0.998), marijuana(OR=0.940), cocaine(OR=0.930) and inhalants(OR=0.972). Although increases in "capacity to act based on ones values" score increases odds of alcohol use (OR=1.027), this effect was buffered when the factor "impetuosity" increased together (OR=0.998). The factor "persistence and self-sufficiency" also decreased the odds of tobacco use(OR=0.929).
Conclusions: Resilience as a whole was not associated with drug use, since the factor "impetuosity" increased the odds of drug use. However, it was suggested that "capacity to act based on ones values" and "persistence and self-sufficiency" could be focus for preventive programs since they decreased the odds of substance use in adolescents.
Financial Support: This research was supported by FAPESP and AFIP

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BRAIN METABOLISM IN LEWIS AND FISCHER 344 RATS AFTER MORPHINE SELF-ADMINISTRATION AND EXTINCTION: A PET IMAGING STUDY.

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Aims: The use of inbred strains of rodents to identify inherited traits that might predict susceptibility to reinforcing properties of abused drugs may be a valuable model. In this work we have examined the brain metabolic response in Lewis (LEW) and Fischer 344 (F344) inbred rats after morphine self-administration and extinction as measured by Positron Emission Tomography (PET).
Methods: Male LEW and F344 rats (N=6-8 in each group) self-administered morphine (1 mg/kg) or saline (0.9 % NaCl) in daily 12-h sessions for 15 days, and they subsequently were submitted to an extinction period (saline substitution) for another 15 days. After finishing the last session of these periods, changes in the 18F-Fluorodeoxyglucose brain metabolism were imaged in a dedicated small-animal PET scanner and analyzed with the SPM5 software.
Results: Control (saline self-administered) LEW animals exhibited higher metabolism than F344 rats in many cortical regions including the motor, somatosensory, insular, piriform, parietal, auditory, entorhinal and visual cortices. LEW morphine self-administered animals also showed a higher metabolism in somatosensory, parietal and auditory regions compared to F344 rats. After the extinction, some of these between strains metabolic differences in morphine self-administered animals were still maintained.
Conclusions: These results suggest that there is an inherent different brain metabolism in many cortical regions of LEW and F344 rats which even is partially maintained after morphine self-administration and extinction in some cortical areas.
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IDENTIFYING IMPULSIVE ACTION IN RATS USING THE ONE-CHOICE SERIAL REACTION TIME TASK.

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Aims: The 5-choice CSRT is an operant task which measures behavioral inhibition in rats, a component of impulsivity, by assessing premature responding before presentation of the stimulus light during the inter-trial interval (ITI). A simplified version (1-CSRT) in which only the center light is utilized places less demand on attentional processes. We tested the hypothesis that an impulsive endophenotype can be identified with the 1-CSRT task.
Methods: Male rats (n=32) were maintained at ~85% free-feeding weight during training. Following a 1 hr habituation, training stages (30 min) involved incremental lowering of stimulus duration, while holding the ITI and limited hold to 5 sec (100 trials). Any correct response (R) resulted in presentation of the reinforcer while incorrect Rs, premature Rs and/or omitted Rs resulted in a 5 sec time out and illumination of the house light. Progression through 8 total trainings occurred after ≥50 correct trials, >80% accuracy and <20% omissions at each stage.
Results: Rats reached criteria in 17.5 ± 0.7 days. Once stable on the final training stage(3-5 days, <20% variability), the upper quartile (32.6 ± 1.1 premature Rs) and lower quartile (17.2 ± 0.6 premature Rs) was identified as low impulsive (LI) and high impulsive (HI), respectively. The # correct Rs was significantly lower in the HI (58.4 ± 1.3) vs. LI rats (72.7 ± 1.6; $p<0.01$, Student's t-test). No differences in % accuracy, # incorrect Rs, perseverative Rs or omissions were observed between HI and LI rats.
Conclusions: We successfully identified an impulsive action phenotype in rats with the 1-CSRT for the first time. Rats require less training than in the more demanding 5-CSRT task. This assay will be useful in investigations and the identification of an endophenotype that has been linked to all stages of the addiction cycle.
Financial Support: Jeane B. Kempner Scholarship, UTMB Center for Addiction Research, NIDA R01 DA06511, P20 DA024157, K02 DA000403

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REDUCED-NICOTINE CONTENT CIGARETTES: KNOWLEDGE, ATTITUDES AND PRACTICE IN DRUG-DEPENDENT PREGNANT AND POST-PARTUM SMOKERS.

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Aims: To determine the knowledge, attitudes, and practice of reduced-nicotine content (RNC) cigarettes in drug-dependent pregnant and post-partum smokers.
Methods: Participants were N=26 drug-dependent, cigarette-smoking patients at the Center for Addiction and Pregnancy (CAP). Participants completed an anonymous survey regarding RNC cigarettes. Study was approved by the local Institutional Review Board.
Results: 43% of CAP patients completed the survey. The majority of participants reported currently being pregnant (85%) and methadone-maintained (92%). Mean (SD) admission duration (days)=73 (75). Mean (SD) reported cigarettes per day=12 (8), and 42% of participants reported current or past use of at least one anti-smoking medication, most commonly the nicotine patch (35%), followed by nicotine gum (19%), and bupropion (15%). A majority (88%) reported current interest in quitting smoking. Patients demonstrated a general lack of knowledge about RNC cigarettes, but most (69%) were interested in learning more about them. Although few patients (4%) reported previous use of RNC cigarettes, 60% reported interest in trying them, and 68% believed RNC cigarettes were at least as safe if not safer than regular cigarettes.
Conclusions: Given the high prevalence of cigarette smoking in drug-dependent pregnant women, there is a need to develop novel treatment strategies in this population. Because nicotine is a known teratogen and because psychological factors play a greater role in continued cigarette use in women than men, RNC cigarettes may have a role to play in helping pregnant smokers quit. These findings suggest that the majority of cigarette-smoking drug-dependent perinatal patients view the use of RNC cigarettes as an appealing approach to aid cessation. In light of these findings and the Food and Drug Administration's new authority to regulate tobacco products, further studies of RNC cigarettes in this population are needed.
Financial Support: none

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MOTIVATIONS NOT TO DRINK ALCOHOL IN ADOLESCENCE.

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Aims: A substantial body of research has examined the role of drinking motives in adolescent and adult alcohol decision-making (Cooper et al, 2004). Cox and Klinger's (1988) motivational model posited an interaction of drinking and non-drinking motives as influences on alcohol-related decision-making. While a developing body of work has examined motives not to drink, there has been little consensus on how the operationalize this construct (Epler, Sher & Piasecki, 2009). The purpose of this investigation was to examine the psychometric properties of a short-form of the MAAQ (Stritzke & Butt, 2001), a measure of motives not to drink developed in an Australian sample of adolescents, and to examine how motives not to drink and drinking motives predict alcohol consumption in adolescence.
Methods: High school students (N=1,088) completed measures of non-drinking motives, drinking motives and alcohol use and problems in a school-based, online survey. Structural equation modeling, particularly MIMIC modeling, was used to examine the measurement of these constructs and their interrelations.
Results: The MAAQ-Short demonstrated high levels of reliability in this sample (α = .86). Girls, non-white students and underclassmen had greater non-drinking motives than boys, Caucasians and upperclassmen. The MAAQ-Short predicted less alcohol consumption among youth as well fewer alcohol-related problems (CFI= 0.92; RMSEA=.072 [CI: .069- .074]). As predicted, motives to drink and not to drink had an inverse relationship. When considered within the context of drinking motives, non-drinking motives accounted for unique variance in the prediction of drinking and drinking-related problems.
Conclusions: Data supports the use of the short-from of the MAAQ in this age group as well as the unique explanatory power of this construct in predicting adolescent alcohol consumption. This work furthers the development of measures of motives not to drink as well as the utility of this construct in developing models of youth alcohol-related decision-making. Discussion of the potential utility of expanding this construct to drug use decision-making will be included.
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ESTIMATION OF A HUMAN SATIETY THRESHOLD FOR COCAINE SELF-ADMINISTRATION.

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Aims: Preclinical work in rodents by Tsibulsky and Norman(1999) have suggested a model of self-regulated cocaine intake. Central to this model is the concept of a "satiety threshold," a bodily amount of cocaine above which the probability of self-administration is low. Given assumptions of first-order cocaine kinetics, they describe an equation relating inter-infusion intervals (T) for self-administered unit cocaine doses (DU), drug half-life ($t_{1/2}$), and the total amount of cocaine at the satiety threshold (DST), as follows: $T=\ln(1+DU/DST)\bullet t_{1/2}/\ln 2$. The current study aimed to estimate a human DST based on a retrospective analysis of human self-administration data.
Methods: 31 non-treatment seeking, cocaine dependent subjects participated in three self-regulated, 2-hour cocaine self-administration sessions under a fixed-ratio 1: 5-min timeout schedule. For each unit cocaine dose (8, 16, and 32 mg/70kg), mean ± SD (i.e., group), inter-infusion interval data were obtained. By fixing the values of $t_{1/2}$ for cocaine between 45 and 60 minutes, non-linear fits enabled estimates of a human satiety threshold.
Results: Mean ± SD inter-infusion intervals of 13 ± 8, 16 ± 10, and 19 ± 14 minutes were obtained for the 8, 16, and 32mg/70kg unit doses, yielding an estimated human DST ranging from 69.5 to 97.3 mg/70 kg.
Conclusions: To our knowledge, these data are the first to describe an amount of cocaine in humans at which satiety is predicted. In analogy to prior rodent studies (Norman and Tsibulsky, 2006) experimental work (now underway) is needed to verify the validity of these estimates.
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COST SAVINGS UNDER PROPOSITION 36 - WHAT GROUPS SAVE THE MOST MONEY?

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Aims: The passage of California's Proposition 36 in 2000 mandated the treatment, rather than incarceration, of drug users. A major impetus for the passage of this law was the assertion that treatment will save tax-payer money by reducing re-offending and the associated costs. Earlier work from our group revealed that indeed, those arrested for prop-36 eligible offenses realized average savings of approximately $2800 per person. Nevertheless, no analysis has specifically examined the relative cost-savings for specific groups under prop 36. The current examination will present cost-analysis and savings reports for racial, as well as gender, groups.
Methods: A comparison group of individuals arrested before the passage of proposition 36 (1997-1998) was compared to those arrested in the first year after the law's passage (2000-2001). Data related to incarceration (jail and prison), arrest, conviction, supervision (probation and arrest), tax revenue, health-care, and treatment costs in the 30 months pre- and post-conviction were compared for gender and racial/ethnic differences.
Results: Our analysis indicates that savings were realized for all groups affected by the passage of prop 36. Nevertheless, significant differences were discovered in savings based on group membership. For example savings for men (μ = $2828) were found to be far greater than savings for women (μ = $474), although some categories produced greater savings for women (e.g., jail costs).
Conclusions: Our results indicate that participation in prop 36 saved money regardless of group membership. Still, the finding that average per person savings varied greatly between groups is important, especially given the current California budget crisis. Groups for which greater savings were realized should be specifically attended to under the current economic conditions in order to refrain from worsening the state's budget by introducing unnecessary additional burden.
Financial Support: This work was supported by funding from California's ADP contract 07-00152 and Dr. Douglas Anglin's private research fund.

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STIMULANT-SEEKING BEHAVIOR IN ADOLESCENT VS. ADULT RATS.

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Aims: Adolescence is a period of increased vulnerability to the initiation and subsequent abuse of drugs. Adolescents may be especially vulnerable to factors that precipitate relapse such as the drug itself, drug-related cues, and stress. Impulsivity, an important factor in drug abuse vulnerability, is also greater during adolescence, and this may further increase drug abuse vulnerability.
Methods: The purpose of this research was to compare adolescent and adult rats on several measures of cocaine-seeking behavior using a Go/No-go procedure (a measure of impaired inhibition), an escalation procedure, and a multi-component reinstatement procedure consisting of drug-, cue-, and stress-induced priming conditions. Adolescents and adult rats were also tested on a delay discounting task that measures impulsive choice, a strong predictor of drug abuse vulnerability.
Results: Results indicated that cocaine-seeking behavior was greater in adolescent vs. adult rats under the Go/No-go procedure. Adolescents also responded more following cocaine and yohimbine (stress-inducing) injections under the reinstatement procedure, while adults (vs. adolescents) showed greater reinstatement responding following presentations of drug-associated cues. Impulsivity under the delay discounting task was also higher in adolescents compared to adults.
Conclusions: These results demonstrate that adolescent (vs. adult) rats exhibit greater vulnerability across several measures of drug-seeking behavior, and they are more likely to engage in impulsive choice, a major liability factor in drug abuse.
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INTEGRATING HIV MEDICAL AND BEHAVIORAL HEALTH CARE IN AN URBAN SETTING.

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Aims: People with chronic diseases, such as HIV, face fragmented care with conflicting demands. Integrating and co-locating medical and behavioral (i.e., mental health and substance abuse) health care is one promising approach to deliver quality care.
Methods: A large urban HIV medical clinic serving over 1700 individuals expanded mental health services to include behavioral health therapists, case/care managers, a psychiatric nurse practitioner (from 50%-80%), a supervising psychiatrist and a pain/addiction medicine specialist. Initial and ongoing staff training on integrated care helped the transition from traditional mental health / substance abuse treatment approaches to a team approach. Communication, both verbal as part of the team and written, between behavioral health staff and medical staff occurs routinely and is monitored via an electronic medical record. Behavioral health contact with patients is presented as a routine component of patient care.
Results: To date 165 patients have formally received substance abuse treatment and completed an assessment interview. Six months later, the patients improved in 13 of 15 areas assessed. Review of services confirmed engagement in behavioral health treatment. CD4 counts increased in 65% of the patients with labs within two months of both the baseline and follow-up assessments.
Conclusions: Integration of medical and behavioral health care for urban people with HIV and substance abuse is both possible and needed as evidenced by the improvements in multiple areas of their lives. Changing the treatment paradigm, however, requires ongoing training, supervision, and emphasis on communication including interdisciplinary meetings.
Financial Support: CSAT grant 79TI 018711 and CMHS grant SM-57651, and Joseph Young, Sr. Funds (State of Michigan)

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DRUGGED DRIVING: PREVALENCE AND TRENDS IN A COLLEGE STUDENT SAMPLE.

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Aims: Drunk driving has long been a major public health concern, but the problem of drugged driving—perhaps just as dangerous—has received much less attention. This study uses data from a longitudinal study of college students to (1) estimate annual prevalence of drugged driving and riding with a drugged driver, (2) evaluate age-related trends and race and sex differences in these two behaviors, and (3) examine the degree of overlap between drugged driving and drunk driving.
Methods: Students (n=1253) were interviewed about past-year frequency of drugged driving, riding with a drugged driver, drunk driving, and whether they had access to drive a car. Annual response rates were excellent (86 to 91%). Repeated measures analyses using generalized estimating equations (GEE) evaluated age-, race-, and sex-related trends (ages 19 to 22).
Results: At age 19, one in five ($20\%_{wt}$) students with access to drive a car had driven under the influence of a drug other than alcohol at least once in the past year. Drugged driving was significantly more prevalent for males and whites (p<.05), with respective prevalence estimates ranging from $9\%_{wt}$ for non-white females to $30\%_{wt}$ for white males. Drugged driving remained stable over time through age 22. At age 19, an estimated $28\%_{wt}$ rode with a drugged driver; and significant race-sex differences were observed ($17\%_{wt}$ for non-white females; $42\%_{wt}$ for white males; p<.05). Unlike drugged driving, significant age-related decreases were observed for riding with a drugged driver. In any given year, about half of drugged drivers were also drunk drivers (range 47% to 60% annually).
Conclusions: The present findings suggest that drugged driving may be just as prevalent as drunk driving in college students. Moreover, conventional estimates of drunk driving prevalence may greatly underestimate the true extent of substance-impaired driving in college students.
Financial Support: R01-DA14845, A. Arria, PI

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ARE THE EFFECTS OF ALCOHOL ON CUE-INDUCED CRAVING MEDIATED BY ATTENTIONAL BIAS?

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Aims: Previous studies have found an association between the attentional bias for drug-related cues and subjective craving. The following study examined 1) effects of alcohol on attentional bias, 2) effects of alcohol on cue-induced craving, and 3) whether cue-induced craving is mediated by attentional bias.
Methods: Participants (n = 72) were randomly allocated to receive 0.000g/kg, 0.014g/kg or 0.400g/kg of alcohol in a between-subjects design. After drink consumption, participants completed a pictorial visual-probe and a modified alcohol Stroop task (counterbalanced), followed by a cue-exposure procedure. Self-reported craving was measured at baseline, pre-exposure and post-exposure.
Results: Data were analyzed within a 2 x 3 mixed model ANOVA with word type / validity (alcohol, neutral) as a within-subjects factor, and challenge condition as a between-subjects factor. For the visual-probe task, there was no significant main effect of validity (p = .27), and no challenge condition x validity interaction (p = .40). For the Stroop task, a significant main effect of word type (F [1, 67] = 13.43, p = .001), indicated slower reaction times for alcohol-related words, but this did not interact with challenge condition (p = .51). A significant main effect of time (F [1, 67] = 51.49, p = .001) was observed, indicating an increase in craving from post-challenge to post-cue-exposure, but this did not interact with challenge condition (p = .19). Pearson correlation coefficients were calculated between bias scores on the two cognitive bias measures and craving change from pre-exposure to post-exposure. All correlations were non-significant (rs -0.10 – +0.11, ps >.37).
Conclusions: Results indicate the cognitive constructs measured by the visual-probe (selective attention) and the modified Stroop (selective processing) tasks are not influenced by an acute dose of alcohol. No significant correlations between attentional bias scores and change in craving following cue exposure were observed. This suggests the cognitive constructs underlying attentional bias and craving may only overlap partially, or be separate, and appear not to be influenced by acute alcohol consumption.
Financial Support: BBSRC

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WHERE THE RUBBER MEETS THE ROAD: AN INTEGRATED MODEL OF TECHNOLOGY TRANSFER IN THE INNOVATION PROCESS.

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Aims: Over a decade ago the Institute of Medicine (IOM) issued a seminal report focusing on substance abuse treatment that specifically acknowledged dissemination of research findings into practice as an area in critical need of improvement and of great importance to the quality of treatment. A key recommendation was increased collaboration between federal agencies, educational and research institutions, and community-based treatment facilities to reduce barriers to the integration of research, treatment, and policy. While impressive Federal initiatives followed, the field continues to lack integrated theories and models of technology transfer to inform and standardize how innovations (research findings, evidence-based practices) are communicated and transferred to the field.
Methods: Through a process of reviewing literature, theory, and 15 years of the ATTC Network's experience, the ATTC Network Technology Transfer Workgroup developed a conceptual model representing the role of technology transfer within the innovation process.
Results: We will present the model along with definitions for seven key terms: development, dissemination, implementation, translation, adoption, technology transfer, and diffusion.
Conclusions: The lack of a conceptual model and an integrated taxonomy related to the innovation process has created confusion and limited the ability of researchers and the public to understand basic principles of technology transfer useful in facilitating the movement of research findings to practice. For example, a pitfall of implementing new treatments is attempting to use a new practice following a brief training. Then when the treatment does not work as expected, it is discarded. The ATTC Network conceptual model and definitions can be used by the addiction treatment and recovery services field to more easily understand the process of innovation, and how technology transfer can speed the use of evidence-based treatments to enhance and improve client outcomes.
Financial Support: This work was supported by SAMHSA/CSAT grants to the ATTC National Office and Regional Centers.

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A 2-YEAR FOLLOW-UP STUDY TO ASSESS EXPERIMENTAL THERAPEUTIC COMMUNITIES IN FRANCE. AN ONGOING STUDY.

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Aims: While Therapeutic Communities (TCs) are generally considered to be an effective method, the bulk of the research evidence is from poorly controlled studies. On French authorities' initiative, experimental TCs have been allowed to open since 2007. This was associated to a research program.
The objective of this presentation were (1) to present objective and methods of this research program and (2) to present comparison of TC residents with outpatient setting subjects. Chi2 or Fisher tests were used to compare qualitative data and Student or ANOVA for quantitative tests.
Methods: Residents are assessed at entry and at 6-, 12-, 18- and 24-month after intake regardless of compliance in TCs. Several questionnaires are used to collect data (ASI, MINI, CAI, CMRS, CAS, SAS) and combined qualitative interviews of both residents and staff following sociological methods.
Results: 1 : Objective of the research program: (1) To describe the construct of TCs, (2) To define the clients' expectations for TCs vs other treatment for addiction, (3) To assess the impact at 2-year after entry into TCs, (4) To determine the associated factor with effectiveness, (5) To compare the evolution of clients entering TCs versus clients in outpatient program for addiction at 2-year after entry into treatment.
2 : 67 residents were assessed. In comparison with clients in outpatient settings, they were older and had received more previous treatments for medical, psychiatric and addiction-related disorders. They reported to use the same type of drugs but started their use younger and were more often polydrug users. They showed higher level of impairment and presented more prevalent psychiatric comorbidities.
Conclusions: By combining a quantitative method and a qualitative method using sociological interviews we expect to better address the issue of TC effectiveness in the French context.
Financial Support: French Monitoring Center (OFDT) and French Health Ministry.

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ASSOCIATION STUDY BETWEEN THE *OPRM1* POLYMORPHISM 17C>T AND HEROIN OR COCAINE ADDICTION IN AFRICAN AMERICANS.

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Aims: The nonsynonymous SNP 17C>T (Ala6Val), located at the N-terminus of the mu-opioid receptor gene (*OPRM1*) in close proximity to the 118A>G, occurs in relatively high frequency in African populations and very low frequency in Asian and European populations. Several groups reported higher frequency of the variant "T" allele in populations with substance dependence but the reports have not been consistent.
This study aims to explore association between 17C>T and heroin or cocaine addiction in African Americans.
Methods: A total of 614 African American subjects (58% males) were analyzed including: a) former severe heroin addicts treated at methadone maintenance treatment programs (n=220), b) cocaine dependent subjects who met DSM-IV criteria for cocaine dependence (n=224), and c) control subjects with no history of alcohol abuse or illicit drug use (n=170). All subjects were recruited in NYC and Las Vegas. The 17C>T SNP was genotyped using TaqMan® technology and verified by sequencing.
Results: Observed genotype distributions were consistent with Hardy-Weinberg equilibrium (p=0.39). The minor allele frequency (the "T" allele) was 0.22, 0.25, and 0.26 (heroin, cocaine, and controls, respectively). No significant difference in allele or genotype frequency was found between heroin or cocaine addicts and controls (p>0.14). No significant difference was found when the analyses were stratified by sex (p>0.2).
Conclusions: The 17C>T SNP is not associated with heroin or cocaine addiction in African Americans.
Financial Support: This study was supported by NIDA-P60-05130 (M.J.K.)

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PROGESTERONE MODULATION OF THE DISCRIMINATIVE STIMULUS EFFECTS OF TRIAZOLAM.

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Aims: Sedative drugs effects among women may be enhanced during the luteal phase of the menstrual cycle and with progesterone pre-treatment, although some inconsistencies have been reported. This study builds on previous research by examining whether sensitivity to the discriminative stimulus effects of triazolam are modulated by progesterone pre-treatment.
Methods: This study examined the discriminative stimulus effects of triazolam, alone and in combination with progesterone, in healthy, premenopausal women (n=9). After triazolam discrimination was established (training dose: .25 mg/70 kg triazolam), test doses (0, .06, .12, and .25) of triazolam were administered alone and in combination with oral progesterone (100 mg). Participants completed cardiovascular measures, verbal reports of drug effect, and computer tasks designed to assess psychomotor and impulsive behavior. Drug effects were analyzed using repeated measures ANOVA with triazolam dose, progesterone dose and time as factors.
Results: Triazolam functioned as a discriminative stimulus in healthy women and engendered prototypical sedative-like effects on subjective measures of drug effect. Progesterone alone substituted for triazolam in a small number of participants (n=2) and produced sedative-like behavioral effects, while no substitution occurred in the other participants (n=7). On average, progesterone pre-treatment had no effect on the discriminative stimulus of triazolam, although progesterone both increased (leftward shift of the dose response curve) and decreased (rightward shift) triazolam sensitivity across participants and dose conditions.
Conclusions: Inconsistencies in the literature relating menstrual cycle and progesterone modulation of sedative drug effects may reflect these individual differences and future research is required to identify factors associated with these individual differences.
Financial Support: DA-024127, RR-15592.

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PREDICTORS OF PRESCRIPTION OPIOID NON-MEDICAL USE, ABUSE AND DEPENDENCE: FINDINGS FROM THE NATIONAL SURVEY ON DRUG USE AND HEALTH.

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Aims: This study utilized data from the 2006 National Survey on Drug Use and Health (NSDUH) to examine predictors of non-medical use, abuse or dependence on prescription opioids.
Methods: The NSDUH is conducted annually in the United States to collect information on the prevalence and correlates of drug use, using a cross sectional design. Participants were 55,279 non-institutionalized civilians aged 12 years and older.
Results: Overall, 13.6% endorsed lifetime and 5.1% past year prescription opioid non-medical use. Rates of prescription opioid abuse or dependence increased approximately 17% from 2005 to 2006 (0.6 to 0.7%). Predictors of non-medical use included male gender [adjusted odds ratio (AOR) 1.30, 95% CI 1.12-1.52], younger age [AOR 2.23, 95% CI 1.86-2.67], lower education [AOR 1.42 95% CI 1.12-1.81], serious psychological distress [AOR 1.42, 95% CI 1.11-1.81], abuse/dependence on alcohol or illicit drugs [AOR 1.55, 95% CI 1.22-1.98], and other substance use, in particular non-medical tranquilizer or sedative use [AOR 15.75, 95% CI 11.22-22.11]. Predictors of abuse/dependence included male gender [AOR 1.56, 95% CI 1.03-2.35], younger age [AOR 1.86, 95% CI 1.23-2.82], serious psychological distress [AOR 3.68, 95% CI 2.4, 3-5.57], needle drug use [AOR 2.75, 95% CI 1.29-5.86], and other substance use, in particular non-medical tranquilizer or sedative use [AOR 28.25, 95% CI 16.86-47.34]). Gender-specific differences in sources and predictors of non-medical use, abuse and dependence were also revealed.
Conclusions: Prescription opioid non-medical use is a common and growing public health problem. The findings may inform screening, prevention and treatment efforts, and alert clinicians to characteristics that may confer increased susceptibility
Financial Support: NIDA grants K23 DA021228 (SEB) and K24 DA00435 (KTB)

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PHARMACODYNAMIC EFFECTS OF 3,4-METHYLENEDIOXYAMPHETAMINE.

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Aims: MDA is an illicitly used drug that is an analog of MDMA (3,4-methylenedioxymethamphetamine, 'Ecstasy'). In vivo MDMA is N-demethylated to MDA. Although MDA is often called a hallucinogen, human studies predate widespread use of MDMA, which is not a classical hallucinogen. Thus, it is not clear if MDA pharmacodynamics are more similar to LSD-like hallucinogens or MDMA. We sought to measure its effects in humans in a controlled setting.
Methods: In a placebo-controlled, double-blind, within-subjects study, 12 individuals received a single 98 mg/70 kg bw dose of MDA. This is the molar equivalent of 105 mg/ 70 kg bw MDMA, a well-studied dose. Hormonal (cortisol, prolactin), physiological (HR, BP), and self-report VAS measures of typical MDMA and hallucinogen effects were obtained.
Results: MDA was well-tolerated by all participants (11M/1F; 5 with prior MDA use, 12 with prior MDMA and hallucinogen use). MDA increased cortisol by 16.39 ug/dL (95%CI: 13.03-19.74, P < 1e-3) and prolactin by 18.37 ng/mL (95%CI: 7.39-29.35, P < 1e-3). These hormonal changes are comparable to those seen after MDMA. Heart rate increased by 9.05 bpm (95%CI: 6.10-11.99, P < 1e-5) and blood pressure increased by 18.98 / 12.73 mm Hg (Systolic 95%CI: 16.47 - 21.49, P < 1e-7; Diastolic 95%CI: 10.82 - 14.63, P < 1e-4). Heart rate and systolic changes were significantly less than and greater than seen in a previous study of MDMA (N = 16), respectively (P < 1e-5 and P = 2.42e-7, respectively). There were robust self-report VAS changes in both MDMA-like (e.g., "closeness to others") and hallucinogen-like (e.g., "familiar things seem unfamiliar", time distortions, closed-eye visuals) effects that were generally similar to those seen after MDMA.
Conclusions: MDA is a psychoactive sympathomimetic phenethylamine with effects similar to MDMA. Although differences may exist in the magnitude of physiological effects, the overall profiles appear remarkably similar.
Financial Support: Supported by DA 016776

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DISCRIMINATIVE, LOCOMOTOR, AND PLACE CONDITIONING EFFECTS OF SALVINORIN A AND ITS SYNTHETIC DERIVATIVES.

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Aims: Current research on the psychopharmacology of the hallucinogenic plant Salvia divinorum is largely motivated by recent trends in recreational use and abuse of this plant and its primary active ingredient, salvinorin A. Additionally, preclinical studies of kappa opioid receptor agonists may have multiple therapeutic applications, including the potential treatment of drug dependence. The current study implemented drug discrimination and place conditioning procedures, two established behavioral assays of the discriminative and appetitive effects of psychoactive drugs, respectively, to examine salvinorin A and two synthetic derivatives of salvinorin B, the ethoxymethyl (EOM) and methoxymethyl (MOM) ethers in male Sprague-Dawley rats.
Methods: In experiment 1, eight rats were trained to discriminate salvinorin A (2.0 mg/kg, I.P. 20 min) in an operant task under an FR 20 schedule of food reinforcement and tested for stimulus generalization with sal B EOM, sal B MOM, morphine, ketamine, and LSD. Experiment 2 assessed the locomotor and place conditioning effects of salvinorin A (0, 0.04 or 0.40 mg/kg administered S.C. 5 min before 30 min conditioning sessions) in 36 rats.
Results: In drug discrimination experiments, both MOM and EOM engendered full substitution for salvinorin A, whereas morphine, ketamine, and LSD failed to substitute. In place conditioning experiments, salvinorin A established a conditioned place aversion and significantly reduced locomotor activity relative to vehicle controls.
Conclusions: Consistent with previous reports, salvinorin A produces unique discriminative stimulus effects that appear to be specific to kappa opioid receptor activities. Additionally, salvinorin A produced conditioned place aversion even at low doses, which conflicts with recent reports that low doses establish conditioned place preference. Additional investigations regarding the psychoactive effects of salvinorin A and its derivatives are warranted.
Financial Support: This research was funded by internal research funds at Western Michigan University.

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FAT CONTENT AND AMOUNT OF CHOW IMPACT THE SENSITIVITY OF RATS TO QUINPIROLE-INDUCED YAWNING.

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Aims: Feeding condition can modify the behavioral effects of drugs acting on dopamine (DA) systems. For instance, food restriction or access to a high fat chow changes sensitivity of rats to yawning induced by quinpirole, a direct-acting DA receptor agonist, suggesting that both content and amount of chow can alter some effects of DA drugs. Because D3 receptors mediate the induction of yawning (i.e. ascending limb of the dose-response curve) and D2 receptors mediate the inhibition of yawning (i.e. descending limb of the dose-response curve), feeding condition might differentially affect drug action mediated through D3 or D2 receptors. This study examined whether differences in content and amount of chow contribute to changes in sensitivity to quinpirole-induced yawning.
Methods: Male Sprague-Dawley rats had either free or restricted (adjusted daily to increase, maintain, or decrease body weight) access to standard (5% fat) or high (34%) fat chow (body weights were matched for separate groups of rats eating different chows).
Results: So long as body weight increased, eating a high fat chow shifted both limbs of the quinpirole dose-response curve leftward, indicating an increased sensitivity at both D3 and D2 receptors. When access to chow was adjusted daily so that body weights were maintained, the descending limb of the quinpirole dose-response curve shifted leftward, indicating an increased sensitivity at D2 receptors. When access to chow was adjusted daily so that body weights decreased, the quinpirole dose-response curve flattened, possibly indicating a further increase in sensitivity at D2 receptors.
Conclusions: Thus, as long as body weight increased, the fat content of the chow impacts sensitivity, but when body weights were maintained or decreased, the amount of chow impacts sensitivity, to quinpirole. Because DA receptors are the target of several drugs of abuse, the content and amount of food might influence vulnerability to abuse of drugs acting on DA systems (i.e. cocaine).
Financial Support: CPF is supported by a Senior Scientist Award (DA17918).

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EFFECT OF ACUTE AMPHETAMINE ON EMOTIONAL MEMORY.

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Aims: This study is designed to assess the effects of a stimulant drug on emotional memory. Drugs of abuse act on neural substrates of learning and memory, which play a central role in addiction. A positive sober memory recollection for experiences encountered during intoxication is likely to contribute to repeated use. Amphetamine (AMP), a prototypic stimulant drug of abuse, enhances memory for motivated behaviors in animal models (i.e. shock avoidance, food reward). In humans, AMP can improve memory for paired word associates and noun word lists. However, its effects on memory for emotional content have not been examined. We hypothesized that AMP would preferentially enhance memory for emotional material. Further, we investigated whether AMP facilitates memory in concert with, or independently of, its effects on subjective arousal state. AMP may improve memory through its ability to produce euphoria, which may result in mood-congruent processing and positive memory biases.
Methods: Healthy human volunteers (N=24; 18-35yrs) receive d-AMP (10mg, 20mg, or placebo p.o.) on three study sessions, before viewing positive, negative, and neutral photographs and personality trait words. Subjects rate stimuli for valence and arousal, and recognition memory is assessed 48 hrs later, while sober. Ratings of stimulus perception, memory improvement, or bias are examined in relation to subjective mood states and drug preference after drug and placebo.
Results: Preliminary results (N=13) suggest that AMP improves memory accuracy for positive > negative photographs, with no improvement seen for neutral photographs or trait words. These effects appear to be independent of AMP-induced changes in arousal state and perceptual alterations.
Conclusions: AMP-induced preferential enhancement of subsequent sober memory for emotional material was found, with the greatest improvement seen for content perceived as positive. This profile may be an important factor influencing repeated use, particularly considering that AMP is often used with the intention of inducing a positive mood state or enhancing celebratory situations.
Financial Support: NIDA DA02812 and T32 DA007255

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EFFECTS OF VOLUNTARY EXERCISE ON MORPHINE ANTINOCICEPTION AND WITHDRAWAL.

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Aims: The present study investigated the effects of voluntary exercise on morphine antinociception and on morphine withdrawal following chronic administration.
Methods: Two groups of C57Bl6J mice were used in each experiment: 1) an exercise (ex) group (n=8) allowed free access to activity wheels in their home cages and 2) a sedentary control (sed) group (n=8). In the first experiment, morphine dose-effect curves (0.32 – 32 mg/kg, s.c.) were obtained with a 56°C hotplate procedure in sed mice and in mice with access to activity wheels in their home cages for 6 weeks. In a second set of experiments, the effect of exercise on spontaneous morphine withdrawal was examined in two other groups of mice. One group of mice received 50 mg/kg morphine (s.c.) twice daily for 5.5 days (11 injections). A second group received 100 mg/kg morphine (s.c.) twice daily for 3.5 days (7 injections). Withdrawal jumping was observed 8 and 32 hrs after the final injection of morphine by placing mice in 4L beakers for 30 min.
Results: In ex mice, the morphine ED50 was 12.6 mg/kg compared to 9.2 mg/kg in the sed mice; however, this did not represent a significant shift in the morphine dose-effect curve. In the withdrawal experiments, mice given 50 mg/kg morphine jumped 16 (ex) and 30 (sed) times 8 hrs after the final injection and 29 (ex) and 17 (sed) times at 32 hrs. Mice given 100 mg/kg morphine jumped 45 (ex) and 54 (sed) times at 8 hrs and 51 (ex) and 78 (sed) times at 32 hrs. At all time points, the ex mice jumped less than sed mice though the differences were not significant due to variability between mice.
Conclusions: Six weeks of voluntary exercise did not produce a significant alteration in morphine's antinociceptive effects in the hotplate procedure. Similarly, exercise did not produce a significant decrease in jumping during spontaneous morphine withdrawal; however, since there was an indication that exercise reduced some of the signs of morphine withdrawal, significant effects may be observed with a larger n or longer exercise durations.
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PRENATAL COCAINE EXPOSURE AND MEMORY AND LEARNING DEFICITS IN EARLY ADOLESCENCE: MALE-FEMALE DIFFERENCES.

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Aims: To assess whether prenatal cocaine exposure (PCE) is associated with memory and learning deficits in early adolescence, with a specific focus on possible sex/gender differences.
Methods: This study was conducted in a subsample of the Miami Prenatal Cocaine Study (MPCS), a large single-site longitudinal study. The prospectively enrolled birth cohort consisted of 476 full-term African American infants (127 girls/126 boys with PCE and 112 girls/111 boys without PCE). Serial multidomain assessments have been conducted. At the 12-year visit, 85% of the original cohort completed the Wide Range Assessment of Memory and Learning (WRAML). Using structural equations modeling (SEM), a memory-learning latent construct was regressed on PCE, with separate models for males and females, and with the 'multiple indicators, multiple independent causes' (MIMIC) model used to estimate possible differential PCE effects on memory-learning subfacets.
Results: With test age held constant, there was a PCE-associated deficit in the latent memory-learning construct ($n=405$; $p<0.05$), but MIMIC analyses showed no differential PCE effects on the memory-learning subfacets. Sex-specific analyses showed a somewhat larger PCE-associated deficit in the memory-learning construct for females. Statistical control for alternative explanations of the memory-learning deficits in adolescence showed some attenuation of the initially observed PCE-associated deficits, for both sexes combined, and for females.
Conclusions: Initial analyses disclosed statistically robust PCE-associated deficits in an overall memory-learning construct, but no differential effects on subfacets as tapped by the WRAML during early adolescence. The observed PCE-associated deficits were somewhat larger for females. Within SEM, multiple regression analyses indicated that the observed deficits might also be influenced by other contextual and environmental factors not specific to prenatal cocaine exposure.
Financial Support: R01 DA 006556;P50 DA 024584;K01 DA 016720

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DEVELOPMENT OF A BEHAVIORAL ACTIVATION INTERVENTION FOR SMOKERS WITH ELEVATED DEPRESSIVE SYMPTOMS IN A RESIDENTIAL SUBSTANCE USE PROGRAM.

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Aims: Higher rates of smoking and related morbidity are found among individuals with co-morbid depression and substance use disorders than in the general population and depressive symptoms impact individuals' ability to quit smoking. Although antidepressants have demonstrated effectiveness for smoking cessation, they do not appear to act through the reduction of depressive symptoms. Moreover, few behavioral smoking interventions meet the specific needs of depressed individuals, particularly those with co-occurring substance use disorders. Thus, the objective of the current study is to develop a novel, behavioral smoking cessation intervention for substance users with elevated depressive symptoms.
Methods: Smoking cessation treatment manuals are being developed for low-income minority substance users with elevated depressive symptoms in residential treatment. Standard smoking cessation techniques, including nicotine replacement therapy will be used, along with behavior activation to combat depressive symptoms. After piloting with 5 patients and considering patient/therapist feedback, manual modifications will be made. Through an iterative process, the manual will be revised based on patient/therapist feedback, will be re-administered to 5 clients, and following feedback, a final version of the manual will be created. Patients will receive five, 90 minute therapy sessions over the course of 2½ weeks. Participants' smoking, substance use, and depressive symptoms will be assessed at baseline, at the 3rd and 5th sessions, and at 2 and 4 week follow-ups.
Conclusions: This intervention has been developed to target the needs of particularly high-risk smokers. Based on initial piloting, treatment feasibility, adherence, and acceptability will be reported. We will comment on the readying of final treatment manuals for a randomized controlled trial with 80 patients where we will compare our treatment to standard smoking cessation. If successful, this treatment will enable us to target smoking among one of the most difficult to treat populations.
Financial Support: N/A

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EFFECTS OF THE MONOAMINE RELEASERS PAL-353 AND (+)PHENMETRAZINE ON CHOICE BETWEEN COCAINE AND FOOD IN RHESUS MONKEYS.

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Aims: Monoamine releasers are one class of compounds being investigated as candidate "agonist" pharmacotherapies for cocaine dependence. The efficacy of monoamine releasers as candidate medications may be influenced by their relative potency to release dopamine/norepinephrine versus serotonin. The aim of this study was to assess the effects of 7-day treatment with PAL-353 (80-fold selective for DA vs. 5HT release) and (+)phenmetrazine (37-fold selective for DA vs. 5HT release) on the relative reinforcing strength of cocaine using a cocaine versus food choice procedure in rhesus monkeys.
Methods: Rhesus monkeys (n=4) were trained under a concurrent schedule of food delivery (1-g pellets, fixed-ratio 100 schedule) and cocaine injections (0-0.1 mg/kg/inj, fixed-ratio 10 schedule). Cocaine choice curves and ED50 values were determined under baseline and test conditions during which PAL-353 (0.032-0.32 mg/kg/h) or (+)phenmetrazine (0.032-0.32 mg/kg/h) was administered continuously for 7 days.
Results: Under baseline conditions, food was primarily chosen during availability of low cocaine doses (0.0032-0.01 mg/kg/inj), and cocaine was primarily chosen during availability of higher cocaine doses (0.032-0.1 mg/kg/inj). Treatment with 0.032 mg/kg/h PAL-353 produced a rightward shift in the cocaine choice curve as indicated by a significant increase in the cocaine ED50. Treatment with (+)phenmetrazine also produced rightward shifts in the cocaine choice curve, but the results were more variable across monkeys than with PAL-353.
Conclusions: These results are consistent with previous studies examining monoamine releaser effects on cocaine self-administration and support the potential of dopamine-selective releasers as pharmacotherapies for cocaine dependence.
Financial Support: This work was funded exclusively from National Institutes of Heath grants R01-DA26946 and T32-DA07027.

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A COMPARISON OF TWO METHODS OF TECHNOLOGY TRANSFER FOR SUBSTANCE ABUSE CLINICIANS.

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Aims: There is a movement to offer technology transfer training workshops in non-traditional formats (i.e., distance learning, web-based, etc.) to facilitate access for substance abuse clinicians. However, there is concern that trainings in non-traditional formats will not offer equivalent training to in-person efforts. The aim of this project is to compare the effectiveness of a behavioral couples therapy (BCT) training workshop offered in two different formats: in-person and via distance learning.
Methods: Data was collected from 81 (51 in-person and 30 distance-learning) substance abuse clinicians who attended one of nine (6 in-person and 3 distance-learning) two-day training workshops. The workshops, designed to be offered in either format, were identical in content, exercises, and length. Participants completed a web-based questionnaire prior to the workshops, as well as immediately after the workshops and at 1 and 6 months after the trainings.
Results: The participants had a mean age of 47.2 years, were largely female (66.7%), Caucasian (70.4%), and earned a graduate degree (M.A. or Ph.D.; 56.8%). Generalized Estimating Equation (GEE) modeling was used to examine participants' BCT knowledge. Participants' computer comfort and years working at current position were employed as covariates. For the overall total knowledge score, and with two subscales (multiple choice and true/false knowledge questions) there were no significant differences on the training (in-person or distance learning) method.
Conclusions: Development of a theory-based workshop training curriculum designed specifically for multiple delivery formats appears to yield positive results. These positive results were found regardless of method of delivery (in-person vs. distance learning).
Financial Support: This project is supported by NIDA (R01DA018295).

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OPIOIDS, CHRONIC PAIN, AND ADDICTION IN PRIMARY CARE.

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Aims: Background: Research has largely ignored the systematic examination of physicians' attitudes towards providing care for patients with chronic non-cancer pain. Aim: To identify barriers and facilitators to treating patients with chronic non-cancer pain by office-based medical providers.
Methods: We conducted qualitative interviews using an individual and group format. Participants were twenty-three office-based physicians in New England. Interviews were audiotaped, transcribed, and systematically coded by a multidisciplinary team using the constant comparative method.
Results: Physician barriers included lack of expertise in the treatment of chronic pain and co-existing disorders, including addiction; lack of interest in pain management; patients' aberrant behaviors; and physicians' attitudes toward prescribing opioid analgesics. Physician facilitators included promoting continuity of patient care and the use of opioid agreements. Physicians' perceptions of patient-related barriers included lack of physician responsiveness to patients' pain reports, negative attitudes toward opioid analgesics, concerns about cost, and patients' low motivation for pain treatment. Perceived logistical barriers included lack of appropriate pain management and addiction referral options, limited information regarding diagnostic workup, limited insurance coverage for pain management services, limited ancillary support for physicians, and insufficient time.
Conclusions: We identified a specific set of physician, patient, and logistical barriers to treating chronic pain patients in office-based settings. Addressing these barriers will be crucial to improving pain management service delivery.
Financial Support: NIDA RO1 DA019511-04, K23 DA024050-02, K12 DA00167, K24 DA000445-04 and Robert Wood Johnson Foundation

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CHARACTERISTICS OF URBAN ADOLESCENTS WHO SCREEN POSITIVE FOR MARIJUANA DEPENDENCE IN INDIGENT PRIMARY CARE CLINICS.

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Aims: Reducing the escalation of marijuana use among adolescents can have a major impact on risk trajectories in adulthood. This paper describes risk and protective factors associated with screening positive for marijuana dependence among adolescents in indigent primary care clinics.
Methods: Patients (ages 12-18) self-administered a computerized survey; participants reporting marijuana use completed a baseline survey. Bivariate and logistic regression analyses were used to compare adolescents screening positive/negative on marijuana dependence (MD) based on demographic and risk and protective factors.
Results: 325 adolescents (34% male; 61% African-American) reported marijuana use and 54% screened positive for MD. Adolescents screening positive for marijuana dependence (MD) were more likely to be older ($p<.05$), engage in binge drinking ($p<.01$), screen positive for non-violent delinquency ($p<.05$), have more sex partners ($p<.01$), and have friends who use drugs ($p<.01$). Regarding protective factors, adolescents screening positive for MD were significantly less likely to report religious activity ($p<.01$), involvement in community activities ($p<.01$), having a mentor ($p<.05$), and having friends who were a positive influence ($p<.05$). There were no significant differences were found for gender, race, work status, grades, school activities, parental drug use, and parental monitoring.
Conclusions: The results of this study indicate that polydrug use, including binge drinking, are important issues to address with inner city teens with marijuana dependence. The varying risk and protective factors associated with the escalation of marijuana use and marijuana dependence among adolescents speaks to the importance of developing tailored interventions to decrease the use of and problems related to marijuana in this population.
Financial Support: NIDA#020075

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NICOTINE-DEPENDENT VS. NON-DEPENDENT METHADONE-MAINTAINED SMOKERS.

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Aims: While the general population estimates for smoking prevalence in the US is 21%, approximately 75% of methadone maintained patients are smokers and are at risk for the adverse effects of smoking. The methadone clinic may be an ideal place to address smoking.
Methods: We evaluated the prevalence of smoking in an urban methadone maintenance program. The time to first cigarette was used as a surrogate for nicotine dependence. Characteristics of nicotine dependent and non-dependent smokers were compared using multivariate logistical regression.
Results: 279 questionnaires were completed. Thirty-six subjects were never smokers, 54 were former smokers, and 187 current smokers. Groups did not differ in age or methadone dose. 70% of smokers were nicotine dependent based on endorsing a time to first cigarette of less than 30 minutes after waking. Neither age, gender, nor methadone dose were associated with nicotine dependence. Factors influencing nicotine dependence included race, number of cigarettes smoker per day, and time of day of heaviest smoking. After multivariate regression, only race and number of cigarettes smoked per day remained significant. Asian smokers were least likely to be nicotine dependent ($p<0.05$) and African American smokers were most likely to be dependent ($p<0.01$). Subjects smoking fewer than 10 cigarettes per day were less likely to be dependent ($p<0.001$). Finally, we asked smokers what cessation services they would like: 38% wanted their smoking ignored; 24% wanted the clinic to help them quit; 21% wanted assistance cutting down; 8% wanted education about smoking; and only 5% wanted referral to a specialist. The desire for these services did not differ between dependent and non-dependent smokers.
Conclusions: Nearly 70% of methadone maintenance patients are current smokers. 70% of these smokers are nicotine dependent. There was no association between methadone dose and odds of being nicotine dependent. Although few of these patients want assistance with cessation, 20% want assistance with cutting down, which may provide an opportunity for future quit attempts.
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KNOCKDOWN OF PRESYNAPTIC D2 RECEPTORS IN DORSAL STRIATUM INHIBITS THE BEHAVIORAL AND NEUROCHEMICAL EFFECTS OF HALOPERIDOL.

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Aims: The D2 receptor mediates the effects of drugs of abuse and neuroleptics. While drugs have been developed with relative specificity for D2 receptors, it is difficult to distinguish their pre- and postsynaptic activities using a strictly pharmacological approach. Likewise, transgenic animal models are hindered by difficulty in targeting specific brain regions. To overcome this we used a viral mediated approach to knock down the D2 autoreceptor from dopaminergic neurons projecting from the substantia nigra to the dorsal striatum and assessed the neurochemcial and behavioral effects of haloperidol.
Methods: Adeno-associated viruses (AAV) that produce short hairpin RNA (shRNA) targeted to the D2 receptor were injected into the dorsal striatum of adult male rats and real time qPCR analysis of D2 mRNA was conducted on the tissue. Since AAV predominately transduces cell bodies at the injection site, we injected the virus into the substantia nigra in order to target the presynaptic D2 autoreceptor in the dorsal striatum. The rats were treated with haloperidol and assessed for catalepsy and DA release as measured by fast-scan cyclic voltammetry. A scrambled shRNA virus was used as a control.
Results: The qPCR demonstrated a significant decrease in D2 mRNA in the D2 shRNA treated tissue. In naïve animals, haloperidol produced a dose dependent increase in electrically-evoked DA release in the dorsal striatum. However, loss of the D2 autoreceptor significantly blunted the effects of haloperidol on DA release, which coincided with a dramatic reduction in haloperidol-induced catalepsy.
Conclusions: These results indicate that the presynaptic D2 autoreceptor in the dorsal striatum regulates haloperidol-induced catalepsy. Furthermore, we have demonstrated that virally mediated genetic alterations in receptor levels provides an effective and flexible technique for dissecting the contribution of pre- and postsynaptic receptor populations in drug action.
Financial Support: DA024763, DA024525, DA007246, DA14030, DA03690, and DA021634

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A CONTROLLED TRIAL OF ON-SITE HEPATITIS C TREATMENT IN METHADONE MAINTENANCE.

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Aims: To conduct the first prospective randomized trial comparing the effectiveness of Hepatitis C (HCV) medical care provided On-site in methadone maintenance treatment (MMT) versus Off-site in a specialized gastroenterology (GI) clinic.
Methods: Opioid-dependent patients in MMT with chronic HCV infection were randomly assigned to HCV care On-site (MMT clinic) or Off-site (GI clinic).
Results: 111 patients were randomized; 55 assigned to On-site and 56 to Off-site HCV treatment. 59 (53%) were eligible for HCV treatment and 52 (47%) were ineligible, primarily due to failure to complete medical assessment. The following HCV treatment outcomes were achieved: Attended initial HCV medical visit: 52 (95%) On-site, 36 (64%) Off-site ($p\leq0.001$). Started HCV treatment: 26 (47%) On-site and 15 (27%) Off-site ($p\leq0.05$). Completed 12 weeks HCV treatment: 20 (36%) On-site, 11 (20%) Off-site ($p=0.059$). Completed 24 weeks: 15 (27%) On-site, 7 (13%) Off-site ($p = 0.06$). Completed 48 weeks: 7 (13%) On-site 3 (5%) Off-site (p=NS). Achieved Early Viral Response (EVR) 18 (33%) On-site, 9 (16%) Off-site ($p \leq 0.05$); End of Treatment Response (ETR): 8 (15%) On-site, 7 (13%) Off-site (p=NS); Sustained Viral Response (SVR): 5 (9%) On-site, 6 (11%) Off-site (p=NS). Of the 41 who started HCV treatment, only 15 (37%) completed. 26 (63%) discontinued treatment, 22 of whom stopped due to inability to tolerate side effects.
Conclusions: Significantly more subjects in the On-site than in the Off-site condition completed HCV medical evaluation, started HCV treatment, and achieved EVR. However, there were no significant differences in achieving ETR or SVR. The most common obstacle to starting HCV treatment was nonattendance at medical visits. Intolerance of side effects substantially limited treatment completion. HCV treatment provided On-site in MMT may therefore be effective in increasing the rates of HCV assessment and HCV treatment initiation but it may have less value in improving rates of achieving SVR.
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PROLONGED REWARD AFTER OXYCODONE TREATMENT IN FEMALES.

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Aims: Oxycodone is a semi synthetic opioid analgesic prescribed for pain management. While oxycodone-induced reward has been shown in male rats, reward pathways have not been systematically investigated in females. Nor has the time course for oxycodone-induced behavioral reward expression and cellular activation in nucleus accumbens been established. To investigate this we tested separate groups of rats for oxycodone-induced conditioned place preference (CPP) and c-fos activation in the nucleus accumbens.
Methods: Exp1:Adult female Sprague-Dawley rats (n=6-7 per group) were given a single baseline 30 min trial in an unbiased CPP paradigm on D0. Rats received water (D1 and D3) or oxycodone 15mg/kg orally (D2 and D4) at time 0 and were paired to their respective CPP compartments at 0hr, 1hr, 2hr or 3hr post treatment for 30 min. Rats were placed back into their home cage between drug treatment and CPP pairing. On D5, the expression of CPP was assessed as time spent on drug-paired side.
Exp2:Separate female rats (n=5-6 per group) received either water or oxycodone (15mg/kg) orally and were perfused 2hr post treatment with paraformaldehyde. Frozen sections (40μm) were assessed for c-fos protein using immunohistochemical procedures.
Results: Exp1:We found that CPP expression was observed at all time points except during the 1-1.5hr block. Interestingly, CPP observed at the later time points of 2 and 3hr post drug treatment was more robust than CPP observed at the early time points.
Exp2:Selective induction of c-fos expression in the core and shell of the nucleus accumbens was observed in the oxycodone group compared to the water group.
Conclusions: These results indicate that behavioral indices of reward are long lasting and accompanied by molecular changes in the nucleus accumbens. These changes provide an insight into the altered processes underlying prescription drug abuse. Future studies will explore the neurochemical mechanisms modulating the expression of oxycodone-induced reward.
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MDMA AND RELATED ANALOGS INCREASE PLASMA SEROTONIN IN RATS.

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Aims: (±)-3,4-Methylenedioxymethamphetamine (MDMA) is a popular illicit drug that targets 5-HT transporters (SERT) in neurons. Because SERT proteins are expressed on platelets and pulmonary cells, it seems feasible that MDMA alters 5-HT function in non-neuronal tissues. Here we examined whether MDMA and related analogs might increase plasma 5-HT by a SERT-dependent mechanism.
Methods: Ex vivo microdialysis was used to assess the effects of MDMA and related analogs on extracellular levels of 5-HT (i.e., plasma 5-HT) in blood specimens obtained from catheterized rats. In vivo experiments were carried out to determine whether changes in plasma 5-HT produced by MDMA could be used to predict changes in brain extracellular 5-HT.
Results: Baseline plasma levels of 5-HT were 0.5 nM. Test drugs evoked dose-dependent increases in plasma 5-HT, with MDMA and its metabolite (±)-3,4-methylenedioxyamphetamine (MDA) exhibiting highest potency. The ability of drugs to elevate plasma 5-HT was correlated with potency as SERT substrates. In vivo data revealed a significant positive correlation between MDMA-induced 5-HT release in blood and brain, but there was a high degree of variability in responsiveness.
Conclusions: Taken together, our results indicate that MDMA and MDA increase plasma 5-HT by a SERT-dependent mechanism, but measures of 5-HT release in plasma may not necessarily reflect SERT activity in the brain. The clinical implications of these findings warrant further study.
Financial Support: Supported by IRP NIDA and IMIM.

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NOVEL JDTIC ANALOGUES BLOCK KAPPA OPIOID RECEPTOR AGONIST-INDUCED DIURESIS AND ATTENUATE STRESS-INDUCED COCAINE REINSTATEMENT.

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Aims: The KOR antagonist, JDTic, is in development as a clinical candidate for preventing stress-induced relapse in cocaine dependent users. Our objective was to determine whether analogues of JDTic, effective in vitro, were effective in vivo as KOR antagonists and could block stress-induced cocaine reinstatement in rats.
Methods: A1-DTic, J-MeO-DTic and J-CA-DTic were evaluated for their ability to block diuresis induced by 10 mg/kg s.c. of the KOR agonist, U50,488, in male Long-Evans hooded rats. Diuresis tests (5 h) were conducted at multiple time points following single s.c., i.p., and i.g. administrations. A1-DTic was additionally evaluated at 3, 10, 30 & 100 mg/kg i.g. in separate groups of 12 rats each for its ability to prevent footshock-induced reinstatement of extinguished lever pressing previously reinforced with 0.5 mg/kg/inf cocaine during 2-h test sessions.
Results: A1-DTic significantly ($p<0.05$) attenuated U50,488-induced diuresis when given i.g., s.c., and i.p. A1-DTic became more effective after one week of its administration. J-MeO-DTic was without effect (0.3 to 10 mg/kg s.c.). J-CA-DTic was ineffective when given i.g. from 3 to 30 mg/kg. J-CA-DTic, however, significantly ($p<0.05$) blocked diuresis at 24 h and 8 days (1, 10 & 30 mg/kg), 15 days (10 & 30 mg/kg), and 22 and 29 days (30 mg/kg) following i.p. administration. Footshock was ineffective in reinstating responding following administration of 10 and 30 mg/kg i.g. of A1-DTic, and levels of responding were reduced relative to those of vehicle, although nonsignificantly so.
Conclusions: A1-DTic and J-CA-DTic are effective KOR antagonists when given systemically, and A1-DTic is now included with JDTic as the only reported agents capable of antagonizing the KOR following oral administration. The failure of stress to reinstate cocaine-seeking in groups treated with A1-DTic is consistent with the increasing reports that KOR antagonists can attenuate stress-related behaviors.
Financial Support: Supported by NIDA U19 DA021002 and Grant DA 09045.

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GREATER PREVALENCE OF MARIJUANA USE THAN TOBACCO USE AMONG LOW-INCOME PREGNANT WOMEN IN DETROIT.

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Aims: The prevalence and teratological effects of marijuana use during pregnancy have received less attention than that for other substances. This is true despite evidence that prenatal exposure to marijuana may cause delayed fetal growth and subtle but lasting cognitive deficits. Self-report data suggests that marijuana is used by pregnant women three times more often than other illicit drugs, but much less frequently than tobacco. However, self-report data may be of questionable validity given the negative socio-legal consequences of drug use during pregnancy. Evidence of greater-than-expected prevalence of marijuana use during pregnancy may suggest the need for re-evaluation of its relative importance.
Methods: A total of 100 low-income, primarily African-American post-partum women were recruited from their private hospital rooms in Detroit, Michigan. All participants completed a brief self-report measure tapping a number of areas, including substance use, then provided hair and urine samples.
Results: By self-report, the prevalence of tobacco and marijuana use in the past three weeks was 11% and 4% respectively; for the past 3 months, prevalence was 17% and 11%. However, objectively-defined marijuana use was more prevalent than tobacco use: 14% of participants tested positive for marijuana by urinalysis, and 28% by hair analysis. Of participants using either substance, approximately 25% used tobacco only, and approximately 25% used both.
Conclusions: Prenatal marijuana use was more frequent than tobacco use in this sample of urban post-partum women. Notably, marijuana is unique in that (a) it has not been the subject of substantial legal or educational efforts aimed at curbing its use during pregnancy; and (b) it enjoys the support of an energetic advocacy network, both formal and informal. The prevalence of use observed in this sample suggests that a broader public health approach to prenatal substance exposure, with explicit inclusion of marijuana, is needed.
Financial Support: National Institute on Drug Abuse, DA R21 018975

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INDIVIDUAL DIFFERENCES IN INCENTIVE SALIENCE ATTRIBUTION TO A FOOD-ASSOCIATED CUE MODULATE BOTH NOVELTY SEEKING AND ACQUISITION OF COCAINE SELF-ADMINISTRATION IN RATS.

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Aims: It has been suggested that incentive salience plays a major role in drug abuse and the development of addiction. Additionally, novelty seeking has been identified as a significant risk factor for drug abuse. However, it is not known how individual differences in the readiness to attribute incentive salience relate to novelty seeking and drug abuse. The present experiments were aimed at examining how individual differences in incentive salience attribution modulate novelty seeking and acquisition of cocaine self-administration in a preclinical rat model.
Methods: Rats (n = 10) were first trained in a novelty place preference task (a measure of novelty seeking) and a sign-tracking task with food (a measure of incentive salience attribution). Rats were then trained to self-administer cocaine intravenously (0.3 mg/kg/infusion) using a modified version of an autoshaping procedure.
Results: The results demonstrated that animals that attributed incentive salience to a food-associated cue were significantly higher novelty seekers and acquired cocaine self-administration more quickly than animals less likely to attribute incentive salience.
Conclusions: The results suggest that incentive salience attribution is a mediating factor of novelty seeking behavior and that incentive salience magnitude may be an indicator of abuse vulnerability.
Financial Support: Supported by NIH grants DA005312 and DA007304

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MARIJUANA AND COCAINE USERS DIFFER IN RESPONSES TO A SOCIAL STRESSOR.

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Aims: In human laboratory and clinical studies, an increased neuroendocrine and behavioral response to stress predicts relapse to cocaine use. Although marijuana treatment is characterized by high rates of relapse, little is known about responses to stress in heavy marijuana smokers. We compared response to a social stressor in primary marijuana and primary cocaine users volunteering for human laboratory research.
Methods: Non-treatment-seeking male cocaine (N=12) and marijuana (N=13) users completed the Trier Social Stress Task (TSST), a standardized laboratory stressor involving both a public speaking and a mental arithmetic task conducted before an evaluative, unresponsive audience. Cocaine users smoked cocaine 3.8 (±1.5) days/week. Marijuana users smoked cannabis 6.8 (±0.6) days/week. All had gone at least several hours without drug prior to the TSST. Outcome measures were heart rate and subjective anxiety, measured with the State-Trait Anxiety Inventory and the Perceived Stress Scale. Salivary cortisol was also collected but data are not yet available. Data collection is ongoing and the final data set will include non-drug using controls. Mixed model ANOVAs followed by t-tests assessed for between group differences.
Results: The TSST increased heart rate and subjective anxiety in both groups. There was an interaction between group and time (during vs after TSST) on heart rate change from baseline ($F(3, 57) = 2.8$, $p < 0.05$), such that marijuana users had marginally higher heart rate responses during the stressor than did cocaine users ($t(19) = 1.8$, $p < 0.09$). There was no effect of group on subjective responses to the stressor.
Conclusions: These data suggest that male marijuana smokers have heightened autonomic stress responding relative to male cocaine users. These findings may have implications for development of targeted treatments for marijuana and cocaine users.
Financial Support: DA19239, DA009236

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EXAMINING THE DIFFERENCES IN THE PROGRESSION TO NICOTINE DEPENDENCE BY GENDER AND ETHNICITY IN THE US POPULATION.

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Aims: Females have significantly higher rates of nicotine dependence than males. Also, African Americans suffer higher incidence of smoking-related health problems than Whites. Research has shown racial/ethnic differences in the process of becoming nicotine dependent, with African Americans being more likely to become nicotine dependent than Whites. The aim of this study was to examine the progression to nicotine dependence focusing on race/ethnicity group and gender differences.
Methods: Data from Wave I of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) were used for this study (N=14,225). Nicotine dependence was operationally defined using DSM-IV criteria in the NESARC. The main independent variables for this analyses included race, gender, age at first nicotine use, and socioeconomic status (SES). Discrete time survival analyses and conditional logistic regression analyses were conducted using STATA version 10.0.
Results: Multivariate survival analyses showed African Americans had 20% lower odds of becoming nicotine dependent than Whites (aHR=0.80; 95% CI=0.74-0.88; p< 0.001), adjusting for covariates Of note, females had 15% lower odds of becoming nicotine dependent than males (aHR=0.85; 95% CI=0.80-0.91; p<0.001). The race-gender interaction showed that compared to White males, the odds of nicotine dependence were lower for White females (aHR=0.88; 95% CI=0.82-0.94; p<0.001), African American males (aHR=0.72; 95% CI=0.64-0.81; p<0.001), and African American females (aHR=0.80; 95% CI=0.71-0.89; p<0.001). Comparisons across gender and race showed that only the difference between White females and Black males was significant (p<0.01).
Conclusions: The lower odds of becoming nicotine dependent suggest the duration of nicotine dependence is less for African Americans and females. Therefore, factors associated with the differences in the odds of becoming nicotine dependent may help explain the tobacco-related disparity by race and gender.
Financial Support: NIH Grants DA 17796, DA 019805, P60-MD 002217

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FUNCTIONAL INTERACTION BETWEEN SDF-1ALPHA IN THE BRAIN AND OPIOID MEDICATIONS.

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Aims: Buprenorphine was approved by the FDA in 2002 for use in supervised withdrawal and maintenance treatment of opioid dependence. Compared to methadone, it is the most common clinically used opioid medication for pain and opioid dependence management. Buprenorphine is a partial mu-opioid agonist, a powerful analgesic in both rodents and humans, has a very long-lasting efficacy, high safety profile and does not posses immunosuppressive properties. The purpose of the present study was to test which of the two opioid medications, buprenorphine and methadone, is the more effective analgesic in the presence of high levels of the chemokine SDF-1 alpha (a condition that occurs with neuroinflammatory diseases, including HIV encephalitis).
Methods: Young adult male Sprague-Dawley rats weighing 200-250 g were used, 8-10 rats per group. A sterilized stainless steel C313G cannula guide (22 gauge, Plastics One Inc., Roanoke) was implanted into the periaqueductal grey (PAG). The latency to flick the tail in cold water (CWT) was used as the antinociceptive index, according to a standard procedure in our laboratory (Pizziketti et al., 1985).
Results: The dose of 1 mg/kg of buprenorphine subcutaneously (s.c.) produced a marked antinociception in the cold-water tail-flick (CWT) test, reaching a peak level (89 ± 10% MPA) at 45 min. Similarly, methadone also produced a marked antinociception (100%). Although the maximum % MPA increase was not significantly different, the dose of methadone was 3 times higher than that of buprenorphine. Either vehicle (aCSF) or SDF-1alpha was microinjected into the PAG before buprenorphine or methadone. Pretreatment with SDF-1alpha failed to alter the analgesic effect of buprenorphine, while it was able to diminish significantly methadone-induced antinociception.
Conclusions: 1) SDF-1alpha in the brain differentially interferes with the opioid medications.
2) Buprenorphine is a more effective analgesic in the presence of high levels of SDF-1 alpha compared to methadone.
Financial Support: This work was supported by the National Institute of drug Abuse 06650 and DA 13429].

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ESCALATED COCAINE SELF-ADMINISTRATION IS PARALLELED BY SIGNIFICANT REDUCTION IN BASAL EXTRACELLULAR GLUTAMATE LEVELS WITHIN THE MEDIAL PREFRONTAL CORTEX.

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Aims: We have previously reported that extended (6 hrs/day), but not brief (1 hr/day), access to self-administered IV cocaine results in increased expression of the NR2 subunits of NMDA receptors within the medial prefrontal cortex (mPFC) after withdrawal. Moreover, while 7 daily sessions of brief access to cocaine did not alter the glutamatergic response within the mPFC to self-administered cocaine, extended access to the drug produced a time-dependent diminution of cocaine-induced glutamate release. Our results are consistent with the hypothesis that extended access to cocaine self-administration results in diminished glutamate function within the mPFC. The present study was designed to test this hypothesis.
Methods: Rats were either trained to lever press for 0.25 mg/infusion cocaine during 7 daily 1-hr sessions (brief access condition), or were allowed additional 10 daily sessions of 6 hrs access to cocaine self-administration (extended access condition). Basal glutamate levels within the mPFC were monitored 24 hrs, before the first and after seventh, session in brief access animals and 24 hrs following the eighth and seventeen sessions (i.e. first and last 6-hrs sessions) in extended access animals.
Results: Relative to the cocaine-naïve condition, brief access to cocaine self-administration failed to alter basal glutamate levels within the mPFC. In contrast, extended access to cocaine self-administration resulted in a session-dependent decrease in mPFC basal glutamate levels.
Conclusions: These data support our hypothesis that extended access to cocaine self-administration results in decreased glutamate function within the mPFC. This neuroadaptation is proposed to play a critical role in the development of escalated cocaine self-administration, a critical symptom of addiction.
Financial Support: NIDA grants: DA017104 to OBS and DA024038 to KKS.

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A RETROSPECTIVE STUDY OF PROTéGéS AND MENTORS OF THE PRAIRIELANDS ATTC LEADERSHIP DEVELOPMENT PROGRAM: THE IMPORTANCE OF THE MENTOR-PROTéGéS RELATIONSHIP.

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Aims: Our self-motivated and idealistic leaders in community based substance abuse treatment (CTP) are getting older and preparing for retirement or getting overwhelmed with the hardships the treatment providers have to endure in financially challenging times. Traditionally, leaders in CTPs have been promoted from clinical positions to leadership roles in the same organizations, with little to no leadership education and development opportunities. In an effort to assist CTP leaders' efforts in succession planning, the Prairielands ATTC has offered five Leadership Development Institutes (LI) the past six years. The goals for this poster are to: 1) share the program characteristics of our LI, with emphasis on the protégé- mentor relationship, and 2) report results from a follow-up survey of both protégés and mentors from our LI.
Methods: Twenty two protégés and eighteen mentors participated in an electronic survey. Response rate was 61.1% for protégés and 62.5% for mentors.
Results: The results indicated that approximately 52.4% of the protégés had changes their job responsibilities after participating in the LI. Both mentors and protégés valued the mentorship process highly, and the protégés attributes their success to their mentors' willingness to spend time with them to discuss their projects and their issues in their organization.
Conclusions: The overall satisfaction with the LI for both protégés and mentors was positive and the relationship between protégés and mentors were the main reasons for the success. The need for continued LI for our CTPs and also succession planning is important to continue.
Financial Support: The project was supported by the Center for Substance Abuse Treatment (CSAT) and Substance Abuse and Mental Health Services Administration (SAMHSA)

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INTER-TEMPORAL CHOICE OF COCAINE ADDICTS: SINGLE AND CROSS COMMODITY DISCOUNTING OF COCAINE AND MONEY.

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Aims: Inter-temporal choice has provided important insights into the understanding of addiction, predicted drug dependence status and the outcomes of treatment interventions. However, such analyses have largely been based on the choice of a single commodity available either immediately or later (e.g., money now vs. money later). Important choices in addiction and its treatment could arguably result from cross commodities, such as between drug and non-drug reinforcers. To date, no published study has systematically evaluated inter-temporal choice using all combinations of a drug and non-drug commodity.
Methods: This study of 46 treatment-seeking cocaine addicts examines their inter-temporal choice of two commodities (equated amounts of cocaine and money). Specifically, the delay discounting procedures were between cocaine now vs. cocaine later (C-C), money now vs. money later (M-M), cocaine now vs. money later (C-M) and money now vs. cocaine later (M-C).
Results: Cocaine addicts discounted C-C significantly more than M-M ($p=.011$), consistent with previous reports. Importantly, the two cross commodity discounting produced a different profile. Discounting in C-M was intermediate, being between C-C and M-M. The greatest degree of discounting occurred in M-C; it was significantly greater than discounting of M-M ($p<.001$) and C-M ($p=.035$).
Conclusions: These data indicate that the commodities alter inter-temporal choice and that the greatest rate of discounting is obtained when the drug is the later available commodity. This profile of results is consistent with the value of drug being high only when more immediately available. Implications for understanding the choices will be addressed.
Financial Support: This work was funded by NIDA Grant R01 DA 12997; Wilbur Mills Chair Endowment; and in part by the Arkansas Biosciences Institute/Tobacco Settlement Proceeds Act of 2000.

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3-AMINOTHIAZOLE DERIVATIVES OF CYCLORPHAN AND MORPHINAN: AFFINITY, SELECTIVITY AND PHARMACOLOGICAL OPIOID PROPERTIES.

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Aims: Previous studies have shown that a primary aminothiazole derivative of cylorphan was long-acting and attenuated heroin self-administration in rats (Wang et al., JPET 2009). The aim of this study was to synthesize and characterize the pharmacological properties of 3-aminothiazole derivatives of cyclorphan, containing a primary, secondary, or tertiary amine. To obtain compounds that might be useful in PET analysis, the N-cyclopropyl group in cyclorphan was replaced with a N-fluoropropyl group.
Methods: The compounds were characterized in receptor binding assays using membranes from CHO cells stably transfected with one type of human opioid receptor. The pharmacological properties of the compounds were characterized in the [^{35}S]GTPγS binding assay.
Results: 3-Aminothiazole derivatives of cylorphan, containing a primary amino group had K_i values of less than 1 nM for the κ and μ opioid receptors. A secondary amino group reduced the affinity of the compounds, but when the secondary amino group contained a methyl group, the compound still bound to the κ receptor with K_i values of less than 1 nM. 3-Aminothiazole derivatives of cyclorphan containing a tertiary amino group had lower affinity at all three opioid receptors. The same pattern was observed when the N-cyclopropyl group in cyclorphan was replaced with a N-fluoropropyl group. The [^{35}S]GTPγS binding assay showed that the compounds were full agonists at the κ and μ opioid receptors.
Conclusions: 3-Aminothiazole derivatives of cyclorphan and morphinan are a class of compounds that bind with high affinity to κ and μ opioid receptors and act as full agonists at these opioid receptors.
Financial Support: This study was supported by DA014251 from the National Institute on Drug Abuse.

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A MONEY MANAGEMENT-BASED THERAPY INCREASES VALUATION OF FUTURE REWARDS.

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Aims: A positive association between delay discounting and substance use has been established, describing the tendency of substance users to discount future rewards at higher rates than non-drug users. However, studies detailing the responsiveness of delay discounting to interventions are lacking, and none have examined how an intervention targeting financial decision-making affects delay discounting and whether changes in delay discounting moderate changes in substance abuse. This study assesses the effects of a money management intervention, Advisor-Teller Money Manager (ATM), on delay discounting over time and the relationship of these effects to changes in cocaine use.
Methods: Ninety patients with histories of substance use receiving psychiatric treatment at a community mental health center were randomly assigned to 36-weeks of ATM treatment or to a minimal-attention control condition. Delay discounting and cocaine use were measured over the intervention period with a 52-week follow up measure of substance use. Analyses were conducted of (a) the effect of ATM on the slopes of delay discounting and cocaine abstinence, (b) the relationship between change in delay discounting and change in cocaine abstinence and (c) the relative timing of changes.
Results: The ATM intervention was associated with significantly less delay discounting of future rewards and less cocaine use over time relative to controls. Increases in delay discounting were associated with decreased abstinence from cocaine. A 10% change in discounting occurred several weeks before the same degree of change in abstinence.
Conclusions: ATM treatment was associated with lower levels of delay discounting and correspondingly higher rates of abstinence. A cognitive re-framing of future events to more concrete conceptualizations with higher perceived probability may account for the increased valuation of future rewards.
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ABUSE DETERRENT ADJUSTED MEASUREMENT MODEL: ADJUSTING FOR LOCAL PRESCRIPTION OPIOID AVAILABILITY AND LOCAL USE OF HEROIN.

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Aims: Recently, pharmaceutical companies have developed abuse deterrent formulations in an effort to address the problem of prescription opioid abuse in the US. The ADAMM™ methodology was created to determine the impact of such formulations on actual levels of abuse. The two-part statistical model adjusts levels of abuse of various prescription opioids by local availability of each prescription opioid ("exposure covariate"). Since the extent to which heroin is locally available has been shown to impact local abuse rates of prescription opioids, addition of a second covariate that provides an indication of local use of heroin is examined. We estimated the relative levels of abuse of several prescription opioids, adjusted for both covariates, and examined the effect local use of heroin has on abusing each prescription opioid.
Methods: Data were analyzed from 3904 patients in substance abuse treatment representing 208 3-digit client home ZIP codes from 2008 ASI-MV data. A negative binomial single hurdle model estimated (1) the odds of abusing OxyContin relative to comparators (any hydrocodone, Duragesic, Kadian, and Dilaudid) at least once in the past 30 days and (2) the rate (# of days/past 30 days) of continued abuse for those reporting any abuse.
Results: Results revealed expected patterns of prescription opioid abuse levels as well as effects of prescription opioid availability and local heroin use on abuse of each opioid product. Local availability was defined as the number of dispensed morphine equivalent milligrams divided by the population in each 3-digit ZIP code, and local heroin use was the number of self-identified heroin users in each 3-digit ZIP code divided by the number of clients in the same ZIP code who completed the ASI-MV. Inclusion of local use of heroin as a covariate may help to "even the playing field" when estimating levels of abuse across prescription opioids.
Conclusions: This model continues to show promise as way of evaluating an ADF's public health impact.
Financial Support: Inflexxion, Inc.

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SEX DIFFERENCES IN THE INFLUENCE OF NEGLECT ON TOTAL INTRACRANIAL WHITE MATTER IN HIGH-RISK ADOLESCENTS.

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Aims: Few studies have examined sex differences in brain morphology in adolescents at-risk for substance abuse. This study examined sex differences in at-risk adolescents in brain morphometric measures of the amygdala nucleus, total intracranial (IC) volumes of grey and white matter and measures of trauma. Relationships between brain morphometric variables and childhood trauma questionnaire (CTQ) responses were also examined.
Methods: At-risk adolescents (26 males; 16 females; ages 14-17 years) from a longitudinal cohort of children followed since birth and well characterized on prenatal cocaine exposure (PCE) and other psychosocial variables participated in a single magnetic resonance imaging (MRI) session. Total intracranial volumes of grey and white matter were automatically computed using BrainSuite software after removal of extracerebral tissue and correcting for possible radio frequency inhomogeneities. The left and right amygdala were traced in the coronal viewing plane using Multitracer software by one rater blind to gender and other variables.
Results: After co-varying for PCE, an overall main effect of sex was found between left ($F(1,37=14.26$, $p=.001$) and right amygdala volumes ($F(1,37)=5.45$, $p=.025$). However, these effects did not hold after adjusting for total IC volume. After adjusting for PCE, males but not females showed significant correlations between IC white matter volume and CTQ score ($r=-.58$, $p=.004$), emotional neglect ($r=-.54$, $p=.008$), physical neglect ($r=-.57$, $p=.004$), and denial ($r=.48$, $p=.021$), resulting in significant differences in the independent correlations of IC white matter volume and measures of trauma between male and females.
Conclusions: These preliminary results suggest significant sex differences in the relationship between IC white matter volume during adolescence and measures of childhood trauma. Further studies using diffusion tensor imaging may be of benefit in elucidating the specific fiber pathways that may be affected in males relative to female children at-risk for substance use disorders.
Financial Support: (Supported by P50-DA016556).

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DAT BLOCKER/SERT SUBSTRATES: COMPOUNDS WITH HYBRID TRANSPORTER ACTIVITY.

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Aims: The aim was to assess very small molecules as neurotransmitter releasers and/or uptake inhibitors at the biogenic amine transporters.
Methods: Standard transporter release and uptake inhibition assays were used to assess these candidates.
Results: It was found that some small compounds are able to block one (or more) transporter, while acting as a substrate of another, releasing whatever is stored in those neurons. For example, 2-(N-cyclopropylamino)-4'-chloro-3'methylpropiophenone (PAL-820) was found to inhibit DAT with an IC50 of 592 nM while inducing serotonin release with an EC50 of 181 nM. PAL-820 also inhibited NET with an IC50 of 3583 nM. A series of analogs will be presented.
Conclusions: It has long been assumed that if a non-selective compound is a neurotransmitter releaser (substrate) or transport inhibitor at one transporter such as DAT, it does so at the other biogenic amine transporters. This assumption has been reinforced by years of study of large molecules as transport blockers, and a lack of recognition that small molecule releasers such as amphetamines are actually substrates of these transporters. This assumption has been found to be incorrect. Compounds with hybrid activity exist. This hybrid activity is unique compared to releasers like amphetamine, which acts as a substrate of multiple transporters (DAT and NET) or venlafaxine, which acts as a blocker of multiple transporters (SERT and NET). Such hybrids represent a novel therapeutic class of compounds.
Financial Support: This work was supported by funding from NIDA (DA12970).

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PERCEPTIONS OF METHAMPHETAMINE/DRUG USE AMONG AGENCY PERSONNEL IN SOUTHWEST NATIVE AMERICAN COMMUNITIES.

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Aims: In 2003, the Indian Health Service reported that methamphetamine use among Native Americans was three times higher than that of the general population. However, little is known about the use and prevalence of methamphetamine and other drug use in Native American populations within New Mexico. Telephone surveys were conducted with providers, counselors and law enforcement personnel to assess their perceptions of drug use throughout New Mexico and the Four-Corners area. Here we present preliminary findings of this ongoing study.
Methods: Treatment providers (n=15), school administrators (n=15), police officers and correctional facility officials (n=7) in Native American Communities in the Southwest were asked to participate in a phone survey regarding their perceptions of Native American methamphetamine and other drug use. The 15-minute structured questionnaire contained questions that were both quantitative and qualitative in nature.
Results: Most respondents (67.5%) identified alcohol as the number one problem substance in their communities, followed by marijuana (17.5%), heroin (5.0%), and methamphetamine (5.0%). Most participants (86.8%) reported that methamphetamine was a mild or moderate problem in their communities; 13.2% said that it was a severe problem. The number of meth users encountered per month ranged widely between participants, with a mean of 13.5(sd 20.6) and median of 3.0. The degree to which participants saw methamphetamine as a problem, and the number of methamphetamine users they saw per month, were not significantly correlated with the rank assigned to methamphetamine as a problem substance (Spearman $\rho = -.143$, $p = .450$; $\rho = -.304$, $p = .068$, respectively).
Conclusions: Methamphetamine was perceived as less of a problem than other substances by most survey respondents. The findings of this survey shed light on the geographic distribution of methamphetamine problems in Indian Country, and will help to focus future efforts in prevention and treatment research.
Financial Support: NIDA CTN

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THE IMPACT OF PSYCHIATRIC AND SUBSTANCE USE DISORDERS ON THE RISK OF FATAL ACCIDENTAL OVERDOSE AMONG VETERANS.

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Aims: The purpose of this study was to examine the risk of accidental overdose death (AOD) for Veteran Health Administration (VHA) patients with and without psychiatric diagnoses, and to examine if co-occurring substance use disorders explain any of the associations between psychopathology and AOD.
Methods: The study cohort (n = 3,291,891) consisted of all individuals who used VHA services in fiscal year (FY) 1999 (10/1/98 to 9/30/99). We used treatment records from FY '98 and '99 to determine psychiatric and substance use disorder (SUD) diagnoses, including Alcohol Abuse/Dependence, Other SUD Abuse/Dependence, Bipolar I or II, Major Depression, PTSD, other Anxiety Disorders, and Schizophrenia. National Death Index data indicated vital status and cause of death during FY '00 to FY '06. AODs were those poisoning deaths due to illicit drugs, medications, and/or alcohol (ICD-10 codes X40-X45). Cox proportional hazards regression models were used to test the association of psychiatric diagnoses with AOD adjusting for (1) age and sex, and (2) SUDs, age and sex.
Results: There were 4,473 AODs during the follow-up. The relative risk of AOD for clinical diagnoses ranged from 36 (95% CI: 3.3, 3.9) for Schizophrenia to 5.2 for Bipolar (95% CI: 4.8, 5.6). All psychiatric diagnoses had a statistically significant relationship with AOD after adjusting for sex and age (all $p < 0.001$, Hazard Ratios [HR] between 2.6 and 3.7). These relationships remained significant (all $p < 0.001$) after adjustment for SUDs, but were attenuated (HR between 1.4 and 2.0).
Conclusions: Veterans who are diagnosed with a psychiatric illness are at an increased risk for AOD. Some, but not all, of this risk is explained by co-occurring SUD diagnoses. Individuals with psychiatric illnesses, particularly those with co-occurring SUDs, may be appropriate for overdose prevention interventions.
Financial Support: This work was supported by the Department of Veterans Affairs Office of Mental Health Services.

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LONGITUDINAL STUDY OF LEVELS OF ADOLESCENT DRUG USE: AN SEM ANALYSIS OF PARENTAL MONITORING.

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Aims: To evaluate the influence of parental monitoring assessed at age 11 on levels of drug use at age 17, while simultaneously examining potential pathways through levels of drug use and deviant peer affiliation at age 11.
Methods: Longitudinal data come from a 1983-1985 cohort of children from southeast Michigan. Drug use was assessed at ages 11 and 17 and parental monitoring and deviant peer affiliation were assessed at age 11. Of the original cohort of 823 children, 714 (87%) contributed data to the analysis. A structural equation model was used to examine pathways of parent monitoring with levels of deviant peer affiliation and drug use modeled as latent variables.
Results: Level of drug use at age 17 was predicted by level of drug use at age 11. Higher levels of parental monitoring at age 11 predicted lower levels of drug use at age 11 and 17 ($p<0.05$ for both), even with level of deviant peer affiliation held constant.
Conclusions: The present study found that the relationship linking parent monitoring and levels of drug use persisted for six years, helping to substantiate the theory that parenting characteristics might exert long-lasting influences on a child's use of drugs.
Financial Support: This work was supported by grants F31DA021040 and K05DA015799 from NIDA, and R01MH44586 from NIMH.

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DEA MONITORING OF ANABOLIC STEROIDS AND EMERGING DRUGS.

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Aims: The illicit drug market and dietary supplement market routinely experience the introduction of new substances with unknown pharmacology. Often, unsuspecting users are unaware of the effects of these new substances which are knowingly substituted and misrepresented. The Drug Enforcement Administration (DEA) utilizes numerous mechanisms to monitor the emergence of new substances to the illicit drug and dietary supplement markets.
Results: Recently, a number of cathinone derivatives and synthetic cannabinoids have been found in seized and analyzed evidence, including N,N-dimethylcathinone, N-ethylcathinone, methylone, 4-methylcathinone, CP 47,497, and HU-210 to name a few. The increased frequency of these substances in seizure exhibits has prompted DEA to collect scientific information on these substances, especially pharmacology. The dietary supplement market is monitored in a similar manner for the introduction of new anabolic steroids. In a profit driven industry, new steroids are routinely introduced in dietary supplements with little or no known pharmacological effect and may or may not be identified on the label. In the absence of scientific information, DEA supports pharmacological testing of these new steroids to investigate their anabolic activity. In both cases, collection of pharmacological information plays a crucial role in evaluating these new substances for a possible scheduling action under the Controlled Substances Act (CSA).
Conclusions: Since 2000, five designer drugs and three anabolic steroids have been placed under the CSA with additional substances currently under evaluation. DEA will continue to identify new substances and work closely with other agencies to assess risk and when appropriate, implement controls. The emergence of new drug substances will continue in both the illicit drug and dietary supplement markets. Thus, it remains critical that these substances be evaluated as a potential risk to public health and social threat.
Financial Support: Not applicable

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CORRELATES OF PRESCRIPTION OPIOID DIVERSION AMONG MIDDLE- AND HIGH-SCHOOL STUDENTS.

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Aims: The diversion of prescription medications has emerged as a growing public health concern, but the correlates of diversion behavior are not well understood. This study examined correlates of prescription opioid diversion in a sample of middle- and high-school students (7th-12th graders).
Methods: A web-based survey was administered to a sample of 977 middle- and high-school students. The sample was 52.6% female with a mean (SD) age of 15.0 (1.8) years; 54.0% of the participants were Black, 43.5% were Caucasian, 0.6% were Hispanic, 1.3% were Asian or Pacific Islander; and 0.6% were Native American.
Results: Lifetime prevalence of prescription opioid use was 44.5%. Among lifetime users of prescription opioids, 19.7% reported that they had ever given or loaned their pain medication to someone else. Diversion was more prevalent among a) females (25.4%) than males (10.7%), $\chi2(1)=13.3$, $p<.05$; and b) 9th graders (24.2%) and 10th graders (31.5%) compared to other grades, $\chi2(5)=16.9$, $p<.05$. Several dimensions of impulsivity were associated with higher odds of diversion, including a) not thinking before doing something (OR=2.4, $p<.05$); and b) a tendency to change interests frequently (OR=2.7, $p<.05$). Diversion was also associated with more frequent feelings of depression (M=0.77 vs. M=0.54, $p<.05$) and sadness (M=.92 vs. M=0.64, $p<.05$). Further, diversion was associated with a higher prevalence of experiencing drug-related blackouts (17.3% vs. 5.1%, $\chi2(1)=6.0$, $p<.05$) and use of alcohol and/or drugs to relax, feel better, or fit in (26.5% vs. 9.2%, $\chi2(1)=13.9$, $p<.05$).
Conclusions: Diversion was associated with being female, being in 9th or 10th grade, some aspects of impulsivity, depressive symptoms, and substance use problems. Results suggest that age-specific screening efforts and interventions targeted toward female students may be useful.
Financial Support: This research was supported by NIDA Grant R01 DA024678 (Boyd, PI).

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THE RELATIONSHIP BETWEEN SUBSTANCE ABUSE HALFWAY HOUSES AND CRIME IN BALTIMORE CITY, MARYLAND.

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Aims: Placement in a substance abuse halfway house has been shown to increase treatment retention in substance abuse patients. However, many communities resist the establishment of halfway houses, at least in part due to concerns about crime. Empirical evidence on the effect of halfway houses on neighborhood crime is lacking. This study used an innovative "microecologic technique" to evaluate crime around 9 substance abuse halfway houses in Baltimore City, Maryland.
Methods: As control sites, 9 residential street addresses (residential points) were matched to the 9 halfway houses based on neighborhood crime and sociodemographic variables. Addresses of halfway houses, residential points, and all Baltimore City police department crime reports from January 1, 1999 through December 31, 2001 were "geocoded" (latitude and longitude assigned by computerized mapping). Concentric circular "buffers" were drawn at 25-meter intervals up to 300 meters around each site. Parameter estimates generated by Poisson regression analyses were used to assess the relationship between crime counts (incidents per unit area) and distance from the site.
Results: Halfway houses had no relationship with crimes committed during the day (7 a.m.-7 p.m.) (parameter estimate -0.1263, $p < 0.831$) or at night (-0.1217, $p < 0.538$). Residential points also had no relationship with crime either during the day (-0.1479, $p < 0.333$) or at night (0.0666, $p < 0.627$). There was no significant difference in crime patterns around the two types of sites, either during the day (interaction term 0.1864, $p < 0.335$) or at night (0.0834, $p < 0.156$).
Conclusions: These findings suggest that halfway houses have no more effect on neighborhood crime than any other residential address. The major limitation of this study is the small sample size, which may have prevented finding significant effects.
Financial Support: Supported by funds from the SAPRP/Robert Wood Johnson Foundation, CSAT/SAMHSA/DHHS, and intramural NIDA/NIH/DHHS.

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KUDZU ROOT EXTRACT DOES NOT AFFECT THE SLEEP/WAKE CYCLE IN MODERATE DRINKERS.

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Aims: Kudzu root extract has been studied as a treatment for alcohol dependence. In heavy drinkers kudzu decreases alcohol consumption both in a naturalistic laboratory setting and an outpatient setting. In dependent populations sleep disturbances secondary to alcohol withdrawal may precipitate relapse. In addition, a number of medications used to treat alcohol abuse can impact sleep. As such, the effect of kudzu on sleep quality may be an important factor in its effectiveness at decreasing alcohol consumption. In this double blind, placebo controlled crossover trial we tested the effects of kudzu root extract on the sleep/wake cycle of moderate drinkers (7.6±0.6 drinks/week).
Methods: Ten healthy adult (age 28.5±2.2 years) men (n=6) and women (n=4) took part in each of 3 phases. For 9 days participants were given kudzu (750 mg/day total isoflavones; NPI-031; Alkontrol-Herbal®, Natural Pharmacia International, Inc.) or placebo in counterbalanced order with an intervening no treatment period of approximately 21 days. Participants kept a daily diary of bedtime and wake time, and wore a wrist actigraphy device (ActiWatch-Score, Mini-Mitter/Respironic) from which sleep parameters were calculated.
Results: The following sleep parameters were similar during kudzu (K) and placebo (P) treatment periods: sleep efficiency index ([K] 79.3±1.5; [P] 79.1±1.6), sleep latency ([K] 28±4min; [P] 31±6min), wake after sleep onset ([K] 6hr 23min ± 11min; [P] 6hr 19min ± 11min), number of wake episodes during the night ([K] 33.5±0.4; [P] 31.5±0.3), and time awake per episode ([K] 1min±7sec; [P] 1min±2sec).
Conclusions: These data suggest that the administration of kudzu root extract does not disturb sleep/wake cycles of moderate drinkers and as such its utility as an adjunct treatment for alcohol dependence remains free of any hidden side effects on sleep quality. Additional studies are needed to determine if kudzu extract can normalize the disturbed sleep/wake cycles of abstinent heavy drinkers.
Financial Support: This work was supported by NIDA grants K05 DA000343, T32 DA15036, and NIAAA grant AA 10536(SEL).

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PSYCHOMETRIC EVALUATION OF THE A-SIDE ASSESSMENT OF RELAPSE RISK FOR YOUTH.

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Aims: Approximately 35% to 75% of adolescents with SUDs relapse to alcohol or other drugs during the first year post-treatment (Tomlinson, Brown & Abrantes, 2004). Gaining a better understanding of the processes underlying relapse for youth is central to designing effective relapse prevention. Developed through extensive focus groups with alcohol and drug using youth and in conjunction with a professional film production team (Anderson & Parent, 2007), the A-SIDE procedure assesses adolescents' in-the-moment cognitions during simulated alcohol and marijuana use situations through open-ended elicitations and semi-structured interviews in response to video stimuli. This investigation is the first psychometric evaluation of this novel method for identifying factors associated with a return to substance use.
Methods: 65 adolescents (ages 15-17; 60% girls) were recruited from substance use treatment programs and local high schools in the Pacific Northwest. Youth completed the A-SIDE and standard measures of substance use, coping, craving, motivation, outcome expectancies, motives, self-efficacy, and laboratory assays across a 5-week period. Cohen' kappas and Chronbach's alpha provided estimates of interrater reliability and stability of constructs across simulated scenes. Concurrent validity was assessed via correlations with contemporaneous measures of substance use and substance-related cognitions.
Results: There was substantial agreement among different raters on coded content for the A-SIDE procedure (mean K = .76, agreement = 85.6%). A number of content codes exceeded the $\alpha > .70$ for reliability across alcohol and drug offer situations. Content areas assessed by the A-SIDE correlated with indices of substance-related cognitions (i.e., expectancies, motives, coping).
Conclusions: This preliminary investigation suggests that the A-SIDE is a reliable measure of substance use decision-making in this sample of youth. While work is underway to examine the construct and predictive validity of this measure, these preliminary findings are encouraging in the development of a process-oriented measure of substance use relapse for youth.
Financial Support: NIDA 019960 (K. Anderson)

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YOUTH PERSPECTIVES ON PRESCRIPTION DRUG NON-MEDICAL USE AMONG THEIR PEERS.

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Aims: The National Monitoring of Adolescent Prescription Stimulants Study (N-MAPSS) detects current levels and types of use and diversion of prescription medications, including 5 commonly prescribed stimulants, among 10 to 18 year olds.
Methods: Prescribing data were used to identify 10 cities with high volume of stimulant prescriptions, with one city chosen from each of the 10 standard federal regions used in the National Survey of Children's Health. Recruitment of respondents took place at entertainment venues such as cinemas, arcades, shopping malls, food courts and sports events. A brief self-administered anonymous survey assessed youth experiences with and attitudes toward prescription stimulants. At the end of the survey, three open-ended questions were asked (n=2,600): How should kids your age be told about prescription drugs and their effects? If you ran the world, how would you stop kids from taking other people's prescription medicines? Why do people use prescription stimulants without a prescription?
Results: Common themes for "How should kids be told…" and "If you ran the world…" were: through education and the schools; warn of the dangers of drug use; by family/parents; by law enforcement; mass media; by medical professionals; and tighter controls. Predominant themes for perceived motivations for non-medical use were: to "get high"; to feel "good, better or happy"; for stress, problems or depression; to be "cool"; just because; and "to fit in". Less than 5% of all respondents mentioned to study, concentrate, stay awake or lose weight as a reason youth are likely to engage in non-medical use of stimulants. Among stimulant users (n=492), 6.5% cited to study, etc.; and among those with a close friend(s) who had tried stimulants (n=740), 9.5% cited to study, etc. as a reason for non-medical use of stimulants.
Conclusions: This research may help identify effective strategies for public education campaigns targeting American youth.
Financial Support: N-MAPSS is implemented by Washington University in St. Louis under contract from Pinney Associates, Inc., with funding provided by Shire Pharmaceuticals.

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SOCIAL DISCOUNTING AMONG PREGNANT CIGARETTE SMOKERS, QUITTERS, AND NEVER-SMOKERS.

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Aims: Smoking during pregnancy is a leading preventable cause of poor pregnancy outcomes, though only approximately 20% of smokers quit upon learning of a pregnancy.
An expectant mother who smokes is faced with a decision to forgo a highly reinforcing activity that she engages in multiple times daily in order to benefit the health of someone else, her fetus. Considering that there is an element of generosity/selfishness in this choice, it is possible that individual differences in generosity/selfishness to others might contribute to this decision to continue or quit smoking during pregnancy. Presently, we aimed to assess generosity/selfishness by using a new instrument measuring social discounting (Jones & Rachlin, 2006).
Methods: Subjects were 130 pregnant women; 91 were continued smokers, 23 were quitters, and 16 were never-smokers. Participants were asked to think of a list of 100 people in their social network and rank them emotionally from close to distant (#1-100, respectively). Then they made choices concerning various amounts of hypothetical money that could be kept for themselves vs. shared with 7 persons from their social-network (persons 1, 2, 5, 10, 20, 50, & 100). Crossover values were assigned when a participant crossed from the selfish to the generous option at each social distance.
Results: Women who continue smoking while pregnant crossed over from the selfish to the generous option later (producing a lower crossover value) compared to quitters and never-smoker controls ($F(2)=12.9$, $p=<.01$). A higher, earlier mean crossover value suggests increased generosity because more money is foregone to give to another. Mean crossover values by smoking status were 42.2±1.2, 50.2±2.2, 55±2.7 for smokers, quitters, and controls, respectively.
Conclusions: Smoking during pregnancy is associated with a choice bias in the direction of less generosity towards others. Understanding that bias could help to elucidate some of the mechanisms involved in the individual differences seen among smoking during pregnancy.
Financial Support: R01 DA14028, R01 DA02249, & T32 DA07242-17 from NIDA

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CANNABIS USE AMONG CONVICTED DRINKING DRIVERS.

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Aims: There is increasing evidence that cannabis adversely affects driving skills and increases collision risk. In this study we examine self-reported use of cannabis among convicted drinking drivers.
Methods: Data are based on 22,277 convicted drinking drivers who completed Ontario's remedial program 'Back on Track' (BOT), including assessment and 6 month follow-up, between 2000 and April 30, 2005. Measures examined included numbers of days using alcohol and cannabis, average drinks per drinking occasion and the number of substance-related problems experienced in the 90 days prior to the assessment and follow-up interviews. Substance-related problems were measured by the Research Institute on Addictions Self Inventory (RIASI), Alcohol Dependence Scale (ADS), Drug Abuse Screening Test (DAST) and the Adverse Consequences of Substance Use Scale (ACSUS).
Results: 1644 individuals (7.4% of program participants) reported using cannabis at least once in the 90 days prior to assessment but no other substances other than alcohol. These individuals were significantly younger (mean ages = 36.5 and 46.1 years respectively) than the 15,461 alcohol-only users, and more likely to be male (proportion males = 95.2 % and 88.8 % respectively). The cannabis and alcohol group, compared to the alcohol only group, also had significantly higher scores on the RIASI, ADS and DAST. However, they reported significantly fewer lifetime drinking driving convictions. They also reported significantly higher adverse consequences of substance use on the ACSUS in all problem areas except for legal problems.
Conclusions: Drinking drivers in remedial programs who report using cannabis and alcohol in the 90 days prior to assessment appear to show important differences from those who report alcohol use only, primarily in the direction of having more severe substance-related problems and consequences. Further research on the use of cannabis in this population is warranted.
Financial Support: Funding was provided by Ontario's Back on Track Program.

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RELATIONSHIP OF IMPULSIVE PERSONALITY TRAITS AND ORBITOFRONTAL RCBF IN COCAINE-ADDICTED AND HEALTHY SUBJECTS.

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Aims: Previous research suggests that impulsivity may have a role in the development and progression of substance use disorders. Alterations in the orbitofrontal cortex (OFC), a brain region important in behavioral inhibition and decision-making, have been documented in cocaine-addicted subjects. The aim of this study was to explore the relationship between personality traits of impulsivity and basal OFC activity in cocaine-addicted subjects compared to healthy controls.
Methods: 48 cocaine-only addicted (2-4 weeks abstinent) and 39 age-matched controls were administered the Temperament and Character Inventory (TCI) and the Revised NEO Personality Inventory (NEO PI-R). Personality variables relevant to impulsivity and decision-making were predicted a priori. Regional cerebral blood flow (rCBF) was assessed with single photon emission tomography (SPECT) immediately following saline administration while subjects were at rest. rCBF comparisons between groups were performed with SPM2 ($p<0.001$).
Results: Neuroticism (N) and the impulsiveness subscale (N5) were significantly higher in the cocaine-addicted subjects relative to controls. Cocaine-addicted subjects showed both right and left posterior lateral OFC regions with significantly lower rCBF relative to controls. Counts per voxel in these bilateral OFC regions were positively correlated with both N ($r=0.41$, $p<0.01$) and N5 ($r=0.46$, $p<0.004$) in controls. Most striking was the relationship between right lateral OFC and N5 in the control group. Significant relationships were not observed in the patients and were in the negative direction.
Conclusions: A significant relationship between N, and specifically N5, was observed with OFC rCBF following saline infusion in the control group only. These findings suggest a neural disconnect between basal OFC functioning and impulsive aspects of personality in cocaine-addicted subjects.
Financial Support: This work was funded by DA10218 & DA11434 and supported by the Department of Veterans Affairs.

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FIRST 5 YEARS OF METHAMPHETAMINE USE: TRAJECTORIES, CHARACTERISTICS OF TRAJECTORY GROUPS, AND PREDICTION OF LATER TREATMENT OUTCOMES.

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Aims: Methamphetamine (MA) continues to be a problem in many western and mid-western states in the U.S. This study examines early (first 5 years after initiation) patterns of use in a sample of individuals treated for MA use, differences in user characteristics across distinguishable trajectory groups, and whether these identified trajectories are associated with differential rates of long-term abstinence after treatment.
Methods: Data (n=348) are from intensive natural history interviews of a random sample of individuals treated for MA abuse in 1995-1997 in Los Angeles county; interviews were conducted 3 and 6 years after treatment. Group-based trajectory analysis was used to identify trajectory classes for patterns of MA use in terms of number of days per month, in relation to 24-month and 48-month abstinence following the studied treatment episode. Differences among trajectory classes in user and treatment characteristics were explored using chi square and GLM.
Results: The analysis sample was 56% male, 30% Hispanic, 17% African American, 47% White, and 6% other race/ethnicity; the mean age of first MA use was 20.0 years; the mean time from MA initiation to the studied treatment episode was 9.3 years. Five trajectory classes were distinguishable: stably low, moderate, and high use groups, increasing use, and decreasing use across the first 5 years of MA use. Rates of 48-month post-treatment abstinence were highest in the groups with generally high early use (37.5%) and decreasing patterns of early MA use (33.0%) compared to other groups with 12.5-21.0% abstinence. Trajectory groups differed significantly in terms of ethnicity and age of first MA use; they also differed on several MA use and treatment-related characteristics.
Conclusions: Consideration of early patterns of MA use may help identify subgroups of individuals for targeting specialized prevention, treatment, and aftercare programs to improve long-term treatment outcomes. Analysis of early patterns may also contribute to a better understanding of recovery.
Financial Support: NIDA grants R01DA11020, R01DA025113, P30DA016383

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FACTORS ASSOCIATED WITH HIGH VS. LOW USE OF EVIDENCE-BASED PRACTICES IN ADDICTION TREATMENT.

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Aims: Use of evidence-based practices (EBPs) in addiction treatment has produced positive outcomes, yet implementation gaps remain in community settings. Researchers and policy makers seek to identify ways to increase the use and fidelity of EBP implementation in treatment programs. Prior research has focused on implementation issues (Simpson et al., 2007), staff motivation, (McGovern et al., 2004) and factors associated with support for EBPs (Fuller et al., 2007). Identifying organizational factors associated with greater EBP use can inform efforts to promote adoption.
Methods: Staff (N = 68) from treatment facilities in central VA were administered surveys assessing self-reported use of 32 empirically or consensus-driven EBPs, as well as measures of organizational culture and climate (Lehman et al., 2002; Taxman et al., 2007). Positive responses to EBP use were summed and categorized using a median split into "high users" and "low users." Differences between high and low users on organizational measures were then assessed using one-way ANOVAs.
Results: Results revealed that high user staff were more likely than low users to obtain treatment knowledge from a variety of sources, such as professional development and membership in professional associations (ps < .05). High users were also more likely to score higher on measures of innovation and adaptation, efficacy, influence, and autonomy. High users also reported having better offices, more internet use, more positive attitudes toward change, and better training.
Conclusions: Increasing the use of EBPs by SA treatment staff may be better facilitated by addressing organizational factors than simply promoting EBPs. These findings are consistent with other research indicating that training resources are associated with the use of EBPs (Friedman et al., 2007) and that, at an organizational level, environmental scanning is associated with use of treatment innovations (Roman & Knudsen, 2004).
Financial Support: This research was funded by NIDA R01DA022081-03

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MINDFULNESS TRAINING AND STRESS REACTIVITY IN SUBSTANCE ABUSE: RESULTS FROM A RANDOMIZED, CONTROLLED STAGE I PILOT STUDY.

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Aims: Addictions are major chronic and public health problems for which few effective treatments exist. Stress has been shown to play a major contributory role in substance use and relapse. Mindfulness training (MT) has shown promise in a number of stress-related maladies. However, no prior studies have compared mindfulness training to empirically-validated treatments for substance use disorders or assessed its impact on stress provocation in individuals with addictions.
Methods: Thirty-six treatment-seeking individuals with alcohol and/or cocaine use disorders were randomly assigned to receive manualized MT or cognitive behavioral therapy (CBT) in an outpatient community setting. After treatment, psychological and physiological responses to personalized stress provocation were measured by self-report, skin conductance, heart rate, and heart rate variability. The primary outcomes were number of days of substance use and stress reactivity.
Results: Individuals assigned to MT showed equivalent abstinence to those assigned to CBT. Additionally, they demonstrated reduced psychological anxiety, and reduced physiological indices of stress during provocation.
Conclusions: This pilot study suggests that mindfulness training may be efficacious as a treatment for substance use disorders by targeting a critical component of addictions: stress.
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PHARMACOKINETIC PROPERTIES OF A BACTERIAL COCAINE ESTERASE TO BE USED AS A TREATMENT AGAINST COCAINE-INDUCED TOXICITIES.

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Aims: In this study we assess the process of elimination of a bacterial cocaine esterase (CocE). CocE is rapidly eliminated from the serum of mice with a half-life of 2.2 hours, thus limiting the *in vivo* duration of action of CocE. Hypothesis: CocE is being eliminated via glomerular filtration.
Methods: 1) Male Sprague Dawley rats (3 per group) were injected intravenously with CocE in different 14-day dosing regimens: 8 mg/kg CocE every 4 days, 8 mg/kg CocE daily, or 24 mg/kg CocE every 4 days. Saline controls were also included. Six hours following the last dose, rats were sacrificed and perfused with saline. Kidneys, livers, hearts and lungs were prepared for immunohistochemical analysis. 2) Male Sprague Dawley rats (3 per time point) were injected intravenously with 8 mg/kg CocE at 30 minutes and 1, 2, 4, 8, and 12 hours before intravenous blood sampling and saline perfusion. Kidneys were prepared for immunohistochemical analysis, additionally protein was extracted. Kidney homogenates were analyzed by Western blotting.
Results: 1) No immunoreactivity was found in the liver, heart, or lungs, but was found in the kidneys, localized to the papilla. Higher immunoreactivity was observed in animals receiving 24 mg/kg CocE than in those receiving 8 mg/kg. No significant difference in reactivity was observed between animals receiving 8 mg/kg daily or every 4 days. 2) Peak concentrations of CocE in the kidney, as assessed by Western blotting and immunohistochemistry, occurs at 1 hour following a bolus intravenous dose of 8 mg/kg. Western blot analysis reveals that full-length CocE disappears in a time-dependent manner after 1 hour, with relatively few proteolytic fragments detected.
Conclusions: Findings demonstrate that CocE is being eliminated through the kidneys. The lack of difference between animals receiving an intravenous dose of 8 mg/kg CocE daily, or once every 4 days, as well as the rapid loss of reactivity observed after 1 hour, suggests that CocE is not accumulating in the kidney, but being rapidly and effectively eliminated from the body.
Financial Support: USPHS grants DA021416, GM007767.

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FEASIBILITY AND EFFECTIVENESS OF COMPUTER-BASED THERAPY IN A COMMUNITY-BASED PROGRAM.

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Aims: Computerized and web-based therapy approaches may expand the reach of evidence-based substance abuse treatment; however, it is unclear how web-based therapies can be optimally integrated into community-based treatment and how effective they will be if they are only partially implemented. We conducted a two-phase pilot study to explore 1) whether client use of the Therapeutic Education System (TES), a web-based Community Reinforcement Approach learning program, would benefit clients in the absence of counselor support, and 2) whether counselors and clients would use the TES in the absence of tangible reinforcement.
Methods: In Phase 1, we randomly assigned 28 cocaine-dependent clients in intensive outpatient treatment to receive either 8 weeks of 1) treatment-as-usual plus cash incentives for completing computerized behavior therapy modules (TES), or 2) treatment-as-usual plus incentives yoked to the performance of a patient in the experimental group, with no exposure to the TES (YC). We assessed client knowledge and coping skills acquisition, as well as urinalysis-verified cocaine use during and after exposure to the TES.
Results: Clients in the TES condition demonstrated large improvements in knowledge acquisition ($F(1, 20) = 8.90$, $p = 0.007$; $d = 1.05$), and small-to-moderate effects on various indices of improved coping skill acquisition. TES clients were significantly more likely to select CBT-style coping responses ($F(1, 20) = 11.95$, $p = 0.002$; $d = 1.16$). We also detected small, non-significant effects indicating decreases in frequency and amount of cocaine used during treatment. In Phase 2, we studied counselor and client use of the TES following brief training, and found that counselors referred only around 10% of their caseloads to the TES, and that without tangible reinforcement, less than 20% of patients engaged with the TES for more than 2 to 3 visits.
Conclusions: Computer-based therapy approaches are viable to improve community-based outpatient treatment, but must be integrated with contingency management systems to insure engagement.
Financial Support: Commonwealth of Pennsylvania SAP Number 4100042753

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JAIL SANCTIONS DURING DRUG COURT PARTICIPATION AND SUBSTANCE ABUSE TREATMENT COMPLETION.

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Aims: In a drug treatment court (DTC) population:
Identify factors associated with failure to complete substance abuse treatment
Examine associations between jail sanctions and their timing and treatment drop-out among participants in the Dane County DTC

Methods: Analyses were carried out using administrative data on all 573 participants in the Dane County DTC achieving a final disposition of treatment completion or failure between 1996 and 2004. A total of 54 variables were available, including descriptors of education, demographics, SES, substance use, prior treatment, current treatment, and criminal history.
Sequential Cox proportional hazards models of time to treatment failure were created framing jail sanctions as time-dependent covariates. A final parsimonious model was built based upon theoretical issues, statistical criteria, and upon previous study in drug treatment court populations.

Results: Cox proportional hazards models of failure to complete treatment demonstrated associations with employment status (hazard ratio in unemployed vs. employed = 1.41, p-value 0.0079), educational attainment (HR in non-graduate of high school vs. high school graduation or more = 1.41, p = 0.02). The application of a first jail sanction achieved significant predictive value (HR 2.71, p < 0.0001); further jail sanctioning did not achieve significance. The association between treatment failure and a first sanction was considerably stronger if the sanction was administered at less than 30 days' participation (HR for sanction 1 at < 30 days 11.34, p-value 0.0002).

Conclusions: Findings are consistent with an effect for jail sanctions during drug court participation, particularly for those without an extensive criminal history and particularly of more serious felony convictions. Offenders with more extensive criminal involvement may require more intensive supervision and service provision.

Financial Support: NIH-NIDA K23 Mentored Career Development Award (1K23DA017283)

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HIV/AIDS-RELATED HEALTH SERVICES IN SUBSTANCE ABUSE TREATMENT PROGRAMS.

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Aims: This report examined availability of HIV services in substance abuse programs and associations between services, characteristics of programs and patients treated.

Methods: In a cross-sectional, descriptive, hypothesis-generating design, 269 of 319 treatment program administrators within the National Drug Abuse Treatment Clinical Trials Network provided information utilizing a standardized survey regarding program characteristics, patient characteristics and availability of HIV services for 3 categories of patients: 6 services for all patients, 6 for newly admitted patients and 11 for HIV infected patients.

Results: The range of HIV-related services provided on-site or via contractual arrangements varied from 10% (Pneumococcal vaccination) to 86% (drug testing). HIV antibody testing was provided by 57% of programs co-located in hospitals, medical schools and universities as compared to 35% of programs in family health or mental health facilities, 30% of free-standing agencies and 50% in other settings (p=0.045). Compared to programs without outpatient pharmacotherapy, programs providing outpatient pharmacotherapy provided a higher mean number of HIV-related services for all patients, for newly admitted patients and for HIV-infected patients (all p<0.0001). HIV-related services were significantly more available in programs where patients engaged in high risk sexual behaviors and had higher HIV infection rates.

Conclusions: The results of this study provide a plausible mechanism of how substance abuse treatment reduces HIV transmission via the availability of HIV prevention and medical services, and provides the basis for future hypothesis-testing examining the utilization, effectiveness and cost-effectiveness of HIV-related health services in substance abuse treatment. Given the public health significance of HIV disease and the role of substance use in its transmission, such studies are imperative.

Financial Support: National Institute on Drug Abuse (2 U10 DA13046)

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THE IMPACT OF HOMELESSNESS ON HIV RISK BEHAVIOR IN DRUG-DEPENDENT PREGNANT WOMEN.

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Aims: This study sought to examine the relationship between recent homelessness and recent sex trade after controlling for other covariates including psychiatric age, education, race, and psychiatric comorbidity.

Methods: Eighty-one pregnant women with drug dependence (59.3% African-American, 37% white, and 3.7% other) currently enrolled in treatment at the Center for Addiction and Pregnancy, a drug dependence treatment program in Baltimore, Maryland, were recruited and completed the HIV Risk Behavior Interview and SCID I/P.

Results: Twenty-one women (25.9%) reported being homeless during the previous six months, and a third of the sample had traded sex during the previous six months. Multiple logistic regression findings revealed that pregnant drug dependent women who had recently been homeless had nearly five times greater odds [Adjusted odds ratio (AOR) = 4.74, 95% confidence interval (CI) =1.42, 15.85, p<.05] of having recently traded sex for money or drugs compared to pregnant drug dependent women without a recent history of homelessness.

Conclusions: Findings suggest that 1 in 4 women recruited from a drug treatment program had been homeless in the previous six months and that recent homelessness was a significant risk factor for women's involvement in sex trade and thus risk for HIV and other infectious diseases. Findings underscore the need for housing services for this population of women. Assisting pregnant drug dependent women find and maintain stable housing can potentially reduce their involvement in sex trade, risk for infectious diseases, as well as improve other psychosocial outcomes in this population.

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LIKELIHOOD OF ASKING FOR HELP OF FAMILY CAREGIVERS OF WOMEN WITH SUBSTANCE USE DISORDERS.

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Aims: While previous research has examined subjective burden and depression for family caregivers of women with SUD (Biegel et al, 2007), little is known about the factors associated with the likelihood of caregivers' asking for help. Data from a NIDA-funded study were used to analyze the association of caregiver stressors, caregiver resources, care recipient and caregiver socioeconomic characteristics and the likelihood of caregivers of women with SUD asking for help.

Methods: Respondents were 82 family caregivers who provided the most support to female clients receiving substance abuse treatment. The dependent variable, likelihood of asking for help, was measured using a four-point likert scale. Measures included the Client Behaviors Scale (Biegel et al, 1994) and the Family Experiences Interview Schedule (Tessler & Gamache, 1995). Data were collected through interviewer administered questionnaires at one time point.

Results: Study participants averaged 40.04 years of age, were 84.1% African American, 12.2% Latino, and 59.8% female. The multivariate model included client behavioral problems, caregiver perceived burden, amount of assistance given to client from caregiver, and caregiver likelihood of asking for help. The regression model was statistically significant, accounting for 15.7% of the variance in desire for help or support. Client behavioral problems accounted for 5% of the variance in caregiver desire for help; while caregivers' perceived burden contributed 5.9% and amount of assistance given to client contributed 3.8%. Results indicate that client behavioral problems, caregiver perceived burden, and amount of assistance given to clients by caregivers are associated with increased likelihood of asking for help in family caregivers.

Conclusions: Caregivers experiencing higher perceived burden who provide greater amounts of concrete support to clients will be most likely to pursue services.This group of family members can be expected to have the highest needs and could therefore benefit from services offered to address their needs.

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INTERNET-BASED POST-MARKETING SURVEILLANCE OF NEWLY MARKETED OPIOID ANALGESICS.

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Aims: The National Addictions Vigilance Intervention & Prevention PROgram (NAVIPPRO™) post-marketing surveillance system monitors a several data streams, including two, near real-time, Internet-based, product-specific datasets: (1) Web-Informed Services (WIS™) monitors Internet prescription drug abuse chatter on abuse related websites, and (2) Geotemporal Real-time Internet-based Intelligence for Drugs (Media-GRIID™) tracks abuse-related media reports over 20,000 news outlets. How these data streams may anticipate abuse rates as new prescription opioid products increase market share is not well understood.
Methods: We examined the relationship of these Internet-based data streams to abuse as measured by NAVIPPRO's ASI-MV® Connect which collects abuse data in the past 30 days from clients in treatment at a network of more than 530 addiction treatment facilities across the US. Data for two opioid products, Opana® ER and EMBEDA™, are examined from product-launch to explore how Internet chatter and media reports may anticipate abuse rates. Time series analyses were conducted for the respective life-span of each product (Opana®: July 2006-present; EMBEDA™: August 2009-present). Cross correlations compared each data stream adjusting for time lags between the data sources and the ASI-MV® Connect measure of prescription opioid abuse.
Results: Significant correlations over time were observed for both Internet-based data streams and ASI-MV® abuse rates adjusting for various time lags. Analyses identified optimal time lags of 7 months for WISTM prescription opioid web chatter (R2=0.73) and 11 months for Media-GRIID prescription opioid-related media mentions (R2=0.38).
Conclusions: These preliminary results raise the possibility that Internet-based data may provide early situation awareness intelligence with respect to abuse levels of analgesic products as market share increases. These data may serve as leading indicators of trends observed in the clinical setting. Implications and robustness of these observations are discussed with respect to Opana® ER and EMBEDA™.
Financial Support: Inflexxion, Inc.

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CHEWING THEN SWALLOWING IN SELF-REPORTED NON-MEDICAL OPIOID USE BY COLLEGE STUDENTS AS REPORTED BY THE RESEARCHED ABUSE, DIVERSION AND ADDICTION-RELATED SURVEILLANCE SYSTEM.

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Aims: To evaluate differences between college students self reporting non-medical use of prescription opioids who swallow opioids whole or chew then swallow.
Methods: College students completed an online questionnaire in August 2009 for the RADARS System College Survey Program, and were sampled equally from 4 US regions. Respondents answered questions about non-medical prescription opioid use and completed a standardized substance abuse screening instrument (DAST-10). DAST-10 scores and the reported number of past-month non-medical opioid use days were calculated as outcome indicators of non-medical use.
Results: Of 2066 survey participants, 124 (6%) indicated only swallowing, only chewing or both routes in the past 30 days of one or more opioid drugs. Of those, 102 (84%) reported swallowing whole and 22 reported chewing then swallowing. Independent samples Mann-Whitney U tests indicated significantly higher DAST-10 scores (p=.001) and past-month opioid non-medical use days (p=.003) for those who chewed then swallowed.
Conclusions: Between group differences on the DAST-10 and past-month opioid non-medical use days suggest that further exploration into chewing/swallowing behaviors are needed as chewing/swallowing may be an important indicator of a progression toward abuse tendencies and increased monthly non-medical opioid use.
Financial Support: Denver Health is a public non-profit organization providing data to industry, regulatory agencies and researchers through the RADARS System.

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HOW ACCURATE ARE ESTIMATES OF COMMUNITY ABUSE MADE BY LOCAL KEY INFORMANTS?

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Aims: Post-marketing surveillance of prescription medications often uses key informants as a primary source to estimate local abuse rates. We examined how key informant report corresponds to direct self-report of clients entering substance abuse treatment using data from the ASI-MV® Connect, a NAVIPPRO(TM) data stream, which collects data from a national network of treatment facilities.
Methods: Treatment facilities having relatively high and low rates of prescription opioid abuse were identified. Counselors at these treatment centers served as local key informants and estimated rates of abuse at their treatment center and in their community on an Internet survey.
Results: Significant differences in the expected direction were obtained for estimates of abuse rates by counselors from high- and low-rate facilities for OxyContin® ($p<0.001$), MS Contin® ($p=0.01$), Lortab® ($p=0.03$), and all prescription opioid products ($p=0.03$). Significance was obtained for counselors' estimates of community rates for OxyContin® ($p<0.001$), MS Contin® ($p=0.003$), and Lortab® ($p=0.008$), Vicodin® ($p=0.006$), Lorcet® ($p=0.006$), Dilaudid® ($p=0.04$), and all prescription opioids combined ($p=0.001$). Closer examination of the relationship of counselor estimates and rates as estimated by ASI-MV® Connect data revealed the relative ranking of these products to be high and significant, $rs = .84$ ($p<0.001$) for high abuse sites, and $rs = .95$ ($p<0.001$) for low abuse sites. Examination of actual estimated percentages, however, suggested that counselors tended to over-estimate rates of abuse of specific products compared to those rates obtained from direct client self-reports, particularly at low abuse-rate sites.
Conclusions: These data suggest that there is general correspondence between client self-report data and key informant reports of abuse despite some discrepancies. Such findings call into question the use of key informant data as primary surveillance data, although key informant reports are likely useful for verification purposes.
Financial Support: NIH Grant # DA024489 & Alpharma Pharmaceuticals LLC

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COMPUTERIZED MET/CBT FOR THE TREATMENT OF CANNABIS ABUSE AND DEPENDENCE.

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Aims: Cannabis Use Disorders pose a significant public health problem. A substantial number of individuals enroll in treatment with a primary diagnosis of Cannabis Abuse or Dependence. A potent intervention comprises motivational enhancement therapy (MET), cognitive-behavioral therapy (CBT), and contingency-management (CM). This project seeks to expand access, reduce cost, enhance fidelity, and improve the efficacy of this intervention by developing a computerized delivery system.
Methods: Thirty-six adults (M=32.8 yrs) participated in a non-randomized, 12-week pilot study comparing therapist-delivered (n=22) and computer-delivered (n=14) MET/CBT/CM. Both treatments included 9 MET/CBT sessions, twice weekly urinalysis monitoring, and an abstinence-based voucher reinforcement program.
Results: The number of MET/CBT sessions attended did not significantly differ between conditions (therapist: M=5.5; computer: M=6.6, p=.59). The longest duration of documented continuous abstinence (therapist: M=4.0 weeks: computer: M=4.1 weeks) and the overall percent of negative tests for cannabinoids (therapist: 34%; computer: 35%) also did not differ. Participant feedback regarding the computer sessions was positive. Across 13 items rated for each session, mean scores ranged from 7.2 to 8.7 on a 10-point scale.
Conclusions: This pilot study suggests that computerized delivery of MET/CBT is acceptable to outpatients and does not adversely impact compliance or outcomes achieved with MET/CBT/CM for Cannabis Abuse or Dependence. Such results are consistent with previous research examining computerized interventions for mental health and substance dependence disorders. Follow-up data and replication in randomized trials are needed to determine the reliability and longer-term effects of these outcomes. Computerized therapies have the potential to increase access to and reduce costs of efficacious treatments without sacrificing and possibly enhancing effectiveness.
Financial Support: NIDA:DA023526; Arkansas Biosciences Institute: Research Component of the Tobacco Settlement Proceeds Act

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BELIEFS ASSOCIATED WITH THE CONSUMPTION AND NON-CONSUMPTION OF TOBACCO IN SCHOOL STUDENTS IN SPAIN.

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Aims: To determine the beliefs associated with the consumption and no consumption of tobacco in school students in Spain.
Methods: The sample is 1324 students, 48% (n = 631) male, mean age 14.89 (SD=3.12). Was given a "Pre-Chat Survey on Drug Addiction; during 2007-2008", elaborated by the Plan Municipal de Drogodependencias (PMD. It was applied logistical regressions, using as covariable the age, with three dependent variables related to smoking tobacco: occasional consumption, daily consumption, and not to have consumed it.
Results: Among those that answer to consume occasionally (e.g. weekends), the associated beliefs are: to believe that "if you control nothing happens" (OR=3.66), it does not harms people of surroundings (OR=1.77), it does not cause problems (OR=2.54). Beliefs potentially associated with not having consumed the tobacco are: it has negative effects on health (OR=2.00), responding negatively "if you control nothing happens" (OR=2.84), it causes many accidents (labour, traffic, etc) (OR=1.88), causes family, labour, scholar or social problems (OR=1.78), harms people of surroundings (OR=1.96), it can cause mental illnesses (OR=1.80), sometimes can lead to commit crimes (OR=2.02), and to respond negatively that it does not cause problems (OR=3.05).
Conclusions: Sense of control on consumption, and beliefs that smoking does not harms people of surroundings and does not cause other problems are with high potential related to occasionally consumption in youth. Beliefs with potential to induce resiliency are that smoking causes negative effects on physical and mental health, causes problems or accidents in many life areas, and in people of surroundings; plus the perception that negative effects can occur also when is perceived that the consumption is control.
Financial Support: Collaboration agreement between the Plan Municipal de Drogodependencias (PMD), Ayuntamiento de Valencia and Univetsitat de València.

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ANXIOGENIC PROPERTIES OF COCAINE-PAIRED CUES IN RATS WITH A PRIOR HISTORY OF SELF-ADMINISTRATION.

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Aims: Clinical research demonstrates that cocaine-paired cues promote craving and may trigger relapse in abstinent users. More recent evidence suggests that these cues may elicit anxiety, and this anxiety may contribute to craving and subsequent relapse. Preclinical research has demonstrated an anxiogenic component of cocaine-paired cues, but only after noncontingent cocaine administration. The current studies sought to examine the anxiogenic nature of cocaine-paired contexts and discrete cues in rats that had previously self-administered cocaine.
Methods: Male rats lever pressed for IV cocaine (0.5 mg/kg/infusion) in 14 daily 2-hr sessions. Each infusion was paired with a 5 sec light+tone stimulus. Two days after self-administration, animals were tested for anxiety on the elevated plus maze (EPM) and the defensive burying paradigm (DBP). Animals were placed into one of three groups. Group 1 received no exposure to either the cocaine paired context or discrete cues before anxiety testing, Group 2 underwent exposure to the cocaine-paired context only, and Group 3 experienced the context and discrete cues.
Results: Exposure to either the cocaine paired context or discrete cues + context significantly increased anxiety in the DBP when compared to non-exposed controls ($p<0.05$). Exposed rats spent significantly more time burying the shock probe than non-exposed controls. Significant differences between groups were not detected in the EPM. There were no significant differences between animals exposed to the cues vs. the context on the EPM or DBP.
Conclusions: These data suggest that craving and relapse to cocaine-associated stimuli may be driven, in part, by the anxiogenic properties of these cues. Treatment directed at reducing such anxiety may be beneficial in craving reduction and relapse prevention.
Financial Support: These studies were conducted in accordance with the Guide for the Care and Use of Laboratory Animals, as adopted and promulgated by the National Institutes of Health. This research was supported by NIH grants RO1 DA21690 and P50 DA16511.

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EFFECT OF VARENICLINE ON CUE-INDUCED ALCOHOL CRAVING: A RANDOMIZED PLACEBO-CONTROLLED STUDY.

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Aims: Alcohol and tobacco consumption are highly comorbid disorders and heavy drinkers are more likely to be heavy smokers. Varenicline is a partial agonist at the alpha4beta2 nicotinic acetylcholine receptor that alleviates symptoms of craving and withdrawal while preventing nicotine from binding to the receptor, thereby reducing the reinforcing effects of nicotine. Recent studies have also shown varenicline to decrease alcohol self-administration in animal models and in one study of heavy-drinking smokers. AIMS: We assessed the effect of 2 weeks of treatment with varenicline vs. placebo on cue-induced craving for alcohol in daily smokers with either concurrent heavy alcohol use (n = 24) or light, social drinkers (n=24).
Methods: Eligible subjects participated in a total of three study visits over 21 days. On the first and last visit, repeated measures of self-reported questionnaires were given at four time-points: baseline; after one cigarette; neutral cue presentation; and tobacco-alcohol cue presentation. Participants also tracked their alcohol consumption in a daily diary.
Results: There was an overall decrease in weekly alcohol consumption in heavy drinkers over the study period, but there were no significant differences between treatment conditions. There was no significant change in cue-induced craving for alcohol (using visual analogue scales) in either the varenicline group (33.4 ± 6.7 to 21.3 ± 5.8; p=0.24) or placebo group (36.1 ± 10.2 to 30.5 ± 10.8; p=0.24).
Conclusions: Varenicline treatment had no significant effects on alcohol consumption or alcohol cue-induced craving compared to placebo in heavy drinkers. Results from a group of social drinkers will also be presented.
Financial Support: This study was supported by the Canadian Institutes of Health Research with a New emerging Team grant on Investigating comorbid substance use and psychiatric disorders: an integrated approach.

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ROUTE OF ADMINISTRATION PATTERNS ACROSS EXTENDED RELEASE PRESCRIPTION OPIOID PRODUCTS.

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Aims: Recently, the first of the abuse deterrent formulation (ADF) products, EMBEDA™ (an ADF version of extended release morphine), was approved and marketed, albeit without abuse deterrent labeling. ADFs attempt to prevent or lessen intentional abuse to get high. Many ADFs are designed to resist physical manipulation thereby limiting abuse through unintended routes of administration (ROAs). These tamper resistant formulations employ barriers to extracting the active ingredient of extended release opioid analgesics, making injecting, snorting, chewing, etc. more difficult. Evaluation of an ADF's success in providing such a barrier requires an understanding of ROA patterns for existing products.
Methods: The ASI-MV® Connect, a NAVIPPRO™ data stream, collects product-specific abuse of prescription opioids in the past 30 days, including routes of administration from adult clients in treatment in a national network of substance abuse treatment centers. 6,363 (9%) of 68,237 unique clients assessed between May 2007 and November 2009 reported abusing an opioid analgesic.
Results: Review of product-specific ROAs revealed that OxyContin was injected (28%) less than Dilaudid (59%; $p < .001$) and less than morphine extended release products as a class (53%; $p < .001$). However, within the morphine ER class, MSContin was injected significantly less often (37%) than either KADIAN (64%) or Avinza (66%; $p<.001$). OxyContin was significantly more often snorted (50%) than Dilaudid (.5%), MSContin (30%), KADIAN (16%) or Avinza (9%). While MSContin was snorted more often KADIAN and Avinza ($p =.001$). OxyContin was chewed (16%) significantly more often than KADIAN (8%; $p=.002$) and Avinza (3%; $p<.001$), but not MSContin (14%).
Conclusions: These findings suggest that different extended release products have characteristic ROA patterns. Evaluations an ADF's tamper resistant qualities should take into account the characteristic ROA pattern of its parent product. Thus, EMBEDA™ should be expected to reduce the high injection rates of KADIAN, but not necessarily reduce a low-rate ROA like chewing.
Financial Support: Inflexxion, Inc.

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EFFECT OF AUDIO COMPUTER-ASSISTED SELF-INTERVIEW ON SELF-REPORTED DRUG USE AND RISKY HEALTH BEHAVIORS.

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Aims: The sensitive nature of HIV risk behaviors poses a challenge for accurate measurement in both epidemiological and clinical contexts. This study sought to determine whether audio computer-assisted self-interviewing (ACASI) is more effective than face-to-face interview methods in eliciting reliable and valid information regarding stigmatized and sensitive behaviors.
Methods: METHODS: Patients admitted to a drug-free outpatient substance abuse treatment program (n=177) were given a face-to-face interview about their drug use and sex risk behaviors using the TCU HIV/AIDS Risk Assessment. Within a week, the same interview was re-administered using the ACASI format.
Results: The findings indicate potentially important interview mode differences in reported high risk behaviors. In the ACASI format, participants reported higher frequency of having sex without a condom while trading for drugs, money, or gifts ($p<.01$). Furthermore, no male participants reported having male sex partners in the face-to-face interview, but the ACASI identified five males who reported engaging in male/male sex ($p<.05$). However, an idiosyncrasy associated with ACASI relative to question complexity is indicated by higher reported frequency of injection drug use in the face-to-face interview ($p<.001$), which is believed to be due to probing by the interviewer.
Conclusions: ACASI was able to capture more reports of sensitive and stigmatized behaviors such as engaging in sex trade and men having sex with men. These behaviors parallel the major transmission categories for HIV infection. ACASI has the potential to yield increased self-disclosure of sensitive risk behaviors relative to face-to-face interviewing. These findings have important public health implications with respect to risk behavior screening and surveillance.
Financial Support: R01 DA011402 (PI: Elizabeth Katz)

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IS RECENT MONOGAMY OR BEING IN A COMMITTED RELATIONSHIP A MARKER FOR LOW SEXUAL RISK IN MEN IN SUBSTANCE ABUSE TREATMENT?

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Aims: Determine the extent to which recent monogamy and/or being in a committed relationship serve as markers for low sexual risk among men in substance abuse treatment.
Methods: Men in methadone maintenance (n=226) or psychosocial outpatient (n=134) treatment participating in the NIDA Clinical Trials Network "Real Men Are Safe" protocol assessed by audio computer assisted structured interview at all time points (baseline, 3 & 6 month follow up) served as participants. Self reported behaviors included number of sexual partners and type of relationship.
Results: The rate of self-reported monogamy in the prior 90 days was stable across assessments (55.3%, 53.6%. 58.3%). However, at each assessment 13-17% of monogamous men identified their single partner as a casual partner. Only 123 (34.2%) men reported being monogamous at every assessment. Of these, 20 (16.3%) reported being monogamous with different partners across assessments. Of the men who reported having multiple sex partners in the 90 days prior to each assessment (35.7%, 31.4%, 23.9%), slightly over half at each assessment also reported having a regular partner in a committed relationship.
Conclusions: Clinicians and researchers should consider individual relationship context and behavior and avoid assuming that recent monogamy or being in a committed relationship automatically denotes lower risk.
Financial Support: Supported by National Institute on Drug Abuse (NIDA) Clinical Trials Network (CTN) grants: U10 DA13714 (Dennis Donovan, PI), U10 DA13035 (Edward Nunes, PI).

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VALIDITY OF A BEHAVIORAL TASK OF NEGATIVE REINFORCEMENT UNDERLYING RISKY ALCOHOL USE.

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Aims: Negative reinforcement has been hypothesized to be a crucial process underlying the development of risky alcohol use behaviors. However, no behavioral tasks have yet been created to examine an adolescent's propensity to act in a risky manner to avoid negative feelings/experiences (i.e., negative reinforcement). The current study presents a newly developed negative reinforcement-based behavioral task for assessing this fundamental pathway to risky alcohol use.
Methods: A sample of 145 college freshmen, ages 18-20, was recruited. Participants completed questionnaires on depressive symptoms, emotion regulation, state/trait anxiety, and an interview regarding alcohol use. The new behavioral task, the Maryland Resource for the Behavioral Understanding of Reinforcement of Negative Stimuli (MR_BURNS), was developed as a negative reinforcement mirror to the positive reinforcement based Balloon Analogue Risk Task (BART). The MR_BURNS creates a situation in which the participant can select a number of pumps to inflate a balloon to reduce the duration of an aversive noise but with the consequence of lowering the probability of receiving a monetary reward later.
Results: About 95% of the sample used alcohol in the last three months and 53% engaged in binge drinking in the past month. Establishing construct validity, higher number of pumps correlated significantly with measures of negative mood and emotional vulnerability including depressive symptoms ($r = .33$, $p < .01$), emotion dysregulation ($r = .37$, $p < .01$), state anxiety ($r = .24$, $p < .05$), and trait anxiety ($r = .24$, $p < .05$). Number of pumps also correlated as expected with younger age of first binge drinking ($r = -.29$, $p < .05$). The number of binges in the past month only significantly correlated with the number of pumps in males ($r = .31$, $p < .05$).
Conclusions: The MR_BURNS demonstrated initial construct validity via correlations with questionnaires related to negative affect and self-reported risky alcohol use, suggesting the utility of the task as a measure of negative reinforcement processes that may underlie the development of problem alcohol use.
Financial Support: Funded by the NIAAA.

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A NATIONAL PRIMARY CARE AND PREVENTION SYSTEM FOR ADDICTIONS IN MEXICO.

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Aims: To present and analyse the current official "Mexican model" for prevention and detection of addiction problems.
Results: By the end of 2007 the Mexican government launched the "National strategy for prevention and treatment of addictions" which included the construction of 310 primary care addiction clinics with the aim of organizing a "National network for addiction treatment". General description: Federal and state funded; community-based, strategic locations; prevention oriented.
Target population: early users, experimenters, problem drinkers(clients with addiction and dependence problems are referred to specialized treatment clinics).
Organization: each clinic has 1-2 outpatient clinical rooms, one social work office, one meeting or multipurpose room. Some have other facilities:sports.
Human resources: at least each clinic has a coordinator, one or two psychologists, one social worker. Some clinics have one medical doctor, which may be a psychiatrist.
Programs: the general approach is through a cognitive-behavioral program for early detection and early intervention including motivational interviewing. In our state (Jalisco) they are running three prevention programs, two prevention-detection programs, and one harm reduction program.
Strengths: there is a potential for high-quality preventive interventions.
Weaknesses: differences in local organization, population attended, heterogeneity in training and college degrees of personnel, in levels of expertise, in previous local basal level of organization, excessive or scarce number of programs and activities,lack of an electronic data system.
Conclusions: These are the first primary care addiction clinics created in Mexico.
Monitoring of different performance parameters (regional and nationally) at different time intervals will ensure an objective method of evaluation. There seems to be a high potential for research on prevention programs and for organizing clinical research and epidemiology networks.
Financial Support: None.

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ON-SITE HEPATITIS C TREATMENT IN METHADONE MAINTENANCE: DESCRIPTION OF A MODEL OF CARE.

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Aims: To describe a model of providing hepatitis C (HCV) medical care on-site in methadone maintenance treatment (MMT).
Methods: Opioid-dependent patients in MMT with chronic HCV infection were randomly assigned to HCV care on-site (MMT clinic) or off-site (GI clinic) as part of a NIDA-funded study. 111 patients completed randomization of whom 55 were assigned to on-site HCV treatment.
Results: Patients assigned to on-site HCV care received interventions intended to facilitate engagement and adherence. Mid-level medical providers trained in HCV care management provided all medical evaluations and treatment interventions following AASLD HCV treatment recommendations. A hepatologist provided HCV treatment supervision and an addiction psychiatrist provided psychiatric supervision and ongoing consultation. All patients underwent a full medical evaluation and psychiatric assessment with a structured clinical psychiatric interview prior to initiation of HCV treatment. All aspects of on-site medical and psychiatric care were coordinated with the MMT clinic staff. HCV appointment reminders were provided on the day prior to and the day of HCV medical appointments utilizing the MMT check-in desk and nursing station. HCV medical treatment staff were readily accessible on a daily basis within the MMT setting to provide reminders and answer questions. On-site laboratory testing, assistance with pegylated interferon injections (if desired), and drop-in access with early morning hours were made available for the convenience of on-site patients. HCV disease and treatment educational sessions were routinely provided to on-site MMT patients as well as to MMT staff. Significantly more on-site vs. off-site subjects attended initial HCV medical visit ($p \leq 0.001$) and started HCV treatment ($p \leq 0.05$).
Conclusions: A model of on-site HCV medical care provided in the MMT setting employing a variety of supportive interventions was associated with significantly more subjects in the On-site condition completing the HCV evaluation process and starting HCV treatment.
Financial Support: NIDA R01 DA 016764

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DISCRIMINATIVE STIMULUS EFFECTS OF THE SYNTHETIC HALLUCINOGEN N,N-DIISOPROPYLTRYPTAMINE.

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Aims: Classic hallucinogens like LSD and DMT are all known to bind to serotonin 5HT2A and 5HT2C receptors. A newer synthetic hallucinogen, N,N-diisopropyltryptamine (DiPT), is known predominantly for its production of auditory hallucinations. Previous research using radioligand displacement binding in HEK cells showed that DiPT also binds to the 5HT2A receptor. Unlike other hallucinogens, DiPT also acts as an antagonist at 5HT3 receptors in electrophysiological studies.
Methods: Two-lever drug discrimination was used to investigate potential mechanisms of action of DiPT in vivo. Adult male rats were trained to discriminate DiPT (5 mg/kg, 15 min) from saline under a FR10 schedule. Training sessions occurred in a double alternating fashion. Training criteria was 85% of responses on the injection-correct lever for both the first reinforcer and total session for nine out of ten consecutive days. The discriminative stimulus effects of DiPT was also tested in rats trained to discriminate LSD, DOM, DMT, MDMA, methamphetamine, and cocaine.
Results: Rats were successfully trained to discriminate 5 mg/kg of DiPT from saline with a 15 minute pretreatment. An average of 60 training sessions (30 drug and 30 saline) were required to meet criterion. In rats trained to discriminate various drugs, DiPT fully substituted for DOM and DMT, partially for LSD, and failed to substitute for methamphetamine, cocaine and MDMA.
Conclusions: DiPT produces discriminable stimulus effects which are at least partially similar to those of other hallucinogens. Research on the mechanisms of DiPT may give further insight into the mechanisms of auditory versus visual hallucinogens, which may be of direct relevance to understanding why humans use hallucinogens and in the mechanism of auditory hallucinations in schizophrenia.
Financial Support: Supported by NIH N01DA-7-8872.

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PATIENT AND STAFF PERSPECTIVES ON MANAGING ADDICTION AS A CHRONIC DISEASE.

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Aims: To describe patient and staff perceptions of managing addiction as a chronic disease through the use of a Long-Term Recovery Management (LTRM) model that combines facilitated therapeutic alliance, contingency management, and the community reinforcement approach.
Methods: Four focus groups were conducted with 10 treatment staff and 23 clients in outpatient treatment to assess their views on managing addiction as a chronic disease. Participants were asked to comment on positive and negative aspects of LTRM. Participants completed an informed consent. Audio-recorded interviews were transcribed and coded.
Results: Results: Among patients, 14 were white, and 9 were African-American; 12 were female. Age ranged from 21-63. Patients and staff highlighted the benefits of long-term care to manage addiction. One patient said, "Your requirements to be in something that's committed, that's long-term, would be great. I'm not used to that. I'm used to this going to the treatment centers, and once I'm done, I'm done." Patients emphasized the importance of being able to develop a trusting relationship with a counselor over time. Staff expressed concern about the challenges that transient patients might pose to Recovery Managers. Patients were delighted with the contingency management component of LTRM, but commented on the kinds of prizes that should be included. Patients also commented on the composition of the LTRM groups in terms of gender relations and relapse among participants.
Conclusions: Conclusions: Staff and patients expressed enthusiasm for the long-term management of addiction and the LTRM model. Patients suggested modifications that were incorporated into a pilot feasibility study of LTRM and a fully powered effectiveness trial comparing recovery trajectories among 200 adults randomly assigned to LTRM or Treatment as Usual.
Financial Support: Wright State University, Maryhaven, National Institute on Drug Abuse, Grant No. 1 RC1 DA028467-01.

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THE INTEGRATION OF DRUG AND HIV SERVICES AT A DRUG TREATMENT CENTER IN DURBAN, SOUTH AFRICA.

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Aims: Formative work conducted between 2005 and 2007 indicated that drug use directly increases users' risk for contracting HIV through influencing their sexual and injection related risk behaviors. It highlighted the need to integrate HIV and drug prevention/treatment efforts.
Methods: In 2007, in collaboration with a local NGO (an in and out-patient drug treatment center), an initiative began to roll out a number of harm reduction strategies for drug users in Durban. In 2008, the second year of this initiative was implemented. The intervention activities include setting up targeted condom and VCT service outlets, community outreach, provision of voluntary counselling and testing (VCT) for drug-using populations and setting up referral mechanisms for drug users in need of other services. The MRC is responsible for the regular monitoring of activities undertaken by the treatment center.
Results: In the first two years of the intervention, 1908 drug users were recruited through outreach activities. A further 495 received VCT and 125 were referred to other services. At baseline, condom use varied, with 40.3% using condoms zero times in Year 1 and 51.5% using condoms zero times in Year 2 of the intervention. Almost all were poly-drug users in Year 1 (97.3%) with considerably less poly-drug use in Year 2(51.3%). Most used substances during sex (76.9% in Year 1, 61.1% in Year 2). Outreach workers assisted drug users in developing risk reduction strategies, and reached 130 for follow-up. A high proportion of drug users received VCT (86.5% in Year 1, 77.5% in Year 2). A higher proportion reported using condoms every time that they engaged in sex in Year 1 (73.1%) than in Year 2 (57.7%).
Conclusions: The intervention to date has demonstrated willingness of the NGO to broaden its service delivery activities and uptake of VCT and other services by drug-using clients. Improved integration of drug treatment, HIV intervention and other services has also occurred, although challenges existed in both Year 1 and 2.
Financial Support: CDC, PEPFAR

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METHODS TO EFFICIENTLY RECRUIT AND EFFECTIVELY RETAIN UNMOTIVATED SMOKERS IN A NATIONWIDE RANDOMIZED CLINICAL TRIAL.

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Aims: For unmotivated smokers (i.e., those unwilling or unable to make a quit attempt), novel strategies for cessation induction are necessary. We describe the sampling and recruitment methods for an ongoing nationwide, single site, telephone-based clinical trial for cessation induction.
Methods: Smokers are recruited proactively via online channels through coordinated efforts with a national market research firm. Potential participants complete a health screener to determine study eligibility. A "behavioral filter" is then used to identify and separate motivated vs. unmotivated smokers, the latter of whom are formally invited into the trial, mailed a consent form, and asked to reply. Consented participants are randomized to one of two treatment conditions designed to promote self-efficacy and motivation to quit: 1) Practice Quit Attempt (PQA) or 2) PQA + samples of nicotine replacement therapy. Outcome measures tested over a 6-month follow-up include additional quit attempts and abstinence, as well as hypothesized mediators of treatment effects.
Results: During the 11 month recruitment period to date, 1899 smokers have been successfully screened and identified as eligible, of whom 943 (50%) have returned a consent, of whom 768 (81%) have been enrolled. Recruitment of non-white smokers has been moderate (11%). Retention rates to date are as follows: 91% of all scheduled calls and 89% of all follow-up calls completed.
Conclusions: High retention rates can be attributed to: 1) coordinated and perseverant calling efforts by research team, 2) a structured database to provide detailed scheduling and reminders for each study contact, and 3) moderate reimbursement (up to $100) for continued participation. Full details of study flow and procedures, including strategies for enhanced retention, will be available for conference presentation. This recruitment methodology may be viable to other researchers engaged in large, telephone based clinical trials.
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INTERACTIONS BETWEEN DELAY DISCOUNTING AND DRD4 GENOTYPE ON SMOKING FOLLOWING A TREATMENT INTERVENTION.

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Aims: Tobacco use is the second leading risk factor for death worldwide. Several factors such as the magnitude of nicotine dependence, impulsivity, and genotype have been shown to influence the likelihood of future abstinence. The aim of this study was to examine the relationships and interactions of delay discounting and DRD4 genotype on abstinence following a smoking cessation intervention.
Methods: Adult smokers who wanted to quit smoking were enrolled (N=97). Participants completed a range of pre-treatment assessments, a six-week course of group cognitive behavioral therapy, and follow-up assessments.
Results: Lower Fagerstrom scores at baseline and the presence of a long DRD4 allele were significant independent predictors of abstinence over the course of the study ($p<.05$). Lower rates of delay discounting at week 4 were also associated with abstinence over the course of the study, but this relationship did not reach statistical significance ($p=.093$). An interaction model that allowed the effect of week 4 discounting to vary with the DRD4 genotype showed that a unit decrease in discounting had more of an effect on the odds of abstinence for participants with a short allele than for those with a long allele ($p=.006$). A one-unit decrease in week 4 discounting for participants with a short allele corresponded to a 1.418 increase in the odds of abstinence (CI95%: 1.105–1.818; $p=.007$), whereas there was no discounting effect for those with the long allele ($p=.346$).
Conclusions: These results suggest that changes in discounting following a smoking cessation intervention are associated with abstinence and are modulated by DRD4 genotype.
Financial Support: Supported by USPHS Grants DA022386 and AA016936.

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DRUG LIFE CYCLE SITUATION AWARENESS: A NOVEL APPROACH TO SIGNAL DETECTION AND POST-MARKETING SURVEILLANCE OF PRESCRIPTION DRUGS.

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Aims: We propose a conceptual and practical approach to signal detection and post-marketing surveillance of newly marketed drugs using principles of situation awareness along the drug life cycle. Introduction of abuse deterrent prescription opioid formulations requires methods of assessing and interpreting the effectiveness of REMS for these products. A critical component will be the ability to identify the behavior of these drugs in the real world. We describe an approach that adopts situation awareness as a model to evaluate misuse, abuse, and diversion along a drug's life cycle.
Methods: Using data from NAVIPPRO™, we identify separate phases of a drug's life cycle and corresponding patterns of abuse behavior.
Results: Three phases corresponding to a drug's prescription volume and time on the market are observed: 1) immediate post-launch/low prescription volume, 2) early market penetration/increasing prescription volume; and 3) established market share with stable prescription volume. Situation awareness and signal detection vary along this continuum moving from an event focused approach to comparative analysis with other drug products and lastly determination of departures from an established baseline profile for the target drug.
Conclusions: This approach is rooted in the concept that signal detection should draw from important event cues and integration of information from disparate information sources to form situation intelligence for a drug. Employing principles of situation awareness moves the concept of signal detection beyond traditional post-marketing surveillance approaches of defining a signal as an a priori quantitative benchmark. Given the paucity of data when a new drug comes to market, this model may allow for predicting future behavior of newly marketed drugs and more timely identification of emerging trends based on the perception of significant event cues. This approach has implications for evaluating the effectiveness of REMS and shows promise for assessing a drug's abuse potential when data are sparse and not amenable to traditional epidemiologic analysis.
Financial Support: Inflexxion, Inc.

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RELATIVE EXPRESSION OF THE FIVE SOMATOSTATIN RECEPTORS MRNA IN THE CAUDATE PUTAMEN OF C57BL/6J AND 129P3/J MICE: STRAIN AND HEROIN EFFECTS.

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Aims: C57BL/6J (C57) and 129P3/J (129) mice differ in their behavioral response to cocaine or heroin. Somatostatin (SRIF) interacts with the dopaminergic system and has a dose-dependent behavioral effect including increased levels of locomotor activity and expression of stereotypy. SRIF acts through binding to membrane bound G protein coupled receptors. There are five distinct somatostatin receptors (SSTR 1-5), each encoded by its own gene. Morphine binds to SSTR-2. Heterodimers within and between SSTRs, dopaminergic and opioidergic receptors are found. To further characterize the C57and 129 mouse strains, we examined mRNA levels of the five SSTRs within the caudate putamen (CPu) in C57 and 129 mice following various doses of heroin.
Methods: 125 male mice (55 C57s and 70 129s) were assigned to treatment groups given different doses of heroin (0, 1.25, 2.5, 5, 10 or 20 mg/kg). Animals received injections of heroin or saline on alternate days for a total of 8 days. Animals were sacrificed and RNA was isolated from the caudate putamen, nucleus accumbens, frontal cortex, hypothalamus and a region containing both the substantia nigra and the ventral tegmental area. mRNA levels of SSTR 1-5 were measured in the CPu with real time PCR. SSTR-3 mRNA was measured in all brain regions. Samples were assayed in duplicate and data were normalized to GAPDH.
Results: The relative expression levels of the five SSTR mRNAs differed between the two strains. Interestingly, in 129 mice SSTR-3 mRNA was not detected in any brain region examined. SSTR-2 and -4 mRNA levels were significantly greater in the CPu of 129 mice than in C57 animals. Heroin administration had a dose dependent effect on the levels of SSTR-1 and -3 mRNAs in the CPu.
Conclusions: These results demonstrate both strain differences in the expression of specific SSTR mRNAs and a heroin-induced dose-dependent elevation of SSTR-1 and -3 mRNAs in the mouse caudate putamen.
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NICOTINE DEPENDENCE AMONG VERY RECENT-ONSET CIGARETTE SMOKERS IN THE USA.

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Aims: We study rapid emergence of nicotine dependence (ND) among smokers with fewer than 90 days of cigarette-smoking (very recent-onset cigarette smokers, VROCS), seeking characteristics associated with risk of becoming dependent soon after smoking onset. Use of menthol cigarettes and age of onset were of particular interest
Methods: Data are from the National Surveys on Drug Use and Health (NSDUH), 2004-2007 (aggregate n=222,221), with the Nicotine Dependence Syndrome Scale and the Fagerstrom Test as ND assessments of the 450 VROCS in the NSDUH nationally representative samples. Estimated associations are from multiple logistic regression analyses for complex sample data.
Results: Among the 450 VROCS, 3/4ths continued to smoke; an estimated seven percent qualified as ND cases (95% confidence interval, CI = 4%, 10%). With sex and age of smoking onset held constant, and with non-Hispanic Whites as reference, there was a robust increased risk of rapid-onset ND among African-American VROCS ($p<0.05$). Early adolescent-onset smokers also had excess ND risk ($p<0.05$). There was no excess risk associated with having smoked menthol cigarettes.
Conclusions: For an estimated one in 14 cigarette smokers, nicotine dependence emerges quite rapidly, especially for African-American smokers, and independently, for early adolescent smokers. We had expected menthol-associated excess ND risk, but did not find it in these data.
Financial Support: NIDA awards K05DA015799, D43TW05819.

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VARIATIONS IN SEXUAL RISK BEHAVIORS ASSOCIATED WITH SEXUALLY TRANSMITTED DISEASES AMONG AFRICAN-AMERICAN AND WHITE FEMALE DRUG USERS.

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Aims: To examine differences in demographics, drug use, and sexual behaviors and their associations with STDs among African-American and white illicit drug-using women.
Methods: Self-reported rates of drug use, sexual risk behaviors, and STDs, including Gonorrhea, syphilis, Chlamydia, genital herpes, genital warts, or trichomoniasis were assessed among 278 drug-using women (62.6% African-American, 37.4% white). Correlates of ever having any one of the six self-reported STDs were tested separately for African-American and white participants.
Results: A higher proportion of African-American women (50.6%) than white women (28.4%) reported a lifetime STD. African-American and white women also differed in terms of their demographic characteristics, drug use behaviors, and correlates of lifetime STDs, but not sexual risk behaviors. Multiple logistic regression findings revealed that African-American illicit drug-using women who had ever had a casual sex partner had nearly four times greater odds [Adjusted odds ratio (AOR) = 3.93, 95% confidence interval (CI) =1.88, 8.20, $p<.01$] of having a lifetime STD compared to African-American drug-using women without a casual sex partner history. In contrast, white women who had ever traded sex for money had approximately three times greater odds (AOR=3.33, 95% CI=1.15, 9.69, $p<.05$) of having a lifetime STD compared to white drug-using women who had not traded sex for money.
Conclusions: Findings suggest African-American illicit drug-using women have greater risk for STDs than their white counterparts despite less risky behavior (i.e. ever having a casual sex partner vs. trading sex for money) which is consistent with studies on women nationally.
Financial Support: This study was supported by grants R01DA014498, T32DA007292, and R03DA024981 from the National Institute on Drug Abuse.

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TYPE OF CONTRACEPTION METHOD USED AT LAST INTERCOURSE AND HEALTH RISK BEHAVIORS AMONG US ADOLESCENTS.

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Aims: To examine associations between health risk behaviors and various contraception methods including dual method (condoms plus another contraceptive method), condoms only, depot medroxyprogesterone acetate (DMPA, marketed as Depo Provera), oral contraceptives (birth control pills), withdrawal, and nonuse of any method at last sexual intercourse among US adolescents.
Methods: Participants were sexually active Caucasian, African American, and Hispanic high school students (9th-12th grade, weighted n = 24,638) who participated in the 1999-2007 Youth Risk Behavior Surveillance System. Multinomial multivariable logistic regression analyses were performed to identify variables associated with type of contraceptive used at last sexual intercourse.
Results: Among males, substance use (i.e., having used all of alcohol, cigarettes, marijuana, and cocaine) was associated with nonuse of any method (odds ratio [OR]: 2.4, 95% confidence interval [CI]: 1.7-3.5) or withdrawal (OR: 2.6 CI: 1.6-4.3) compared to use of condoms only. In contrast, females with higher number of sexual partners were more likely to use withdrawal (OR: 2.9 CI: 2.1-3.9 for 6+ sexual partners versus 1 sexual partner) or contraception methods that offer no STI protection (i.e., birth control pills, OR: 1.8 CI: 1.4-2.5, and DMPA, OR: 2.6 CI: 1.6-4.2, for 6+ sexual partners versus 1 sexual partner).
Conclusions: Prevention efforts should focus on adolescents who are at highest risk of STIs and unplanned pregnancies.
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COMORBIDITY AMONG DRUG USE, ANXIETY, DEPRESSION, AND CONDUCT DISORDER FROM ADOLESCENCE TO YOUNG ADULTHOOD IN A POPULATION-BASED PROSPECTIVE COHORT STUDY.

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Aims: The relations between substance use and mental health problems over the lifecourse remain largely unknown. We assessed concurrent and sequential comorbidity among substance use and symptoms of anxiety and depression (ANX/DEP), and conduct disorder (CD) from adolescence to young adulthood.
Methods: We used data from the Project on Human Development in Chicago Neighborhoods. Respondents were 12-15 years old in 1994-1997 (early adolescence) and were e-interviewed in 1997-2000 (late adolescence) and in 2000-2002 (young adulthood) (n=1517). Analyses: We applied clustered multivariate transition models and used pairwise odds ratios to quantify concurrent comorbidity.
Results: We found that: (a) SU and CD co-occurred at all ages studied [Wave 1 ΔPOR=3.3 (95% CI: 2.3, 4.7); Wave 2 ΔPOR=1.9 (95% CI: 1.3, 2.8); Wave 3 ΔPOR=2.5 (95% CI: 1.3, 4.8)]; (b) using drugs in early adolescence was associated with a higher likelihood of reporting CD in late adolescence (P=0.6) and the latter was associated with using drugs in young adulthood (P=0.4); (c) using drugs in early adolescence was also associated with ANX/DEP in late adolescence (P=0.7); (d) ANX/DEP and CD were likely to co-occur in mid- and late-adolescence [Wave 1 ΔPOR=2.0 (95% CI: 1.2, 3.2); Wave 2 ΔPOR=1.6 (95% CI: 1.1, 2.3)]; and (e) CD in early adolescence predicted ANX/DEP in late adolescence [Transition probability (P) = 0.4], while ANX/DEP in late adolescence predicted CD in young adulthood (P=0.3).
Conclusions: Future research on the determinants of comorbidity can make a critical contribution to the design of health policies that can effectively reduce the burden of comorbid drug use and mental disorders.
Financial Support: Funding for this work was provided by the Robert Wood Johnson Foundation Health and Society Scholars Program and by National Institutes of Health grants including grants DA 022720, MH 082729 and MH 078152.

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IS CANNABIS AN APHRODISIAC OR SEXUAL SUPPRESSANT? A VIEW FROM THE PAST.

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Aims: In the 1890s, the Indian Hemp Drugs Commission (IHDC) surveyed hundreds of key informants about health effects of cannabis consumption and one focal point was to test propositions about the relationship between cannabis and sexual function, in light of many centuries of experience with cannabis in traditional Indian medical practice. The aim of this research is to quantitatively analyze these surveys to characterize this relationship.
Methods: For this project, a random sample of 117 records was drawn from the IHDC roster of 251 key informants in the province of Bengal, India. The Commission's informants were medical professionals, administrators, revenue officials, missionaries, and others judged to be knowledgeable about cannabis in Bengal. Two of us independently coded the texts, and conferenced all discrepancies until reconciliation. The responses were tabulated for evidence of patterns linking cannabis use with sexual function and dysfunction.
Results: 86% of the key informants were knowledgeable about the use of cannabis as an aphrodisiac. Just over one-half asserted that moderate use of cannabis as an aphrodisiac was not more detrimental to health than the consumption of other drugs, but excessive cannabis use was considered to be both damaging to health, and to lead to sexual impotence (85% and 77% of the sample, respectively). Informants from Great Britain were more likely to assert health-damaging effects of cannabis, relative to other drugs; fewer Indian informants made this assertion (86% versus 45%). With respect to cannabis-caused impotence, 64% of the British informants and only 36% of the Indian informants knew of evidence on this adverse effect.
Conclusions: This project's evaluation of the historical IHDC records illuminates an interesting view of cannabis-associated benefits and potential hazards in the domain of sexual medicine. The traditional use of cannabis in India as an aphrodisiac appears to be balanced by concern about potential sexual dysfunction.
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ALTERED DEFAULT MODE RESTING BRAIN NETWORK IN HIV-INFECTED INDIVIDUALS.

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Aims: Approximately 50% of patients infected with human Immunodeficiency virus (HIV-1) still have associated cognitive disorders (HAND). The brain activation during cognitive tasks on blood-oxygenation-level-dependent functional MRI (fMRI) of HIV infected individuals is often abnormal prior to manifestation of cognitive symptoms. However, whether the resting state (or the "default mode") brain networks are also altered is unknown, and was evaluated.
Methods: 37 HIV+ subjects (ages 51.3 ±9.0 years, 15.1±2.7 years education) and 38 HIV-seronegative controls (ages 52.9 ±13.2 and 15.2 ±2.5 years) were studied. Each participant was scanned with eyes closed on a 3T Siemens Trio scanner. Single-shot gradient-echo echo-planar MRI (TE/TR=30/3000ms, 3 mm slices, ~42 axial slices, 642 matrix, 20cm FOV, 120 NEX) was performed with motion and distortion corrections, and motion monitoring in real-time to assure <1mm translations and <1 rotations. The Melodic FSL software tool was used to perform Probabilistic Independent Component Analysis (ICA) on the fMRI data using linear models.
Results: Ten ICA components showed significant activation in one or both subject groups. Despite eye closure, the visual and visual attention networks were activated in both groups ($p<0.0001$). The control group showed significant activation in the left parietal lobe ($p<0.04$), while the HIV group tended to show activation in the right parietal lobe ($p<0.08$). Furthermore, the HIV subjects, but not the controls, activated the dorsal attentional network in the parietal regions ($p<0.04$) and the auditory cortices ($p<0.02$).
Conclusions: These patterns of altered default mode networks are consistent with the neuroadaptation seen on prior fMRI studies in HIV patients, and may be associated with neuroinflammation. Further analyses will evaluate those with and without HAND, and the relationship with cognitive performance and clinical data.
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EMOTIONAL AND PHYSIOLOGICAL RESPONSE TO STRESS AND SUBSTANCE USE IN ADOLESCENTS.

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Aims: Aims: Adolescence is a critical period for the development of emotional arousal and regulation. Also during adolescence, rates of substance use increase. The present study aimed to examine relations between adolescents' substance use and their physiological and emotional responses to a stressor. We predicted that greater arousal in response to stress would be associated with substance use.
Methods: Methods: Participants were 78 14-17 year olds (50% boys, 80% African-American) drawn from a larger longitudinal study of high risk low-income youth. Youth participated in the Triers Social Stress Test, a standardized social stressor. Salivary cortisol, HR, BP, and self-reported anxiety were measured before, during, and at repeated time points after the stressor. Facial, vocal, and postural emotion expressions during the stressor were coded from videotape, using a system based on emotion theory (e.g., Ekman & Friesen, 1975). Adolescents' current substance use was based on self-report, urine toxicology, and breathalyzer. Substance users were not different from non-users in gender, race, or maternal education level.
Results: Results: For heart rate, a significant substance use group X time point interaction was found ($F[6, 433.40) = 2.51$, $p < .05$, indicating that substance users had higher heart rate during the stressor than non-users, $F(1, 129.23) = 4.80$, $p < .05$). For observed anxiety, substance users had lower anxiety expression during the stressor than non substance users, $t(64.59$ – equal var not assumed) $= 2.40$, $p < .05$.
Conclusions: Conclusion: Substance-using adolescents had higher heart rate arousal, but did not show that arousal in their emotion expression. This finding is consistent with research finding that emotion "suppression" is associated with negative health outcomes (John & Gross, 2004), including substance use initiation in youth.
Financial Support: Supported by NIH grants: P50-DA16556, K01-DA024759, & R01-DA06025.

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BEHAVIORAL DRUG AND HIV RISK REDUCTION COUNSELING IN MMT PROGRAMS IN WUHAN CHINA.

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Aims: We evaluated whether the efficacy of a standard methadone maintenance treatment (MMT) is improved by providing additional manual-guided behavioral drug and HIV risk reduction counseling (BDRC).
Methods: A 6 month pilot clinical trial, with 3 months of active treatment phase and 3 months of follow-up, enrolling heroin dependent individuals (N=45) was conducted in two MMT clinics in Wuhan China. All study participants received standard MMT services, consisting of daily medication at the clinics and infrequent additional services on demand (e.g., visits/discussion with physicians or MMT nurses). Participants in the MMT+BDRC group additionally received weekly individual counseling provided by trained drug counselors. The first 8 study participants, 4 at each MMT clinic,2 for each counselor, were assigned to MMT+BDRC condition in order to give the nurse counselors opportunity to continue improving their mastery of the newly learned BDRC intervention. The remaining 37 participants were randomly assigned to either standard MMT or MMT+BDRC. Primary outcome measures included reductions of illicit opiate use (based on urine tests) and HIV risk behaviors.
Results: Participants were 85% male; mean (SD) age 36.5 (6.9) years; there were no significant baseline differences between the two groups. Participants in MMT+BDRC achieved both greater reductions of illicit opiate use, as indicated by the overall proportion of opiate negative test results during the active phase of the study (74% vs. 55% $p< 0.01$) and greater reductions of HIV risk behaviors at the end of the active phase of the study, as indicated by the scores on a short version of the AIDS Risk Inventory. 83.3% in the MMT+BDRC group and 76.2% in the standard MMT group were still actively participating in their MMT programs at 6 months.
Conclusions: BDRC is feasible to deliver by the trained MMT nursing personnel and appear to be a promising approach for improving the efficacy of standard MMT services in China.
Financial Support: NIDA DA14718-05A1S1, DA013108, K24 DA00445

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CXCR4 INVOLVEMENT IN THE GP120 ANTAGONISM OF THE ANTINOCICEPTION INDUCED BY OPIOIDS IN THE COLD WATER TAIL-FLICK TEST.

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Aims: We have reported that both the chemokine CXCL12/SDF-1alpha and the human immunodeficiency virus-type 1 coat protein, glycoprotein 120 (gp120), reduced the antinociception induced by opioids. Because gp120 binds to the same receptor, CXCR4, as CXCL12/SDF-1alpha the present experiments were designed to use the CXCR4-selective antagonist, AMD3100, to investigate the receptor's involvement in the effect of gp120 on the antinociception induced by morphine and the mu- delta- and kappa-selective opioid receptor agonists, DAMGO, DPDPE and dynorphin, respectively.
Methods: Rats were housed individually after surgical implantation of cannulae into the periaqueductal grey (PAG). Experiments began 1 week postoperatively. The cold-water tail-flick test was used as an antinociceptive index. A cutoff time was set at 60 sec. The percent of maximum possible antinociception (%MPA) for each animal at each time was calculated using the following formula: %MPA = [(test latency - baseline latency)/(60 - baseline latency)] x 100.
Results: The results showed that (1) AMD 3100 (100 pg, 10 ng, 100 ng and 500 ng, PAG) itself has no effect in this range; (2) gp120 (100 ng, PAG) can reduce the antinociception induced by DAMGO (400 ng, PAG), DPDPE (50 ng, PAG) and dynorphin (20 μg/μl, PAG); (3) AMD 3100 can reverse the gp120 antagonism of antinociception.
Conclusions: These results indicate that CXCR4 receptors expressed in the brain of rats are involved in the gp120 antagonism of antinociception induced by opioids.
Financial Support: Supported by NIDA Grants DA 06650 and DA13429

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CRAVING INTENSITY AND WITHDRAWAL SEVERITY ACROSS PHASES OF OPIOID DETOXIFICATION WITH BUPRENORPHINE.

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Aims: The occurrence of craving and withdrawal symptoms may contribute to relapse to drug use during treatment episodes and recovery efforts. Craving compels drug seeking behavior, and withdrawal symptoms are a barrier to sustained abstinence. Research on craving and withdrawal indicates that the first few weeks after attempts to reduce drug use are the most problematic. The current study examines indices of craving intensity and withdrawal symptom severity across time in a detoxification program, and addresses the association between craving and withdrawal symptom severity and drug use.
Methods: The study analyzed data collected in a recently completed 28-day detoxification taper trial conducted as part of NIDA's Clinical Trials Network (CTN), The Visual Analog Scale (VAS) is a self-report measure used to collect craving intensity, and the Clinical Opiate Withdrawal Scale (COWS) collected clinically observed withdrawal symptoms from 516 opiate-dependent study participants. The COWS and VAS responses were computed for each week of the 4-week induction/stabilization phase and weekly urine drug results were used as a measure of opioid use.
Results: Results demonstrate that patterns of craving and withdrawal occurred in parallel across the 4 weeks, with a sharp reduction in both craving and withdrawal symptoms from week 1 (COWS = 4.07; VAS = 39.09) to week 2 (COWS = 1.65; VAS = 19.98), followed by a slower reduction from week 2 to week 3 (COWS = 1.22; VAS = 15.57). Both craving and withdrawal symptoms leveled out from week 3 to week 4 (COWS = 1.08; VAS = 14.19).
Conclusions: Understanding changes in craving and withdrawal across time in a detoxification program is useful in guiding clinical treatment plans, such as scheduled clinic visits and number of weekly behavioral sessions.
Financial Support: NIDA 2U10 DA13045

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ASSESSING THE RELIABILITY AND VALIDITY OF COCAINE USE ALGORITHMS IN CLINICAL TRIALS.

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Aims: Accurate measurement of cocaine use over time is critical to the validity of clinical trials on drug abuse. Currently, four widely used approaches to assess cocaine use in trial participants include the use of urine toxicology (U), self-report (SR), a corroboration of urine toxicology and self-report (USR), and an assessment of urine toxicology based on Preston's rules (Preston). However, the sensitivity and reliability of these algorithms have not been widely explored. We therefore examined the comparability of these algorithms to assess their reliability and estimate their sensitivity.
Methods: The data on cocaine use of 81 patients randomized to a 12-week randomized, placebo-controlled trial of memantine for cocaine dependence were used. Patients provided urine samples and self-reports at each of their thrice-weekly visits. Cocaine use was determined if: (U) the urine samples had a >300ng/ml BE concentration; (SR) self-report of at least one day of use since last visit; (USR) the urine samples were BE positive or SR of at least one day of use since last visit; or (Preston) the urine samples were positive according to Preston's rules. Cohen's Kappa's were calculated to evaluate the concordance between all pairs across the four algorithms. Cross-tabulations of cocaine use results based on U, SR, Preston and SR algorithms were conducted to assess the distribution of discrepancies.
Results: Kappa's ranged from moderate (K=0.52) to very good (K=0.72) across different pairs of the four algorithms. Cross-tabulations of cocaine use results indicated substantial discrepancies between positive U's and negative SRs, and negative Preston's and positive SR's.
Conclusions: The observed discordance alluded to imperfect validity of the algorithms. Negative SR and positive U discordant pairs may be due to patients' inaccurate recall. Negative Preston's and positive SR's may be due to Preston's rules being too lenient. SR's appeared to be a highly valid algorithm. Preston's rules should be modified to include SR.
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PSYCHIATRIC COMORBIDITY AS PREDICTOR OF RELAPSE AFTER LONG-TERM ABSTINENCE FROM SMOKING.

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Aims: Further understanding of the risk of relapse in smokers following long-term abstinence is needed to inform treatment planning. We investigated the impact of psychiatric comorbidities on relapse in daily smokers who had abstained at least one year.
Methods: Using longitudinal data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), 5381 former daily smokers who had not smoked cigarettes in the year prior to the baseline interview were identified. Risk of relapse (smoking at least 100 cigarettes at any time in the three-year follow-up period) was compared by presence of DSM-IV psychiatric disorders in the year prior to baseline.
Results: Mood, anxiety or substance use disorders signaled increased risk of smoking relapse. The relative odds of relapse for those with versus without major depressive disorder (MDD) was 2.2. Cannabis and alcohol dependence were associated with increased odds of relapse (OR = 3.4 and 2.3, respectively). After adjustment for demographic characteristics, duration of abstinence, and amount previously smoked, the magnitude of these associations diminished (MDD, OR=1.5; cannabis, OR=1.2; alcohol, OR=1.3). Younger age at baseline signaled a high probability of relapse (e.g. age 18-24 vs 50+, OR=3.5) independent of smoking characteristics and psychiatric comorbidity. There was an inverse association between duration of abstinence and probability of relapse.
Conclusions: Those with psychiatric comorbidity are at increased risk of relapse, although this risk mostly is accounted for by duration of abstinence and age of the smoker. Nonetheless, it is important to consider addressing any mood, anxiety and other substance use disorders to improve the patient's probability of long term smoking abstinence success, particularly in the context of age and abstinence duration.
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A WHOLE-BRAIN CLASSIFIER APPROACH FOR REAL-TIME FMRI FEEDBACK TRAINING IN COCAINE ADDICTION.

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Aims: Region-specific real-time fMRI feedback has enabled subjects to control pain-modulating brain activity, and to achieve pain relief. These pioneering studies encourage similar rtfMRI feedback attempts for "craving circuit modulation" in addiction, but the relevant brain regions are not yet fully characterized, may be spatially distributed, and may vary across individuals. We are thus testing whether a "whole brain" classifier approach may be used 1) to rapidly distinguish the brain states associated with viewing cocaine vs. non-drug videos, and 2)to provide rtfMRI feedback for controlling the brain state associated with viewing a cocaine video.

Methods: BOLD fMRI at 3T with a partial least squares (PLS)linear classifier was used to characterize the whole brain response to alternating 30 sec cocaine vs. non-drug videos in cocaine patients (n=5; ongoing) and controls (n=2; ongoing). Real-time visual feedback based on this classifier was provided to two controls via a cursor adjacent to the ongoing video, with instructions to attempt control of the cursor by increasing or decreasing the state associated with viewing the target video.

Results: The whole-brain classifier based on PLS regression robustly distinguished ($15<t<34$; $p<0.0000$) between the brain states associated with viewing a cocaine vs. a non-drug video in cocaine patients; this classification was rapid (~ 5 minutes) and occurred in all patients. Real-time visual feedback (1-2 s lag) based on the classifier was also achieved, and one of the two controls demonstrated rapid control of the cursor.

Conclusions: This is the first evidence that a whole-brain classifier is feasible for rtfMRI feedback studies; it may provide a rapid and sensitive approach for training brain control. These technical milestones are critical to clinical testing of rtfMRI feedback in the addictions.

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CIGARETTE SMOKING AND NEONATAL OUTCOMES IN DEPRESSED AND NON-DEPRESSED OPIOID-DEPENDENT AGONIST-MAINTAINED PREGNANT PATIENTS.

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Aims: To compare neonatal outcomes in agonist-maintained pregnant cigarette smokers, with and without depression.

Methods: Participants were N=124 agonist-maintained pregnant smokers enrolled in a multi-site randomized controlled trial comparing maternal/neonatal safety/efficacy of methadone and buprenorphine in pregnancy. Data were obtained from N=131 opioid-using pregnant patients recruited for the parent study between July 2005 and November 2008. All participants signed local IRB-approved informed consent for study participation.

Results: Smoking, controlling for other drug use, was associated with lower birth weight and increased prematurity in depressed and non-depressed patients. However, the association between smoking and NAS requiring medication treatment differed between depressed and non-depressed patients. Among non-depressed patients, each additional cigarette per day (CPD) increased the odds of NAS treatment by 11% [OR:1.11;95%CI:(1.02-1.22)]. While depression alone did not appear to alter odds of NAS treatment [OR:2.53;95%CI:(0.48-13.25)], there was a statistically significant interaction between depression and average CPD [ratio of ORs:0.87;95%CI:(0.77-0.99);p=0.03] such that, among depressed patients, there was no association between CPD and NAS treatment [OR:0.98;95%CI:(0.89-1.06)].

Conclusions: This finding was unexpected and possibly spurious; after the removal of a single outlying data point (a depressed patient smoking 40 CPD who delivered at 34 weeks with no NAS treatment), the estimated effect of each additional CPD on odds of NAS treatment was unchanged, but the interaction between depression and CPD was no longer statistically significant [OR: 0.89; 95%CI:(0.78-1.03)]. Further investigations are needed to clarify the complex relationships between cigarette smoking, depression, and NAS.

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CO-OCCURRING MENTAL HEALTH AND SUBSTANCE USE DISORDERS AMONG RECENTLY BOOKED ARRESTEES.

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Aims: The aims of this study were to assess the prevalence and particular characteristics of the dual-diagnosed arrestee population in Maricopa County, Arizona. Secondary aims consisted of testing the co-occurring quadrant model along key indicators of criminal activity and violence among the study population.

Methods: Interview data obtained from 1,426 recently booked male and female arrestees at three booking facilities were used in these analyses. These interviews included a core instrument as well as a detailed 35-item Dual Diagnosis addendum, modeled after the NIJ's ADAM data collection protocols. The interview assessed captured core demographic information, substance use patterns, and functional status indicators, along with crime related variables. Nearly 1900 arrestees were approached, with 1,690 consenting to be interviews and 1,427 providing valid urine samples.

Results: First, we found that county jail intake facilities frequently deal with arrestees with co-occurring substance use and mental health problems; 24.8% of our respondents satisfied criteria for a co-occurring disorders. Second, co-occurring respondents were significantly more likely to be recidivists. Finally, co-occurring disordered arrestees were more likely to be affiliated with a gang and were at significantly greater risk for violent victimization.

Conclusions: These findings suggest that the proportion of arrestees with co-occurring disorders is sufficiently large to justify attention and that certain socio-demographic and criminal justice characteristics of this subpopulation may require innovative strategies to adequately address these challenges.

Financial Support: This study was supported, in part, by a contract from the Maricopa County Board of Supervisors.

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USE OF THE MICHIGAN AUTOMATED PRESCRIPTION SYSTEM TO MONITOR AND MANAGE DIVERSION IN AN URBAN METHADONE CLINIC.

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Aims: Diversion (i.e. transferring a drug from a lawful to unlawful distribution or use) includes illegal drugs (e.g. heroin), prescription narcotics (opioids and benzodiazepines), and legally obtained prescriptions that are illegally distributed. These practices threaten recovery of opioid dependent patients in methadone treatment.

Methods: Standard documentation of drug abstinence in a methadone clinic involves urine drug screens (UDS). Patients with negative UDS are usually judged to be abstinent and recovering. Problems with this approach include limitations of the assay (results often not confirmed), lack of sensitivity (potent benzodiazepines may be missed), and inability to identify specific opioids or the illegal diversion of "legitimate" prescriptions for sale/bartering.

Results: Our patients are monitored with UDS and online queries of the Michigan Automated Prescription System (MAPS), a database of controlled substances filled at Michigan pharmacies. Information is available up to 4 weeks from the query. MAPS reports are compared to UDS results and patients without these drugs in their urine are identified. Reports are monitored for evidence of multiple prescribers, early refills and potentially dangerous drug combinations. Patients are confronted and take home dosing is cancelled for 90 days using the "8 point criteria" (SAMHSA). Because discharge from a methadone clinic increases risks of morbidity and death, we do not automatically discharge patients from the program. We will report our intervention of graduated return to take home privileges, designed to minimize loss of patients who return to street drug use.

Conclusions: A statewide-computerized prescription search in a methadone clinic can be useful to identify and control diversion. Diversion contracts, education, and graduated return to take home dosing can minimize loss of these patients from the clinic, and the probability of medication overdose and criminal activity.

Financial Support: Department of Psychiatry

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AN ELECTRONIC HEALTH SYSTEM IN OPIOID AGONIST TREATMENT CLINICS: STUDY DESIGN AND BASELINE CHARACTERISTICS.

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Aims: Electronic health systems (EHS) are commonly included in healthcare reform discussions; however, their impact in addiction treatment has not been examined. We report pre and post implementation quality, productivity, patient and staff satisfaction, and financial performance results of an integrated EHS in an outpatient opioid agonist treatment program consisting of 7 clinics providing primary medical and HIV care for approximately 3000 predominantly minority adults in New York City.
Methods: Specific aims were selected using a pre-study needs assessment of stakeholders. Quality measures included viral load assessment in hepatitis C virus (HCV) infected patients and timely assessment of medical and addiction status at various intervals. The number of counseling, primary care, and HIV case management visits represented productivity measures. Using an anonymous survey, patient and staff satisfaction were assessed. Financial performance was measured as revenue per capita staff and cost per patient visit.
Results: Pre-implementation results were as follows: (1) Quality: HCV viral load was appropriately performed in 92% of cases; annual medical assessments were timely for 83% of cases; annual addiction assessments were timely at 30 days, 90 days, and annually for 81%, 46%, and 70% of cases, respectively. (2) Productivity: There were 64345 counseling visits, 5221 primary medical care visits, and 2680 HIV case management visits. (3) Satisfaction: Seventy-four percent of patients were satisfied/very satisfied with their care, while 33% of clinicians and managers were satisfied/very satisfied with the pre-EHS system for providing care. (4) Financial performance: Revenue per capita staff was $66,900 and cost per patient visit was $31.34. Post-implementation data is being compiled.
Conclusions: These results provide insight into the state of primary care and addiction treatment delivery in one large program and a basis for assessing the impact of an integrated EHS, further informing healthcare reform discussions.
Financial Support: National Institute on Drug Abuse: R01 DA022030

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ASSOCIATION BETWEEN CINGULATE VOLUME AND IMPULSIVITY IN ADOLESCENT CANNABIS SMOKERS.

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Aims: Cannabis is the most frequently selected drug of choice for initiates 12 years and older in the U.S and is thought to have a neurocognitve impact related to early use. Increased impulsivity during adolescence may be related to substance use initiation. Further, functional neuroimaging studies have shown altered activation of the cingulate cortex, a region known to mediate impulsive behavior and cognition, in cannabis abusing adults. Therefore, we hypothesized that adolescent cannabis abusers (CA) would differ from healthy controls (HC) in both impulsivity and cingulate volume.
Methods: Thirty-six subjects from the Salt Lake City area completed diagnostic interviews and drug screens. Structural imaging data was acquired on eighteen CA subjects (17.7 ± 0.9 years) and eighteen HC subjects (17.2 ± 0.8 years) using a T1-weighted 3D MPRAGE sequence on a 3T Siemens Trio magnet. Volumetric segmentation was performed with Freesurfer and adjusted volumes were obtained by taking the ratio of segmented cingulate volumes to total segmented brain volume. The Barratt Impulsivity Scale (BIS) was used to assess impulsivity.
Results: CA subjects had significantly higher scores on the BIS planning subscale ($p = .01$), a measure of decreased future orientation, when compared to controls. Compared to HC, the CA group also showed a strong trend ($p = 0.06$) toward increased volume for the right rostral anterior cingulate region. Moreover, for the CA group, total right cingulate volume was correlated with both total BIS score ($r = .52$, $p = .02$) and with the BIS planning subscale ($r = .74$, $p = .001$).
Conclusions: These findings suggest a relationship between levels of self-reported impulsivity, future orientation, and cingulate volume in adolescent cannabis abusers. Protracted development of prefrontal cortical systems during adolescence is thought to contribute to delayed behavioral maturation and increased impulsivity. These findings suggest that morphometry of the cingulate may play a role in the onset of drug use.
Financial Support: Research supported by funding from NIH grant DA020269

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RISK OF DEATH AND CRIME AMONG PROGRAM-QUITTERS.

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Aims: Mortality rates typically increase among opioid maintenance treatment (OMT) terminators.
The observed increase in death-risk may be due to the "absence of treatment", or it may be explained by selection effects. This study investigates crime (criminal charge) rates prior to treatment as a predictor for death after treatment termination, in order to highlight possible selection mechanisms.
Methods: Criminal charges are considered as a proxy variable for "risk behaviour". Data on all opiate dependents in Norway (1997-2003) who applied for and/or were accepted for OMT (n=3789) were cross linked with the Norwegian death registry. In addition registry-data on recorded criminal charges from the National Crime registry for the three years prior to first application date (n=>20.000 charges) for treatment was included.
Data were analysed according to pre-treatment crime levels and post-treatment group comparisons between survivors (n=711) and deceased (n=46).
Results: Pre-treatment crime levels varied significantly between treatment terminator survivors and deceased.
Mean number of criminal charges during the 3 years prior to treatment application, were 10 and 16 for survivors and deceased, respectively. Both groups had higher rates of pre-treatment criminal charges compared to treatment compliers with mean; 6 and 7 criminal charges for survivors and deceased, respectively.
Conclusions: Already prior to OMT application those who later terminate treatment and particularly those who die post-treatment differ in terms of higher levels of criminal behaviour than those who comply with treatment. The observation of high death risk post-treatment seems to be partly caused by selection mechanisms, not only the "absence of treatment".
The findings imply that prior to treatment high criminal activity is a detectable predictive factor associated with treatment adherence and outcome. This opens an opportunity for earlier interventions in order to avoid treatment termination and ultimately post-treatment death.
Financial Support: The study has received a 3-year PhD-grant from the Research Council of Norway.

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PRESCRIPTION OPIOID ABUSE PREDICTS FIRST ADMISSION INTO METHADONE MAINTENANCE TREATMENT.

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Aims: To determine which prescription opioids (POs) (as well as other factors) contribute to first admission into methadone maintenance treatment (MMT)
Methods: A national survey was conducted among 22,846 patients enrolling in 85 MMT programs between Jan. 2005 and Sept. 2009. (Regions where PO abuse was believed to be prevalent were oversampled.) A logistic regression model for predicting first MMT episode was constructed. Interview date, age, gender, race, region, chronic pain, craving, withdrawal severity, and urbanicity were included as covariates. Past month heroin use and 10 POs (buprenorphine, hydrocodone, morphine, hydromorphone, fentanyl, extended release oxycodone, immediate release oxycodone, methadone liquid, methadone disks, and methadone pills) also were included as potential predictors. (Separate methadone formulations were included because disks and liquid are typically dispensed at MMT programs and pills are typically prescribed to pain patients and dispensed at pharmacies.) Adjusted odds ratios (AOR) for effects $p < .01$ are reported.
Results: Mean age was 34, 79% were white, 40% female, 60% living in counties with > 1M residents, 41% chronic pain, 56% used heroin and 72% used one or more POs. First admission MMT enrollees (50%) were more likely to be using hydrocodone (AOR=1.48), extended release oxycodone (AOR=1.42) and immediate release oxycodone (AOR=1.29) and less likely to be using heroin (AOR=0.56), methadone liquid (AOR=0.38), and hydromorphone (AOR=0.83). New enrollees were also more likely to be younger, living in non-urban areas, male, white, have chronic pain, have higher drug craving, and a more recent enrollment date.
Conclusions: First MMT episode is associated with several, but not all types, of POs. Characteristics correlated with first MMT episode suggest a different demographic than has traditionally been associated with MMT enrollment.
Financial Support: Funded by Rocky Mountain Poison and Drug Center as part of the Researched Abuse Diversion and Addiction-Related Surveillance (RADARS®) System.

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IMPLEMENTING RESEARCH IN TRADITIONAL COMMUNITY TREATMENT PROGRAMS: FINDINGS FROM A CTN TRIAL.

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Aims: The dissemination and adoption of new evidence-based treatment into traditional treatment settings continues to be fraught with many obstacles and challenges.

The NIDA Clinical Trials Network was established to provide a mechanism for bridging the gap between research and practice, by conducting clinical trials research in community treatment programs (CTP), as well as to facilitate the adoption of evidence-based treatment in these settings. An example is provided for this presentation by a recently completed CTN project, "Starting Treatment with Agonist Replacement Therapies" (START; CTN 0027) designed to evaluate the hepatic safety of two medications, Suboxone and methadone, used in the treatment of opioid dependence. Discussed will be the organizational experiences of two of the eight participating CTPs, both affiliated with the CTN Pacific Regional Node; Bay Area Addition, Research and Treatment (BAART)in San Francisco and Matirx Institute on Addictions in Los Angeles, in implementing a new evidence-based technology, Suboxone, into programs best described as "traditional methadone" settings. Descriptions of both programs their patients, organizational cultures and treatment philosophy, staff and research experience are presented. The presentation will focus on individual and shared experiences including; study implementation, recruitment and retention challenges, study impact on existing program culture and the clincial and programatic benefits the study afforded, expanding patient access to treatment, increased staff and patient knowledge related to partial agonist treatment and and sustainability considerations.

Conclusions: Clincial trials research can be successfully conducted in community treatment program settings and may facilitate the diffusion and may serve in the adoption of new treatments into traditional treatment programs.

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DISTRESS TOLERANCE AND ADOLESCENT SMOKING CESSATION.

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Aims: More than half of adolescent smokers report attempts to quit each year (YRBS, 2005; Riedel et al., 2002) but only a small percentage actually succeed (Moss, Allen, Giovino & Mills, 1992; Zhu et al., 1999). In efforts to understand the underlying reasons for failed cessation attempts, the current study investigated negative emotionality and resulting avoidant coping styles, specifically distress intolerance, as a contributing factor to relapse. Low psychological distress tolerance is defined as the inability to persist in goal-directed behavior in the face of affective distress and has predicted poor cessation outcomes among adult smokers.

Methods: The study is currently in the data collection process. The available sample consists of 22 adolescent daily smokers who reported a desire to quit smoking within 30 days upon enrollment (mean age =16.8, 57.1% male, 61.9% White, mean cigarettes per smoking day (CPSD) = 8.7). Outcome variables were assessed during baseline, quit date, and at 7-day intervals over the period of a month post-quit date. Psychological distress tolerance in the current study was measured using computer-based behavioral tasks, including the Mirror Tracing Persistence Task (MTPT) and the Paced Auditory Attention Serial Task (PASAT).

Results: To date, 82% of participants reported making a quit attempt (mean duration = 15.6 days) and 91% of participants indicated a reduction of CPSD. Lower distress tolerance was associated with younger age of smoking onset, higher baseline CPSD, and heaviest lifetime smoking. Prospective analyses indicated that lower distress tolerance predicted shorter quit attempt duration and smaller reductions in CPSD across the follow-up period, after accounting for baseline smoking.

Conclusions: Preliminary results of the current study elucidate processes that may predispose adolescents to fail in their smoking cessation attempts. Low psychological distress tolerance should be considered as a basic mechanism to target in smoking cessation treatments for adolescents.

Financial Support: NIDA K23 DA23143

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REPEATED ADMINISTRATION OF A LONGER-ACTING MUTANT COCAINE ESTERASE: INTERACTIONS WITH THE ACUTE CARDIOVASCULAR EFFECTS OF COCAINE AND IMMUNE RESPONSES IN FREELY MOVING RHESUS MONKEYS.

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Aims: Cocaine (COC) is the most common illicit drug related to emergency room visits, with the majority of cases due to chest pain resulting from increases in blood pressure (BP) and heart rate (HR). These studies were aimed at characterizing 1) the capacity of a mutant COC esterase (T172R/G173Q; DM CocE) to ameliorate the cardiovascular effects of COC, and 2) the development of anti-CocE antibodies following repeated dosing with DM CocE in rhesus monkeys.

Methods: Four rhesus monkeys (2 male and 2 female) were implanted with telemetric probes (DSI; D70-PCT) capable of continuous measurement of BP and HR. DM CocE (0, 0.032, 0.1, 0.32, 1.0, or 3.2 mg/kg; IV) was administered 10 min after an IV dose of 3.2 mg/kg (n=3), or 1.0 mg/kg (n=1) COC, with BP and HR recorded for an additional 110 min. Blood was collected 24h prior to test sessions to allow for anti-CocE antibody titer determinations.

Results: In general, IV COC resulted in persistent increases in BP and HR. DM CocE produced dose-dependent and rapid decreases in BP in all four monkeys, with BP returning to control levels within the first 5-10 min following doses of 0.32, 1.0, or 3.2 mg/kg DM CocE. Similar decreases in HR were observed in 3 of the 4 monkeys, although these changes occurred over a longer time course. Repeated dosing of DM CocE failed to produce significant increases in anti-CocE antibody titers.

Conclusions: These studies demonstrate that DM CocE is capable of producing a rapid, and robust amelioration of COC-induced elevations in BP, and to a lesser degree HR, in rhesus monkeys. In addition, the effectiveness of DM CocE to reverse the cardiovascular effects of COC was unaffected by repeated dosing, and occurred in the absence of significant immune responses. Together, these results suggest that DM CocE may provide a novel and effective therapeutic for the treatment of acute COC toxicity.

Financial Support: NIDA grants DA023213 & DA021416

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DRUG-SEEKING IN RESPONSE TO A PRIMING INJECTION OF MDMA IN RATS: RELATIONSHIP TO INITIAL SENSITIVITY TO SELF-ADMINISTERED MDMA AND DORSAL STRIATAL DOPAMINE.

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Aims: In laboratory animals, exposure to priming injections of 3,4-methylenedioxymethamphetamine (MDMA) produced drug seeking following extinction of MDMA self-administration. The present study aimed to evaluate whether the magnitude of drug seeking was related to latency to acquisition of MDMA self-administration and increases in striatal dopamine.

Methods: Rats (n=23) were given daily access to MDMA self-administration until they earned a total of 240 infusions (total intake of 165 mg/kg MDMA). An additional group of rats (n=7) were yoked to some of the rats that self-administered MDMA so that they passively received the same amount of MDMA. Two days later, drug-seeking tests were conducted and all animals received a MDMA (10.0 mg/kg, i.p.) priming injection while changes in extracellular dopamine in the dorsal striatum were measured by in vivo microdialysis.

Results: Fourteen of the 23 rats acquired self-administration within the temporal limits of the study and the latency to meet the criterion ranged from 9-37 days. An experimenter administered injection of MDMA produced drug seeking in these rats, and the number of responses was significantly higher than responses produced by rats that failed to meet the criterion or by yoked control rats. For rats that met the criterion, drug seeking was negatively correlated with the number of days to self-administer the criterion number of MDMA infusions and positively correlated with MDMA-produced dopamine in the dorsal striatum. Importantly, MDMA-produced dopamine overflow was greater for the rats that met the criterion.

Conclusions: These findings suggest that drug seeking is influenced by initial sensitivity to the reinforcing effects of MDMA and related to drug-produced increases in striatal dopamine.

Financial Support: Neurological Foundation of New Zealand and Wellington Medical Research Foundation.

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CLINICAL FEATURES ASSOCIATED WITH ALCOHOL DEPENDENCE EMERGING SOON AFTER DRINKING ONSET.

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Aims: In this project, the aim was to study very early emergence of clinical features associated with alcohol dependence, as they are experienced within 90 days after drinking onset. Research on these very recent onset users (VROUs) may shed light on new early outreach and intervention approaches, as well as possible biobehavioral pathways leading toward alcohol dependence.
Methods: Data are from years 2004-2007 of the nationally-representative National Surveys on Drug Use and Health (NSDUH). The study population includes VROUs age 12 years or older whose first full drink of alcohol occurred within 90 days prior to NSDUH assessment (termed VROU-90d, n=6422). The assessment of clinical features was guided by DSM-IV-TR criteria. We used a GLM/GEE approach to estimate male-female and other subgroup variations in risk of clinical features.
Results: The majority of VROU-90d were under the age of 18 (64%) and many (42%) had not yet had more than one drinking occasion. Tolerance was the most commonly experienced clinical feature, followed by spending a lot of time on drink-related activities, and drink-related reduced participation in other activities. Among these VROU-90d, males and females did not differ in these experiences; in comparisons of adolescent-onset and older drinkers, there were no age of onset-related variations. Tolerance, using more than intended, continuing to drink despite recognition of health problems, and withdrawal-associated complaints were experienced more often by VROU with prior tobacco or other extra-medical drug use ($p<0.05$).
Conclusions: Some very recent onset drinkers are experiencing clinical features associated with alcohol dependence shortly after onset of drinking. Some anticipated subgroup variations were not found (e.g., male-female; age-of-onset). Variation with prior drug experience deserves more study.
Financial Support: NIDA award K05DA015799

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ANALGESIC EFFECTS OF SMOKED MARIJUANA AND ORAL THC IN HEALTHY MARIJUANA SMOKERS.

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Aims: Compounds that act on the cannabinoid system produce analgesia in laboratory animals; however, it is unclear the extent to which these effects are generalized to humans. To better understand the potential clinical application of cannabinoids for pain management, the following placebo-controlled, double-blind, double-dummy, within-subject study compared the analgesic efficacy of smoked marijuana (MJ) and oral tetrahydrocannabinol (dronabinol; THC) using the Cold-Pressor Test (CPT), a laboratory model of pain that has predictive validity for clinical use of analgesics.
Methods: Non-treatment-seeking marijuana smokers (N=26) participated in this 5-session, outpatient study. During each session, a MJ cigarette (0, 1.98, or 3.56% THC) was smoked 45 min after THC administration (0, 10, or 20 mg); only one drug was active per session. Analgesic, subjective, and physiological effects were measured throughout each session. For the CPT, participants immersed their hand in cold water (4°C) for up to two minutes, and the amount of time to report pain (pain threshold) and withdraw the hand from the water (pain tolerance) was recorded. Subjective pain ratings were also measured immediately after each CPT.
Results: Compared to placebo (P), high-dose THC increased pain threshold and tolerance, whereas the high strength of MJ only increased pain threshold. The effects of THC peaked later and lasted longer than those of MJ. High-dose THC also decreased subjective ratings of painfulness compared to P, whereas both active strengths of MJ decreased these ratings. Similarly, both MJ strengths increased positive drug effects such as 'Good Effect,' 'Like,' and 'High' relative to P, whereas only the high THC dose increased these ratings.
Conclusions: Oral THC and MJ effectively decreased the pain response elicited by the CPT; THC produced longer-lasting increases in pain threshold and tolerance, whereas MJ only altered the subjective pain experience. MJ also increased measures of abuse liability.
Financial Support: US NIDA (DA09236-12&DA19239).

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DOUBLE-BLIND FLUOXETINE IN COMORBID MDD-CUD YOUTH.

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Aims: We recently completed a first double-blind, placebo-controlled trial of fluoxetine (20 mg) in adolescents and young adults with comorbid major depressive disorder (MDD) and an cannabis use disorder (CUD) (R01 DA019142) to determine whether fluoxetine decreases the cannabis use and the depressive symptoms of that youthful comorbid population.
Methods: All subjects also received motivational and cognitive behavioral psychotherapy. Subgroups of those subjects also participated in a related genetics sub-study and in a related fMRI sub-study.
Results: A total of 70 subjects participated in that 12-week trial, including 43 males (61%) and 27 females (39%). Fluoxetine was well tolerated in that study population. During the clinical trial, significant decreases ($p<0.001$) were noted in observer-rated and self-rated depressive symptoms and in the number of cannabis use days across the entire study sample. However, no significant differences between the fluoxetine group and the placebo group were noted on any of the depression-related or the substance use-related variables on repeated measures ANOVA.
Conclusions: No efficacy was demonstrated for fluoxetine for treating MDD/CUD youth. However, the within-group improvements in depressive symptoms and cannabis use days across both treatment groups suggest that MET/CBT may have been helpful for treating those symptoms.
Financial Support: NIDA grants R01DA019142, R01DA019142-04S1, K02DA017822, P50DA05605; NIAAA grants R01AA15173, R01AA013370, K24AA015320, and K02AA00291.

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COMPARISON OF INTERVENTIONS FOR THE REDUCTION OF HCV AND HIV RISK BEHAVIORS.

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Aims: This paper reports on the results of a five year study comparing a peer network intervention to an individually-focused intervention for injection drug users (IDUs). Outcomes included reduction of HCV and HIV risk behaviors and improvement of self-efficacy for reducing risk behaviors among index and peer network members.
Methods: Six hundred and fifty-eight injection drug users were recruited through street outreach in Denver from May 2004 through December 2008. Index subjects were recruited and asked to bring in two network members. Index subjects were randomly assigned to receive either a peer network intervention (n=141 for index and 188 for network) or the Indigenous Leader Outreach Model (ILOM) (n=144 for index and 185 for network), which was individually-focused. Participants were followed and data were collected at 6 and 12 months.
Results: Participants were 61% white, 70% male and averaged 40 years old. Only data at 6 months were analyzed for this study. Compared to ILOM, the peer network intervention had a marginal effect in the reduction of the number of times having unprotected sex in the last 30 days for index subjects (-6 vs. -1, $p=0.06$), and a marginal effect in the improvement of self-efficacy regarding sex (5-point Likert scale) for network members (0.14 vs. -0.03, $p=0.08$). There was a marginal effect in the reduction of the number of times substances were injected in the last 30 days (-43 vs. -16, $p=0.09$) for methamphetamine-using network members.
Conclusions: Findings suggest some evidence of the effectiveness of a peer network intervention compared to an individually-focused intervention in reducing HCV and HIV risk behaviors, and in improving self-efficacy for reducing HCV and HIV risk behaviors. Index subjects and network members had different outcomes for which the peer network intervention was effective. Some effects were stronger for methamphetamine users. Complex modeling will be performed and may yield more significant results. Findings will be presented.
Financial Support: This study was supported by the National Institute on Drug Abuse, DA016994.

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NATIONAL MONITORING OF ADOLESCENT PRESCRIPTION STIMULANTS STUDY: STIMULANT MEDICATION USE AMONG 10 TO 18 YEAR OLDS.

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Aims: N-MAPSS is an innovative national study that estimates the prevalence of use, misuse, abuse and diversion of prescription stimulants among youth 10 to 18 years old.
Methods: An entertainment venue intercept method was used to collect data from teens in ten cities: Boston, Cincinnati, Denver, Houston, Los Angeles, New York City, Philadelphia, Seattle, St. Louis and Tampa. Youth completed an anonymous two-part survey covering demographics, ADD/ADHD diagnosis, pill identification, risk behaviors, stimulant use, misuse and diversion, as well as use of other prescription drugs, alcohol and illicit drugs. The survey assessed adolescent experiences with using and reasons for taking prescription stimulants, including whether or not they had ever been told by a doctor or parent to do so.
Results: Overall, 19% of youth reported stimulant use in their lifetime (any use, not limited to misuse/abuse); of which half (~9%) reported any use in the last 30 days. Use increased with age and diagnosis of ADHD. Half of the past 30 day users misused their stimulants. Among the youth with ADHD, those who misused stimulants were more likely than those who did not misuse to report current smoking, an alcohol binge in the last 30 days, and illegal drug use.
Conclusions: This study provides important information to address sociological, demographic and behavioral factors associated with medical and non-medical use of prescription stimulants which may aid in detecting misuse of stimulants in the future.
Financial Support: N-MAPSS is implemented by Washington University in St. Louis under contract from Pinney Associates, Inc., with funding provided by Shire Pharmaceuticals.

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FRENCH SURVEY ABOUT STUDENTS' HEALTH IN 5 UNIVERSITY HEALTH AND PREVENTION CENTERS.

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Aims: To describe students' health and quality of life, evaluate psychoactive drugs consumptions and motivations to come to the University Health and Prevention Centers (UHPC) some of them being as dispensaries too
Methods: 1572 students were included during 5 weeks in 5 different sites (Clermont Ferrand, Savoie, St Etienne, Lyon, Grenoble). Sociodemographic data, SF 36(short version), EPICES Score (French deprivation index) alcohol, tobacco and cannabis use as well as motives for consulting were analyzed in each center whether they are only UHPC or dispensaries too. Logistic regressions were processed to determine specific profiles of students
Results: Significant differences ($p<0.001$) exist in many items showing higher age, alcohol experimentation and EPICES score, lower QoL in dispensaries. Logistic regressions about alcohol experimentation, binge drinking, tobacco and cannabis use. They provide models of drug consumption focusing on gender, SF 36 and EPICES score (Male, french native with low vitality being the main factors associated with higher odds ratio and significant p value)
Conclusions: Results confirm previous data collected in 2007 about 718 students. They could be helpful to build an observatory about students'health and therefore focus prevention programs towards specific groups
Financial Support: Institutional

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PREDICTORS OF TREATMENT COMPLETION AMONG OFFENDERS ENROLLED IN A COMMUNITY-BASED OUTPATIENT PROGRAM.

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Aims: Despite the well established link between crime and substance abuse, many offenders do not receive treatment, or once enrolled, do not complete treatment. Research has consistently demonstrated that substance abusers who stay in treatment longer have less subsequent drug use and commit fewer crimes. The aim of the present study was to assess the predictors of treatment completion among a sample of offenders attending a community-based drug-free outpatient program.
Methods: Currently, the sample consists of 107 offenders enrolled in a study assessing the effectiveness of a six month treatment protocol that integrates drug and employment counseling. The offenders are under various levels of supervision including county and state probation/parole, a treatment court and an alternative disposition program. Research assessments are collected at baseline, every other week during the six month treatment phase and at six, 12 and 18 months post-treatment entry. Urine drug screens are collected weekly.
Results: The sample is predominately male (91%) and the majority are African American (62%). The average age of subjects is 34 years and the average amount of time participants spent incarcerated is nearly 3½ years. One-third are dependent on cannabis (33%), one-third are alcohol dependent (32%), 30% are dependent on cocaine and one-fifth (20%) are opioid dependent. Preliminary findings from logistic regression analyses indicate that those who are mandated to treatment, such as treatment court or the alternative disposition program, are six times more likely to complete treatment (OR=6.1,CI=1.2-32.1,p=.033), whereas those who are opioid dependent are 3.7 times less likely to complete the six month treatment protocol(OR=3.7,CI=1.1-12.6,p=.035).
Conclusions: Requiring offenders to attend treatment may be an effective way to increase treatment compliance, and hence reduce drug use and recidivism. However, offenders with an opioid dependence diagnosis may require medication assisted therapy to experience positive treatment outcomes.
Financial Support: Supported by NIDA grant R01DA019600.

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HUMAN MDMA USE IS ASSOCIATED WITH INCREASED ACTIVATION IN ANTERIOR CINGULATE GYRUS DURING FLANKER TASK PERFORMANCE: AN FMRI STUDY.

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Aims: MDMA (Ecstasy) is a widely used party drug that produces serotonergic axon toxicity. Human MDMA users have impairments across a broad range of cognitive domains, including attention, concentration, psychomotor, and executive functions. MDMA use is associated with reduced gray matter concentration in the anterior cingulate gyrus.
Methods: To investigate the neural basis of MDMA effects on cognition, we used fMRI at 3 Tesla to examine anterior cingulate activation in abstinent human MDMA users (N=7) during performance of a flanker task (in which a central arrow is flanked by arrows pointing in an incongruent or congruent direction) that included a response inhibition component. This task taps multiple neurocognitive domains. We examined activation for incongruent stimuli and response inhibition within 3 subregions of the anterior cingulate (Brodmann area [BA] 24, 31 and 32).
Results: Lifetime MDMA use was non-significantly positively correlated with signal intensity and spatial extent of activation across all 3 regions. For incongruent stimuli, Spearman's correlation coefficients were: $r=0.60$ for BA 24; $r=0.164$ for BA 31; and $r=0.491$ for BA 32. For response inhibition stimuli: $r=0.436$ in BA 24; $r=0.164$ in BA 31, and $r=0.436$ in BA 32. There was no association of task performance with MDMA exposure.
Conclusions: MDMA use was associated with increased task-evoked activation across all stimuli and all regions but not with task performance. While these preliminary findings from a small sample set did not achieve statistical significance, the results are consistent with our earlier results showing that MDMA use is associated in a dose-response manner with increased activation across multiple tasks and brain regions. This overall pattern of increased activation and preserved task performance following MDMA exposure is suggestive of altered cortical excitability or reduced cortical efficiency, potentially secondary to altered serotonin signaling.
Financial Support: NIDA: DA015137, DA020149 and DA00366 to RLC; NCRR: Vanderbilt UL1 RR024975.

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RACIAL/ETHNIC DIFFERENCES IN RECENT DRUG DETOXIFICATION ENROLLMENT AND THE ASSOCIATION BETWEEN DISCRIMINATION AND NEIGHBORHOOD FACTORS IN NEW YORK CITY DRUG-USERS.

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Aims: Drug dependent minorities may be less likely to access drug detoxification (detox) services, and continue drug treatment beyond detox (i.e., inpatient or outpatient services).
Methods: We assessed individual (race/ethnicity, discrimination) and neighborhood-level factors (% black, % Latino, %< poverty level, and Townsend disadvantage scale) associated with recent detox by combining census data with baseline data from "Social Ties Associated with Risk of Transition in Injection Drug-use" (START), a prospective study of 653 new injection drug-users (IDUs) and non-injecting heroin/crack/cocaine users (non-IDUs) recruited by respondent driven sampling and targeted outreach in New York City. PROC-GLIMMIX to account for hierarchical-level data was used.
Results: Fewer blacks (19.7%) reported recent detox compared to Hispanics (28.3%) and whites/others (27.4%;p<0.06). Drug-use discrimination, higher % Latinos, neighborhood disadvantage, and drug used most often (heroin/crack/cocaine) were independently associated with detox. After adjustment, drug-use discrimination (AOR:1.87;95%CI:1.20-2.34) and more neighborhood disadvantage (AOR:0.65;95%CI:0.42-1.00) were significantly associated with detox. Among detox enrollees only, fewer blacks (20.2%) received additional methadone maintenance, cocaine treatment, inpatient/other treatment compared to Hispanics (45.8%) and whites/others (28.6%;p<0.01). After adjustment among detox enrollees, blacks remained less likely to receive an additional long-term treatment modality, but persons who experienced drug-use discrimination and lived in high poverty neighborhoods were more likely to receive additional long-term treatment modality compared with detox services only.
Conclusions: Race/ethnic differences in perceived drug-use discrimination may systematically filter persons into detox and treatment. Understanding how race influences discrimination, subsequent healthcare access and health-behaviors is dire for improving access to detox and retention in subsequent long-term treatment.
Financial Support: NIDA

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DRD2/ANKK1 IN RELATION TO REGULAR ALCOHOL AND CANNABIS USE AMONG ADOLESCENTS: DOES PARENTING MODIFY THE IMPACT OF GENETIC VULNERABILITY? THE TRAILS STUDY.

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Aims: The aims of the present study were to determine the direct effect of the A1 allele of the TaqIA polymorphism (rs1800497), and its interaction with parenting (i.e. rejection, overprotection and emotional warmth), on the development of regular alcohol and cannabis use in a large, general population sample of Dutch adolescents.
Methods: Information was obtained by self-report questionnaires. Perceived rejection, overprotection and emotional warmth were assessed at age 10-12. Regular alcohol and cannabis use were determined at age 15-18 and defined as the consumption of alcohol on 10 or more occasions in the past four weeks, and the use of cannabis on 4 or more occasions in the past four weeks. In the vast majority of cases, DNA was extracted from blood samples. Models were adjusted for age, sex, and parental alcohol or cannabis use.
Results: Carrying the A1 allele was not related to regular alcohol or cannabis use, neither directly nor in interaction with perceived parenting. Main effects for parenting indicated that overprotection increased the risk of regular alcohol use, and that the risk of cannabis use was enhanced by parental rejection and buffered by emotional warmth.
Conclusions: Our findings do not support a genetic predisposition for regular alcohol and cannabis use in adolescent carriers of the A1 allele of the TaqIA polymorphism. Given the substance-specific influences of rejection, overprotection and emotional warmth, these parenting factors might be promising candidates for prevention work.
Financial Support: Supported by ZonMW research grant 60-60600-98-018.

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RESULTS OF A PILOT RCT OF BURPRENORPHINE FOR WOMEN IN THE CRIMINAL JUSTICE SYSTEM: PRELIMINARY ANALYSES.

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Aims: Recent studies have demonstrated the efficacy of both methadone and buprenorphine among male prisoners transitioning from prison to the community, but no studies have been conducted with women. The aim of this study was to determine the efficacy of buprenorphine for relapse prevention among women in the criminal justice (CJ) system transitioning back to the community.
Methods: 27 women under CJ supervision were recruited from an inpatient drug treatment facility that treats CJ individuals returning back to the community. Initially 9 women were enrolled in the single, open label buprenorphine arm and then 18 were randomized to buprenorphine (n=11) or placebo (n=7; double-blind). All women signed informed consent, completed baseline measures, and started study medication prior to release. Participants were followed weekly in the community, provided urine drug screens (UDS), received study medication for 12 weeks, and returned for a 3 month follow-up. Intent-to-treat analyses were performed for all time points through end-of-treatment (EOT).
Results: The majority of participants were Caucasian (88.9%), young (M=32.6+9.3), divorced/separated (59.2%) women with at least a high school/GED education (74.1%). GEE analyses showed that buprenorphine was efficacious in maintaining abstinence across time compared to placebo (p<0.001). Point prevalence opiate positive UDS were lower across all time points for active vs. placebo participants. By EOT, 40% of active and 100% of placebo participants were positive for opiates (p<0.001), while across the entire treatment phase, 34.6% of active and 78.6% of placebo UDS were positive for opiates (p<0.001).
Conclusions: Women in the CJ system who received buprenorphine prior to release had fewer opiate positive UDS at all time points after release compared to women receiving placebo. Initiating buprenorphine in a controlled environment prior to release appears to be a viable strategy to reduce opiate relapse when transitioning back to the community.
Financial Support: Supported by NIDA R21DA019838 and product support from Reckitt Benckiser.

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CLUSTERING OF TOBACCO USE: RESULTS FROM THE PERUVIAN MENTAL HEALTH SURVEY, 2002-2006.

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Aims: As with childhood diarrhea and other communicable infections, tangible neighborhood-level clustering of drug use has been observed in the United States and elsewhere — even with individual level covariates held constant. Nonetheless, there is little published evidence on neighborhood clustering of tobacco use. Here, the aim is to estimate clustering of tobacco use within Peruvian neighborhoods and districts, with due attention to individual-level influences on recent tobacco use, including ethnic variations observed within this country.
Methods: Data are from mental health surveys conducted by our institute in 18 cities of Peru (n= 22,281 adults 18+ years), including assessment of tobacco use. Alternating logistic regressions (ALR) produced estimates for clustering of recent tobacco smoking.
Results: Tobacco experience in Peru is common: almost 3/4ths had smoked; two-fifths are recent smokers. Estimated clustering for recent tobacco use was gauged via ALR neighborhood and district pair wise odds ratios, both of which were in the 1.1-1.3 range, not appreciably distant from estimates for clustering of diarrheal disease in villages of low-income countries. Male sex, ethnic affiliations, and educational attainment all were associated with recent tobacco use, but did not account for observed clustering.
Conclusions: This new study evidence is consistent with neighborhood and district-level clustering of recent tobacco use in Peru, similar to clustering of illegal drug use in the US. Individual level characteristics explain only part of this clustering. Other explanations must be sought.
Financial Support: NIH/FIC/NIDA, D43TW05819, K05DA015799 & T32DA021129

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URB597, A FATTY ACID AMIDE HYDROLASE METABOLISM INHIBITOR, EFFECTS LOCOMOTOR ACTIVITY IMMEDIATELY AFTER THE FORCED SWIM TEST.

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Aims: The effects of CB1 receptor activation in the forced swim test (FST) and on locomotor activity (LMA) were examined by manipulating the endogenous receptor agonist anandamide with URB597. URB597 inhibits the enzymatic activity of fatty acid amide hydrolase (FAAH) and thereby increases the concentration of anandamide and activates the CB1 receptor.
Methods: C57Bl/6 mice (n=9-10) were exposed to the FST (6 min in 25° C water) following an intraperitoneal (i.p.) injection of vehicle or a dose of 0.03 mg/kg or 0.1 mg/kg URB597. Immediately after the FST, the mice were placed in a locomotor activity chamber (30 min; LAC). The effect of CB1 receptor activation and FST exposure was measured by time spent immobile (sec) in the FST and by distance traveled (cm), the average velocity (cm/sec), total entries into the center zone (#), and total time spent in the center zone (sec) in the LAC. LMA was measured before the FST (Pre-FST1), immediately after the FST (Post-FST1), and a week after the FST (LMA-FST1).
Results: Time spent immobile in the FST was similar in C57Bl/6 mice treated with vehicle and URB597 at doses 0.03 mg/kg and 0.1 mg/kg. LMA was reduced significantly during the Post-FST1 session compared to LMA during the Pre-FST1. Also, a significant increase in the total time spent in the center (0-10 min) was observed in mice treated with 0.03 mg/kg URB597 compared to vehicle in both the Post-FST1 and LMA-FST1. In addition, the average velocity increased significantly in mice treated with 0.03 mg/kg URB597 compared to vehicle in the Post-FST1 (20-30 min).
Conclusions: These data suggest an interaction between CB1 receptor activation and responses in the FST and LAC. Under these conditions, URB597 did not decrease time spent immobile in the FST as reported with antidepressants such as desipramine (Lucki, 2001). However, a low dose of URB597 increased time in the center immediately after the FST in the LAC.
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MECHANISMS OF PRESCRIPTION DRUG DIVERSION AMONG IMPAIRED PHYSICIANS.

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Aims: To investigate mechanisms of prescription drug diversion among a population of physicians being monitored for substance abuse and to explore policy options for preventing the specific methods of diversion uncovered. The authors hypothesize that methods of diversion used by physicians are a function of the access to prescription drugs that they have by virtue of their profession.
Methods: A qualitative study using focus groups was conducted to gather information about prescription drug diversion among impaired physicians being monitored by a state physician health program (PHP). Non-probabilistic, purposive sampling was used to obtain a geographically diverse group of physician participants. PHP monitors arranged the focus group sessions and recruited all participants. Nine focus groups, which included a total of 54 physicians, were conducted. Focus groups were anonymous. Physicians were not compensated for participation. Audiotapes of the focus group sessions were transcribed and loaded into Atlas.ti for coding and analysis.
Results: Physicians reported using five primary methods to divert prescription drugs: stealing from patients; stealing from health care organizations; utilizing samples provided by prescription drug reps; ordering large shipments of drugs from pharmaceutical warehouses for personal use; and self-prescribing or prescribing in the name of patients and/or friends for personal use. The most commonly diverted drugs included prescription opioids, followed by prescription sedatives. Many physicians reported diverting for several years before being caught.
Conclusions: Mechanisms of prescription drug diversion used by physicians result from their increased access to prescription drugs relative to the general population. The development of policies to require funding of state prescription drug monitoring programs as well as policies to restrict the distribution of drug samples has the potential to mitigate the amount of prescription drug diversion that occurs among physicians as well as other health care personnel.
Financial Support: This work was supported by a NIDA Diversity Supplement to R01DA020791, LB Cottler, PI.

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DOPAMINE β HYDROXYLASE INHIBITOR SYN117 DECREASES SUBJECTIVE EFFECTS OF COCAINE.

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Aims: The non-selective DβH inhibitor disulfiram blocks the subjective effects of cocaine and reduces its use. We tested the hypothesis that the selective DβH inhibitor SYN117 will reduce the positive subjective effects of cocaine in a double-blind, placebo-controlled, inpatient study with fewer side effects than disulfiram.
Methods: Non-treatment seeking, cocaine dependent subjects were randomized to placebo (n=5) or placebo/80 mg/160 mg of SYN117 for 13 days (n=15). The pharmacokinetics of cocaine and its cardiovascular and subjective effects were measured at ascending doses of 0, 10, 20 and 40 mg of intravenous cocaine in subjects treated with placebo or SYN117.
Results: SYN117 was well-tolerated and there was no difference in adverse events observed after the combination of SYN117 and cocaine vs. cocaine alone. The pharmacokinetics of cocaine was unaltered. A main effect of SYN117, cocaine and an interaction were observed (ANOVA) for some measures on the Visual Analogue Scale (VAS). 'Drug effect,' 'high,' 'good effects,' and 'stimulated' significantly decreased in subjects receiving SYN117 plus cocaine vs. placebo plus cocaine. SYN117 significantly increased ratings of 'depressed' and 'anxious'. 'Craving' did not change.
Conclusions: These data show that SYN117 significantly alters the subjective effects of cocaine and is well tolerated by human subjects. In comparison to disulfiram which resulted in increased levels of plasma cocaine and decreased cocaine clearance, SYN117 did not alter the pharmacokinetics of cocaine in keeping the selectivity of SYN117 as a DβH inhibitor. Thus, the present phase I analysis suggests that further examination of SYN117 for efficacy in treatment of cocaine dependent subjects is warranted.
Financial Support: Synosia Therapeutics, Inc., UTMB Center for Addiction Research, UTMB Clinical Research Center, DA009262, DA024157, DA020087

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DIFFERENTIAL ANTAGONISM OF THE BEHAVIORAL EFFECTS OF NICOTINE, VARENICLINE, AND CYTISINE IN MICE.

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Aims: Although nicotine replacement therapy is effective in promoting abstinence from cigarette smoking, there is margin for improvement. Varenicline is reported to be more effective than nicotine replacement therapy and comparatively less is known about cytisine, a pharmacotherapy for tobacco dependence in Europe. To examine the possibility that nicotine acetylcholine receptor subtypes differentially mediate behavioral effects, nicotine, varenicline, and cytisine were combined with antagonists differing in their selectivity for receptors containing α4β2 subunits.
Methods: Male C57BL/6J mice (n=7) responding on a fixed ratio 30 schedule of food delivery received i.p. nicotine, varenicline, and cytisine, alone and in combination with the non-selective nicotine antagonist mecamylamine and the α4β2 nicotine receptor-selective antagonist dihydro-β-erythroidine (DHβE).
Results: Nicotine, varenicline, and cytisine dose-dependently decreased responding; nicotine was more potent (ED50 = 0.72 mg/kg) than varenicline (ED50 = 1.8 mg/kg) and cytisine (ED50 = 2.7 mg/kg). The agonists had a similar time course of activity, including a rapid onset (<5 min) and relatively short duration of action (40 min). Mecamylamine (1 mg/kg) produced surmountable antagonism, evidenced by rightward shifts (95% confidence limits) in the dose-effect curves for nicotine, varenicline, and cytisine of 3.3 (2.2-4.8), 3.1 (2.0-4.9), and 2.3 (1.8-2.9)-fold, respectively. The rate-decreasing effects (7.9% of non-drug control) of nicotine (1.78 mg/kg) were partially antagonized (42% of maximum) by DHβE (3.2 mg/kg); however, DHβE did not antagonize the rate-decreasing effects of varenicline.
Conclusions: Differential antagonism of nicotine and varenicline by DHβE as well as a quantitative difference in antagonism of cytisine, relative to nicotine and varenicline, by mecamylamine suggests that these smoking cessation treatments differ in their site of action at nicotine acetylcholine receptor subtypes.
Financial Support: Supported by USPHS grant DA25267.

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ACUTE EFFECTS OF BENZYLPIPERAZINE ON COGNITION AND EXECUTIVE FUNCTIONING USING FUNCTIONAL MAGNETIC RESONANCE IMAGING USING THE STROOP PARADIGM.

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Aims: Party pills containing BZP have been marketed as safe and legal alternatives to illicit recreational drugs, such as 3,4-methlenedioxymethamphetamine (MDMA) or methamphetamine. BZP is a stimulant with similar subjective effects to dexamphetamine (DEX). There is a paucity of information known about the effects of BZP in humans. This study is a randomized double blinded cross-over trial to determine the effects of BZP on impulse control and executive function in comparison to DEX and Placebo using fMRI
Methods: 12 healthy participants aged 18-40, were recruited from the Auckland area. Subjects were imaged by fMRI, at the Centre for Advanced MRI, at the University of Auckland. Imaging was performed whilst participants undertook the Stroop paradigm 90minutes after an oral dose of BZP (200mg), DEX (20mg) or Placebo. The participants were tested with each condition on a separate occasion. Echo-planar images were collected on a MRI scanner (Siemens Magnetom Avanto 1.5 T, Germany).Data was pre-processed, analysed with SPM8 and then used to identify regional activation
Results: Analysis of the overall Stroop (incongruent-congruent) condition (p=0.001) resulted in significant change in activation for both the BZP and DEX group in the Dorsolateral Prefrontal Cortex (DLPFC) compared to Placebo, in addition, BZP caused accentuated change in activation in the Anterior Cingulate Cortex compared to placebo. Reaction Time (RT) was increased by BZP and DEX compared to Placebo. There was no trend with accuracy
Conclusions: This study is the first to investigate the effect of the combination of BZP and TFMPP on cognition and executive functioning using fMRI. Our results suggest that BZP displays characteristics typical of other psychostimulants such as DEX in the effect on the DLPFC, and its effects on RT
Financial Support: School of Pharmacy, The University of Auckland

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COGNITIVE BEHAVIORAL THERAPY SESSION ATTENDANCE, RETENTION AND OPIOID USE IN PRIMARY-CARE-BASED BUPRENORPHINE/NALOXONE TREATMENT.

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Aims: Aims: To determine whether greater cognitive behavioral therapy (CBT) session attendance is associated with higher patient retention and lower levels of illicit opioid use in primary-care based buprenorphine/naloxone (BUP) treatment.
Methods: Methods: We conducted a 24-week randomized clinical trial of BUP in 135 opioid dependent patients, 64 of whom were randomly assigned to receive CBT in addition to physician management (PM). CBT, by doctoral and master level clinicians, was available for 50 minutes weekly for the first 12 weeks. PM (20 minutes) was provided every other week for the first 6 weeks and then monthly. Urine toxicology analyses for opioids were obtained weekly.
Results: Analysis: Patient retention was evaluated using a Cox regression. The association between number of sessions attended and weeks of continuous opioid-negative urine samples obtained during the two 12-week time periods was examined using a Pearson's coefficient. Missing urines were considered positive for opioids.
Results: Overall, patients randomized to CBT were predominately male (74%), never married (70%), white (88%), and reported heroin as the primary drug of abuse (65%); 41% were employed full-time. Patients' mean age was 33.2(SD = 8.9). The average number and length of CBT sessions attended were 8.0 (SD= 3.4) and 40.0 minutes (SD = 9.0), respectively. Retention levels were correlated with CBT session attendance ($p < .001$). Increased session attendance was associated with a greater number of consecutive weeks opiod negative urines during the first 12 weeks ($r = .30$, $p < .001$) and second 12 weeks of treatment ($r = .48$, $p< .001$).
Conclusions: Conclusion: Since greater cognitive behavioral therapy (CBT) session attendance is associated with retention and reduced illicit opioid use, strategies to increase session adherence are warranted.
Financial Support: Supported by NIDA RO1 DA019511-03

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PRESCRIPTION OPIOID ABUSE IN ADULT AND ADOLESCENT SUBSTANCE ABUSE TREATMENT CENTER POPULATIONS: EARLY FINDINGS FROM CHAT™

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Aims: This study examines early data from CHAT™, a real-time, product-specific data stream from a sample of adolescent substance abuse treatment centers and compares prescription opioid abuse among this sample population to patterns observed among an adult treatment center population.
Methods: NAVIPPRO ™data from 127,409 adult treatment center admissions (patients age 18 and older) and 278 adolescent treatment center admissions (patients age 18 and younger) were examined. Clients reported past 30 day abuse of prescription opioids in general and at a product-specific level. Data on routes of administration, source of the drug, and reported use of other drugs were reviewed and compared among the two populations.
Results: A greater percentage of adults in treatment report past 30 days abuse of any prescription opioid compared to adolescents (9.6% vs. 5.4%, $p<0.01$).More adults than adolescents reported injection of opioids (19.1% vs. 6.7%), while a greater percent of adolescent patients used alternative non-oral routes of administration (snorting 46.7%, smoking 20.0% vs. adults 34.7% snorting, 3.4% smoking). Reports of drug source among the two populations indicate more adults than adolescents (44.6% vs. 6.7%) abuse of their own prescriptions. Adolescents more frequently report stealing (13.3% vs. 7.1%), trading for the drug (13.3% vs. 1.3%) and other sources (26.7% vs. 13.5%). Lastly, other drug use among these populations show 51.7% of adult prescription opioid abusers also report past 30 days abuse of heroin (23.7% vs. 6.7%) and cocaine (33.3% vs. 26.7%), though adolescents more frequently report problematic alcohol use (46.7% vs. 33.2%).
Conclusions: Early findings from adolescent patients in substance abuse treatment suggest age-related patterns of prescription opioid abuse that differ from the adult treatment center population. Findings suggest that early intervention and education strategies targeted at the adolescent population may prevent or reduce high risk behaviors that are more prevalent among older age groups.
Financial Support: Inflexxion, Inc.

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A COMPARISON OF INDEPENDENT AND SUBSTANCE-INDUCED DEPRESSION IN CANNABIS-, COCAINE-, AND OPIOID-DEPENDENT TREATMENT SEEKERS.

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Aims: The DSM-IV has identified two distinct categories for depression coexisting with substance use disorders (SUDs) – independent depression (ID) and substance-induced depression (SID). While this distinction has important therapeutic and prognostic implications, it remains difficult to make in clinical practice for the reason that patients may be unable to precisely provide important chronological and symptom severity criteria. Predictors, associations, and other markers may be helpful in guiding the diagnostic process. We therefore examined the differences between cannabis, cocaine, and opioid dependent individuals contending with ID and those contending with SID in regards to several variables, hypothesizing that ID is more commonly found in females and cannabis dependent individuals, and that it is associated with higher symptom severity and psychiatric comorbidity.
Methods: Cocaine, cannabis, and/or opioid dependent, treatment-seeking individuals underwent a SCID at our clinical research site; those with coexisting ID or SID diagnoses were provided with further questionnaires(n=242). 2x2 tables were created and a chi-squared analysis was performed for independent variables. Binomial logistic regression was performed in order to ascertain which of the variables were significant predictors.
Results: Men were more likely than women to suffer from SID (Chi-2<0.05), while women were more likely than men to suffer from ID(chi-2<0.005). Cannabis dependence was highly associated with ID(chi-2<0.001), while cocaine dependence was most associated with SID(chi-2<0.05). ID was associated with higher HAMD scores (16 vs. 10, $p<0.005$), and was more highly associated with the comorbid diagnosis of PTSD (chi-2<0.05). Cannabis dependence was a significant predictor of ID ($p<0.05$), and female gender was a near significant predictor of ID ($p=0.06$).
Conclusions: Gender, cannabis dependence, psychiatric severity, and psychiatric comorbidity have variable, statistically significant associations with ID and SID, and may be helpful in guiding the diagnostic process.
Financial Support: SUPPORTED BY NIDA GRANTS,R01DA15451, K0DA20046,P50DA09236.

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MORPHINE IN COMBINATION WITH METABOTROPIC GLUTAMATE RECEPTOR ANTAGONISTS IN A MODEL OF INFLAMMATORY PAIN.

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Aims: The present study examined the effects of the mGluR1 antagonist [(3,4-dihydro-2H-pyrano[2,3-b]quinolin-7-yl)-(cis-4-methoxycyclohexl)-methanone] (JNJ16259685) and the mGluR5 antagonist 2-methyl-6-(phenyl-ethynyl) pyridine hydrocholoride (MPEP), alone or in combination with selected doses of morphine in the capsaicin-induced hyperalgesic tail withdrawal model of inflammatory pain in rats.
Methods: Baseline latencies to withdraw the tail from a 45°C water bath were determined in male Fischer 344 rats following capsaicin admininstration to the tail . After baseline determinations, morphine (0.3-10.0 mg/kg), JNJ16259685 (1.0-3.0 mg/kg), or MPEP (1.0-10.0 mg/kg) were administered alone or in selected dose combinations 30 min prior to testing. 15 min prior to testing, rats received 0.3 μg capsaicin into the tail under isoflurane anesthesia, with animals recovering within 2-3 min. Latencies to withdraw the tail from the 45°C water bath were recorded 15 min following capsaicin injection.
Results: JNJ16259685 produced no significant antinociceptive effect alone and did not shift the morphine dose effect curve at any dose tested. Similarly, low doses of MPEP (1.0-3.0 mg/kg) produced no antinociceptive effect alone and did not shift the morphine dose effect curve; however, the highest dose of MPEP (10.0 mg/kg) produced a significant antinociceptive effect alone and a small, but significant attenuation of the high morphine doses (3.0-10.0 mg/kg).
Conclusions: These results indicate that the effects of mGluR antagonism on morphine antinociception in an inflammatory pain model depend on the dose and type of antagonist as well as the dose of morphine.
Financial Support: R01-DA002749 and T32-DA007244.

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DISTRESS TOLERANCE AND ADOLESCENT SUBSTANCE USE PROBLEM SEVERITY.

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Aims: The problem of substance use in adolescence continues to grow despite large-scale public health efforts to reduce both its incidence and prevalence. This is particularly troublesome given that adolescent substance use and especially misuse often signals future impairments in physical health, mental health and social and occupational functioning. To enhance prevention efforts, theorists have attempted to understand factors that contribute to the etiology and maintenance of substance misuse, with particular emphasis on the role of negative emotional states. Initial evidence suggests that pre-adolescents with low distress tolerance, defined as the inability to persist in goal directed activity in the presence of intense emotional discomfort, are significantly more likely to have used alcohol in the past year (Daughters et al., 2009). However, limitations of this study included low levels of past year alcohol use indicative of a pre adolescent sample, as well as lack of inclusion of a measure of behavioral disinhibition, which is consistently associated with higher rates of delinquent behavior among adolescents.
Methods: In attempts to replicate and expand on this finding, we examined the relationship between distress tolerance, behavioral disinhibition (i.e., impulsivity), and the total substance use problem index of the Global Appraisal of Individual Needs (GAINS) scale among a sample of 150 15-17 year old adolescents.
Results: Hierarchical linear regression was used to example the unique and interacting effects of distress tolerance and impulsivity on substance use total problems. Findings indicate that among girls, but not boys, the interaction of low distress tolerance and high levels of impulsivity significantly predict greater substance use total problems ($R2 = .21$, $F = 6.6$, $p < .001$; $B = 0.22$, $sr2 = .09$, $p < .001$).
Conclusions: Future research directions and implications for translating this basic research into effective prevention and intervention programs will be discussed.
Financial Support: NIDA R21DA022741

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LOPERAMIDE-INDUCED TASTE AVERSIONS IN F344 AND LEW RATS: ASSESSMENT OF PERIPHERAL OPIOID ACTIVATION.

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Aims: The inbred F344 and LEW rats display strain differences in the aversive effects of systemically administered morphine, but display no differences in the aversive effects of centrally administered DAMGO, a selective mu opioid receptor agonist. These discrepant results suggest that the strain differences in morphine's aversive effects between these animals could be a function of differential activation of peripheral mu opioid receptors.
Methods: To test this hypothesis, male F344 (N = 67) and LEW (N = 67) rats were conditioned with loperamide, a peripheral mu opioid receptor agonist, in the CTA design. Animals received saccharin to drink followed by an injection of loperamide (0, 10, 18 or 32 mg/kg, s.c.; a total of three such pairings).
Results: Repeated-measures ANOVA revealed no strain differences, i.e., loperamide induced aversions of comparable strength in LEW and F344 rats, suggesting that peripheral mu opioid activation does not differ between the two strains. In follow-up assessments in which rats of both strains received saccharin without a subsequent loperamide injection, only the LEW rats conditioned with10 mg/kg loperamide extinguished the CTA; extinction was not evident in any other group.
Conclusions: The fact that loperamide induced dose-dependent aversions in both strains with no significant differences in acquisition of the aversions suggests that factors other than peripheral opioid activation accounts for the reported differences in morphine-induced CTA between the two strains (F>L). One possibility is that the aversive effects of morphine are peripherally mediated and similar for the F344 and LEW rats. Morphine's central (rewarding) actions may be different between F344 and LEW rats and it is this central activity that may modulate morphine's perceived aversive effects, i.e., the centrally mediated rewarding effects of morphine may impact the degree to which it can condition an aversion in the two strains.
Financial Support: Supported by a grant from the Mellon Foundation to ALR.

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MANUFACTURE, CHARACTERIZATION, AND STABILITY OF STANDARDIZED MARIJUANA CIGARETTES.

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Aims: The NIDA Drug Supply Program requires a constant supply of standardized marijuana cigarettes at specified potencies for use in scientific research and clinical studies. These cigarettes are manufactured per current good manufacturing practices regulations and released per established specifications for Δ9-THC and moisture content.
Methods: RTI has been manufacturing marijuana cigarettes for NIDA since 1974. The marijuana cigarettes are standardized for size and weight. The manufacturing parameters are kept consistent between batches. Potency is controlled through selective blending of bulk marijuana batches to produce a uniform, homogeneous lot of starting material for cigarette manufacture. For controls or placebos, Δ9-THC is extracted to produce plant material with less than 0.1% Δ9-THC. During manufacture, the cigarettes are tested for weight variation, moisture by a gravimetric method, and Δ9-THC content by a validated capillary gas chromatography (CGC) method. Analyses obtained via three extraction procedures provide profile of the cannabinoid content of cigarettes. Stability of cigarettes is monitored at ambient, refrigerator, and freezer conditions. At three-month intervals, the stored cigarettes are analyzed for Δ9–THC and other cannabinoids by CGC. The quantitative analytical data obtained from these analyses is examined for trends over time. Data for each batch of marijuana cigarettes is placed in a FDA Drug Master File and included in IND applications by NIDA investigators.
Results: The analytical data obtained demonstrate that each batch of standardized marijuana cigarettes meet established specifications for Δ9-THC and moisture content. The cigarettes are found to be stable at frozen conditions.
Conclusions: Standardized marijuana cigarettes manufactured at varying potencies as required by NIDA, stored under frozen conditions and shipped to NIDA investigators are of appropriate quality for use in research programs.
Financial Support: By NIDA under a contract to the University of Mississippi and subcontract to RTI.

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DRINKING AND DRIVING IN A DRIVER PROBABILISTIC SAMPLE FROM ALCOHOL OUTLETS OF PORTO ALEGRE, BRAZIL: PRELIMINARY FINDINGS.

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Aims: Brazil has 35,000 traffic accidents (TA)/year and Porto Alegre data show that 10 to almost 40% of TA victims have positive Blood Alcohol Concentration (BAC). In June 2008, a law changing the legal BAC limit to zero for drivers was passed. Aims: to assess risk factors for DUI of drivers who drink at alcohol outlets (AO) in Porto Alegre after the law.
Methods: A driver probabilistic sample was selected in 3 phases: 1) census tract with probability proportional to size (PPS- AO number), stratified by AO density (after statistical spatial analysis); 2) AO and time period (PPS based on time lag); and 3) drivers (inverse sampling with the screening of any adult who left AO). Selected drivers were interviewed, breathalized, and had saliva tested for drugs when they left the premises.
Results: So far, 2911 subjects have been approached, and 931 met inclusion criteria. Among those, we interviewed everyone who would drive in the next 60 min (G1: n= 450, male 76%, 37.2 y) and one fourth of those who were not (G2: n=159, male 64.2%, 37.7 y). Refusal rate was 5.7%. The overall prevalence of DUI was 52%, ranging from 7.9 % (Thursday) to 19% (Saturday). Binge drinking (in the last 12 months) differences were not significant (G1 73.1%; G2 78%). DUI in the last 12 months was significantly higher in G1(95.6% vs. 57.2%), as well as previous DUI accident (G1 19.6% vs. G2 12.6%). Although 62% of drivers were favorable to the law (G1 59.1% vs. G2 70.4%), only 45% reported changing their behavior (G1 42.1% vs. G2 53.3%).
Conclusions: DUI prevalence was extremely high, and data point to a recurrent behavior among those who were going to drive, regardless of the law. This should probably be related to the lack of enforcement of the law changing BAC legal limit in Porto Alegre.
Financial Support: SENAD

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IMPACT OF RIVASTIGMINE TREATMENT ON METHAMPHETAMINE-INDUCED SUBJECTIVE AND REINFORCING EFFECTS.

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Aims: To characterize the effects of treatment with rivastigmine (0, 3, or 6 mg, b.i.d.) on craving produced by experimental administration of methamphetamine (METH: 0, 15, and 30 mg, IV) in non-treatment-seeking, METH-dependent volunteers.
Methods: This is a double-blind, placebo-controlled, within-subjects, inpatient study. Participants receive METH on day 1, and are then randomized to placebo or rivastigmine on days 2-8. METH dosing is repeated on day 5. On day 6, participants are exposed to a METH sample session of 10 non-contingent infusions of METH (0 and 5 mg, IV). On day 7, participants choose between an infusion of METH (0 and 5 mg, IV) or no infusion.
Results: To date, participants (N=10) are primarily Caucasian males who are 34.5±2.6 (mean±S.E.M.) years of age. Participants report using METH for 11.1±2.2 years and have used METH 14.2±3.5 days out of the last 30 days. Preliminary analyses of the data include mean maximum subjective effects at post-randomization (day 5). The data indicate that METH, but not saline, increased subjective effects of High and Desire, and that rivastigmine (3 and 6 mg) reduced these responses by ~25%. Self-administration data reveal that participants chose METH infusions more often than saline ($p<0.001$), and that rivastigmine treatment reduced the total number of choices for METH, though this did not reach significance.
Conclusions: The results indicate that rivastigmine treatment is well tolerated and there is evidence indicating efficacy for rivastigmine in attenuating the subjective and reinforcing effects produced by METH. Data acquisition is continuing and a larger sample size (N=16) will be presented at the conference. Additional outputs will include cardiovascular data and a complete analyses of subjective effects across the full time course.
Financial Support: DA023964

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COCAINE REWARDS ACTIVATE NEURAL PROCESSING USED FOR PERFORMANCE OF COGNITIVE TASKS IN NONHUMAN PRIMATES.

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Aims: Analyses of behavioral, neurophysiologic and imaging data in nonhuman primates (NHPs) performing two different well-trained cognitive tasks, show that trials that signal delivery of cocaine vs. juice rewards, activate different brain regions as reflected in brain images of local cerebral metabolic activity from the same animals.
Methods: Rhesus monkeys were trained to perform a 1) multi-image delayed-match-to-sample (DMS) or 2) GoNogo, task in order to receive either cocaine (IV) or juice as a reward for successful performance on individual trials. PET imaged [18] FDG was employed to visualize local cerebral glucose metabolic rates while animals performed the tasks. Single neuron recordings were also obtained from neurons in the prefrontal cortex and dorso/ventral striatum to correlate firing with task performance for cocaine and juice rewarded trials.
Results: Accuracy on cocaine trials was dose-dependent and produced different types of brain activation patterns using PET [18]FDG imaging than sessions employing only juice rewarded trials. Neurons in the prefrontal cortex and ventral striatum recorded during task performance reflected differential firing on juice vs. cocaine rewarded trials. On cocaine trials striatal neurons were more responsive than on juice trials while prefrontal neurons were affected by cocaine only as a function of trial difficulty.
Conclusions: The findings suggest that cocaine rewards activate different neural systems within the brain than juice rewards. If is likely that cocaine acts by "hijacking" normal reward processes that are activated by appetitive conditioning, suggesting that some reward systems cannot discriminate between cocaine and appetitive elements delivered in a behaviorally contingent manner. This bias in a specific population of prefrontal and striatal neurons to respond to both cocaine and juice when delivered as rewards, makes these brain regions more susceptible to activation when exposed to abused substances.
Financial Support: This work was supported by DA06634 and DA0235373 and DA026487 to S.D.

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PROMOTING THE USE OF DEPOT NALTREXONE WITH AN EMPLOYMENT-BASED CONTINGENCY MANAGEMENT INTERVENTION.

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Aims: Naltrexone is an effective opiate antagonist, but its utility in treating opiate dependence has been limited by poor patient acceptance. Recently developed depot injections of naltrexone provide opiate blockade for up to 4 weeks and should simplify adherence. However, given the rejection of oral naltrexone by most patients, concurrent behavioral treatment may be needed to encourage patients to take the depot injections consistently. The purpose of this study is to evaluate the effectiveness of the Therapeutic Workplace, an employment-based intervention that uses salary for work to reinforce clinically important behavior change, in promoting use of depot naltrexone in unemployed heroin-dependent adults.
Methods: After completing opiate detoxification and induction onto oral naltrexone, participants were randomly assigned to a Prescription or Contingency group. All participants could attend a therapeutic workplace for 26 weeks, where they could work for 4 hours every weekday and earn about $10 per hour in vouchers. All participants could receive depot naltrexone injections every 4 weeks at no cost. Participants in the Contingency group could work and earn vouchers only if they took their scheduled injections. Participants in the Prescription group could work and earn vouchers independently of whether they used depot naltrexone.
Results: Preliminary results from the first 20 participants (10 from each group) who completed the study showed that 2 participants in the Contingency group received all naltrexone injections compared to 7 in the Prescription group. The percent of injections received by the Contingency group was significantly higher than the Prescription group (85 vs. 50%, respectively, $p=.01$). The randomized controlled trial (n = 38) and associated statistical analyses will be completed by the time of this presentation, and updated results will be presented.
Conclusions: The study shows that employment-based reinforcement can increase use of depot naltrexone.
Financial Support: This work was supported by R01DA019497 and T32DA07209.

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ALCOHOL CONSUMPTION OVER 11 YEARS IN A PROBLEM DRINKING AND DEPENDENT GENERAL POPULATION SAMPLE.

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Aims: Compared to treatment-seeking alcohol drinkers, the course of alcohol consumption among problem and dependent drinkers in the general population has seen limited study. The primary goal of this work was to examine how informal support and community services impact the course of alcohol disorders by examining the trajectories of alcohol consumption over 11 years in a randomly selected sample.
Methods: Both alcohol dependent and problem drinking adults (n=672) were identified through probability surveys in the general population of a single California county. Participants were interviewed at baseline and again 1, 3, 5, 7, 9 and 11 years later. Models of consumption, controlling for demographic characteristics, problem severity, community services, and recovery-oriented social networks, were estimated.
Results: Total volume of alcohol consumed declined over time (p<.0001) in an accelerating fashion (p=.0001). Women drank less than men (p=.0012), and Whites more than Blacks (p=.0060) and Hispanics (p=.0091). Baseline severity was positively related to drinking volume (ASI severity p=<.0001) but negatively related to number of dependence symptoms (p=.0081). Interestingly, a risk indicator based on family alcohol history was not significant (p=.4566). Recovery-oriented social networks (p<.0001) and AA participation (p<.0001) significantly predicted decreased consumption for both groups. Of particular interest, contacts with medical, mental health, welfare, and legal systems were predictive of reduced consumption (p<.0001).
Conclusions: Results both confirm and extend earlier our earlier work on this topic. Findings point to the importance of developing mechanisms for better identifying problem drinkers in the course of contacts with health and social service systems, and for facilitating use of self-help groups and positive changes in social networks. Development of recovery-oriented social networks should be emphasized to extend the benefits of treatment for dependent individuals.
Financial Support: Supported by grant funding from NIAAA and NIDA

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FRENCH MODIFIED ADDICTION SEVERITY INDEX: PSYCHOMETRICS PROPERTIES IN TOBACCO USERS AND VALIDITY OF THE ADDED TOBACCO SECTION.

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Aims: Tobacco is the most prevalent substance used in the general population as well as in clinical samples such as substance-dependent clients.
Objective: To assess the validity of the Tobacco section of the French modified ASI in 833 tobacco users.
Methods: The validity of the tobacco section of the ASI in clients of outpatient addiction clinics was examined by assessing its internal consistency, its convergent validity with other measures such as DSM-IV tobacco dependence diagnosis and Fagerström Test for Nicotine Dependence (FTND) score, and its discriminant validity.
Results: Internal consistency was similar to that reported for the ASI in other substance user samples. Internal consistency of the tobacco section was good (Cronbach's alpha = 0.77) and a principal components analysis indicated that the four items comprising the Tobacco composite score loaded in one factor. ASI tobacco scores showed good convergent validity with FTND score and DSM-IV tobacco dependence diagnosis. The ASI tobacco scores could discriminate tobacco users who reported tobacco use as a problem from those who reported no problem with their tobacco use. They could also discriminate subjects who met DSM-IV tobacco dependence criteria.
Conclusions: The French modified ASI is the first tool that permits a multifactorial assessment of tobacco use. The systematic assessment of tobacco use will better allow for the opportunity to discuss and plan treatment for tobacco addiction management in addiction clinic settings.
Financial Support: PHRC 2006

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FOUR-YEAR OUTCOMES FROM THE EARLY RE-INTERVENTION EXPERIMENT WITH RECOVERY MANAGEMENT CHECKUPS.

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Aims: Ongoing monitoring and early re-intervention have become standard practice when managing numerous chronic conditions. This experiment tested the feasibility and effectiveness over 4 years of providing quarterly Recovery Management Checkups (RMC) to adult chronic substance users.
Methods: Participants (n=446) were recruited (93% participation) from sequential substance abuse treatment admissions and were 54% Male, 80% African American, 77% between the ages of 30-49, 88% with dependence, 56% with co-occurring psychiatric problems, and 54% with moderate to high levels of crime and violence. Participants were randomly assigned to the RMC or control condition (assessment only) and interviewed quarterly for 4 years with an average of 95% completion per wave. RMC included quarterly monitoring; utilized motivational interviewing to provide personalized feedback and to resolve ambivalence about substance use; and used treatment linkage, engagement, and retention protocols to increase the amount of treatment received. Measurement was based on urine testing, record logs, and self report using the Global Appraisal of Individual Needs (GAIN).
Results: Participants assigned to RMC where significantly more likely than those in the control condition to re-enter treatment (70% vs. 54%, OR=2.31), return to treatment sooner (45 vs. 13 months, d=0.41), return to treatment more times (1.9 vs. 1.0 times, d=0.63), receive more treatment (112 vs. 79 days, d=0.23), have fewer successive quarter in the community using (5.9 vs. 7.5, d=-0.30), have fewer substance problems per month (2.02 vs. 2.83 problems, d=-0.29) and reported more total days of abstinence (1026 vs.932 days, d=0.24).
Conclusions: RMC is an effective method of monitoring and re-intervening with chronic substance users and is associated with better long-term outcomes. While RMC increased the likelihood of reentering treatment and improving outcomes, almost half were still using or having problems 4 years later.
Financial Support: The National Institute on Drug Abuse Grant number R37 DA11323.

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THE RELATIONSHIP BETWEEN INCREASED EXERCISE AND SMOKING CESSATION.

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Aims: Exercise is increasingly recognized as an important aid in helping people manage multiple chronic conditions in general and specifically to quit smoking. This is important because co-occurring emotional problems are common in substance abuse treatment and predict relapse, but less than half of those who need it receive mental health services. The goal of this observational study is to evaluate the extent to which increased physical exercise is associated with reduced smoking in the same quarter and the extent to which any gains are sustained into the next quarter.
Methods: Data are from 446 participants in the Early Re-Intervention (ERI) experiments who were interviewed using the Global Appraisal of Individual Needs (GAIN) quarterly for 4 years (over 95% completion per wave, 80% completing all waves). Participants were 54% Male, 80% African American, 77% between the ages of 30-49, 88% with dependence, and 56% with co-occurring psychiatric problems. They were recruited (93% participation) from sequential substance abuse treatment admissions at Haymarket Center's central intake on the west side of Chicago. Each quarter, participants were classified into those who increased their days of exercising 20 or more minutes per day versus those who did not (including those who decreased their exercise).
Results: Increased exercise was associated with significantly greater reductions in the number of times participant smoked than those who did not (+10 vs -35 times per quarter, $F(2,12122) = 5.153$, $p<.01$) and the resulting changes were sustained in the next.
Conclusions: This suggests that exercise can be a useful adjunct to treatment or recovery support services and should be explored further in a prospective experiment.
Financial Support: National Institute on Drug Abuse Grant # R37 DA11323

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EFFECTS OF PREWEANLING, PREADOLESCENT, AND ADOLESCENT METHYLPHENIDATE TREATMENT ON MORPHINE-INDUCED CONDITIONED PLACE PREFERENCE.

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Aims: Early exposure to methylphenidate (MPH) alters the rewarding properties of abused drugs in adult rodents; however, some investigations have found enhanced rewarding effects while others have reported decreased rewarding effects. Although the reason for these apparent discrepancies is unknown it is possible that age at onset of MPH exposure may be important. Specifically, rats exposed to MPH during adolescence and the preweanling period showed increased cocaine self- administration and morphine-induced CPP while preadolescent MPH exposure decreased cocaine-induced CPP. Therefore to determine if age at onset of MPH exposure differentially affects the rewarding value of morphine, we assessed morphine-induced CPP in adults rats exposed to MPH during the preweanling, preadolescent, or adolescent phase.
Methods: Rats were injected with MPH (0, 2, or 5 mg/kg, IP) once a day from postnatal day (PD) 10, 20, or 30 for 10 consecutive days. Morphine-induced CPP was assessed starting on PD 60. CPP was conducted using a 12-day biased CPP procedure which included one preconditioning day, eight conditioning days (consisting of alternating daily injections of saline or morphine (0 or 5 mg/kg, SC) and three test days. The three test days occurred 24 hr, 4 weeks, and 8 weeks after the last conditioning day.
Results: Rats conditioned with morphine showed morphine-induced CPP regardless of MPH treatment. MPH exposure changed the persistence but not the acquisition of morphine-induced CPP in an age-dependent fashion. In rats exposed to MPH at PD 20, morphine-induced CPP was not altered at any time point, whereas; morphine-induced CPP was enhanced in rats exposed to MPH (2 or 5 mg/kg) at either PD 10 or PD 30 on the later to test days. Interestingly, the increased persistence was only seen in male rats.
Conclusions: The present data showed that early MPH treatment may increase the vulnerability to abused drugs but this enhanced vulnerability is dependent on the age at onset of MPH exposure.
Financial Support: Supported by NIH grant GM073842

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WITHDRAWN

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A ZERO-INFLATED HIDDEN MARKOV MODEL OF COCAINE USING BEHAVIOR.

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Aims: Paradigms for stress- and cue-reactivity research involve acute pharmacological or stressful stimulation designed to elicit stress and craving responses in substance-dependent individuals. It is unclear whether participation in stress- and cue-reactivity research increases drug-seeking behavior. Markov models are frequently used in behavioral research to model longitudinal processes. We proposed a 2-state zero-inflated hidden Markov model for Poisson counts to model the frequency of drug use per week among cocaine-dependent individuals before and after study participation.
Methods: Timeline follow-back for cocaine use was collected for 12 weeks prior to and 4 weeks after participation in a stress- and cue-reactivity study. Two latent states corresponding to high and low use were hypothesized to describe weekly use behavior. To account for a preponderance of "zero" uses, we assumed a zero-inflated Poisson process for the weekly counts. Markov model transition probabilities depend on the prior week's latent state, demographic variables, and time-varying covariates. We adopted a Bayesian approach to model fitting, and used the conditional predictive ordinate statistic for model comparison.
Results: The the zero-inflated Poisson hidden Markov model provided the best data fit (log pseudo marginal likelihood = -1008.4). The population mean (standard error) number of days used per week for participants in the high use state was 3.4 (1.7) versus 1.0 (1.0) days in the low use state. The log odds ratio [95% credible interval] of remaining in the high use state at time t given that the subject was in the high use state at time t -1 was 6.46 [5.02, 8.29]. The odds of transitioning to or remaining in the high use state in any given week after participation in the study was 0.06 [0.01, 0.17] of what it was in the 12 weeks prior to the study.
Conclusions: The zero-inflated Poisson hidden Markov model is useful for monitoring longitudinal drug use. Participation was not associated with increased drug use.
Financial Support: NIDA P50 DA016511, P20 DA022658, K24 DA00435, M01 RR001070

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GENDER DIFFERENCES IN THE PREVALENCE OF CO-OCCURRING MENTAL HEALTH DISORDERS IN A SUBSTANCE ABUSE TREATMENT POPULATION.

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Aims: The high rate of co-occurring mental health disorders in people with substance use problems has been identified in both community samples and clinical populations. In a recent study to validate four screening tools for mental disorders in a Canadian substance abuse treatment population, structured clinical interviews were conducted to assess the presence of a mental disorder. The purpose of the present study is to examine the co-occurrence of mental health disorders in this population, and to identify gender differences in the prevalence of these disorders. A second objective is to explore differences in the prevalence of particular mental health disorders within groups when examined by different substance use diagnoses and gender.
Methods: 544 clients were recruited from three large treatment centres in Ontario, Canada (68.6% male; mean age 37.3 years). Clients completed several screening tools and self-report measures, followed by an independent same-day structured clinical interview (SCID). Pearson chi-square analysis was used to examine differences between groups, and univariate logistic regression was used to examine the strength of the association between specific variables.
Results: Compared to men, women were found to have a significantly higher lifetime prevalence of mood disorders (70.2% vs. 57.6%), anxiety disorders (71.3% vs. 53.9%), eating disorders (17.0% vs. 2.9%), and mental health disorders overall (88.3% vs. 77.2%). In addition, women were found to have a greater number of comorbid psychiatric disorders, while men were found to have a greater number of lifetime substance use disorders. Significant relationships were also identified between mental health disorders and specific substance use disorders.
Conclusions: The results of the present study contribute to the growing evidence concerning gender differences in co-occurring mental health and substance use disorders within different treatment-seeking populations.
Financial Support: Canadian Institutes for Health Research

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CHARACTERISTICS OF TREATMENT RESPONDERS TO A CONTINGENCY MANAGEMENT INTERVENTION FOR HOMELESS, OUT-OF-TREATMENT, SUBSTANCE-ABUSING MEN WHO HAVE SEX WITH MEN.

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Aims: Homeless, out-of-treatment, substance-abusing men who have sex with men (MSM) have high HIV seroprevalence rates, frequently engage in exchange sex, and suffer from untreated mental health issues. This study assessed the efficacy of a Contingency Management (CM) intervention to homeless, out-of-treatment, substance-dependent MSM seeking low-intensity HIV prevention services at a community-based organization.
Methods: A total of 131 participants were randomized to a 24-week CM or control condition. Both groups earned points for attendance at the parent program and study activities; CM participants earned additional points for drug/alcohol abstinence and for accomplishing health-promoting behaviors. Assessments were conducted at baseline and 7, 9 and 12-month follow-up.
Results: Preliminary findings indicated a main effect of CM for both health-promoting behaviors (M_{CM}=15.9, $M_{control}$=1.7;p<.01), and drug/alcohol abstinence [β_{CM}=0.35 (SD=0.17); Z=2.11;p<.05]. However, further parsing of the data revealed differential effects based on race and HIV status. HIV-negative participants across both treatment conditions achieved greater alcohol/drug abstinence [M_{CM}=19.7 (SD=5.3), $M_{control}$=15.3 (SD=5.0); χ^2=27.36;p<.01], but accomplished fewer health-promoting behaviors (F=7.80;p<.01) relative to HIV-positive participants. Similarly, Caucasian participants achieved greater alcohol/drug abstinence than all other ethnic groups [M_{White}=10.2 (SD=3.1), M_{Black}=3.3 (SD=1.7); $M_{Hispanic}$=2.5 (SD=1.5); M_{Other}=1.0 (SD=0.9); F=408.8;p<.01], but this trend was not significantly different with health-promoting behaviors.
Conclusions: Identifying specific characteristics of treatment responders will inform the development of more specifically targeted and designed interventions to this high-risk population.
Financial Support: Supported by NIDA grant #1 R01 DA 015990-03

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HIV TRANSMISSION RISK BEHAVIORS AND GENOTYPIC DRUG RESISTANCE AMONG HIV+ PATIENTS ON OPIOID AGONIST TREATMENT.

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Aims: Opioid dependent HIV+ patients may harbor and transmit virus that is resistant to antitretroviral therapy (ART). Opioid agonist treatment (OAT) can improve adherence to ART and reduce HIV transmission risk behaviors. Our objective was to determine the prevalence of HIV transmission risk behaviors and HIV drug resistance among HIV+ patients receiving OAT.
Methods: We assessed demographics, ART adherence, urine toxicology, prior ART resistance, and self-reported HIV transmission risk behaviors via self-report and chart review. We collected blood samples for ART resistance testing. We evaluated the association between HIV transmission risk behaviors and ART resistance.
Results: 59 HIV+ patients receiving OAT were included in the analysis. 64% were male, 34% white, 53% on methadone, and 47% on buprenorphine. Of 47 patients on ART, 70% reported taking their medications daily. 42% had at least one urine toxicology test positive for illicit substances in the prior 6-mos. Of patients reporting sexual activity (n=35), 23% had unprotected sex; of patients reporting IDU (n=8), 38% reported sharing needles/works. 90 unprotected sexual encounters occurred and 12 were with HIV- or status unknown partners. 21 needles/works sharing encounters occurred and 19 were with HIV- or status unknown partners. 32% of patients (n=19) had a detectable viral load. Of these, 9 had evidence of ART resistance; 4 had single class, 2 double class, and 3 had triple class resistance. One patient with double class resistance and 2 patients with triple class resistance reported having sex >10 times each and one patient with triple class resistance reported sharing needles 7 times, all with HIV- partners.
Conclusions: We conclude that some HIV+ opioid dependent patients receiving OAT continue to engage in HIV transmission risk behaviors that can expose others to ART resistant virus. Strategies are needed to minimize the risk of transmitting of drug resistant HIV.
Financial Support: NIMH, 2P30MH062294-06A1; The Robert Wood Johnson Foundation; VA Merit Award

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ENVIRONMENTAL ENRICHMENT DAMPENS THE EFFECTS OF PRENATAL COCAINE ON COCAINE REWARD AND DOPAMINERGIC MARKERS IN ADOLESCENT MALE AND FEMALE RATS.

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Aims: Behavior of children exposed to cocaine prenatally has been shown to be altered by environment. A rat model was used to assess the effects of prenatal cocaine and environmental manipulation on reward circuits during adolescence.
Methods: Female rats were administered cocaine (0, 30 or 60 mg/kg/day prior to and during pregnancy. Following weaning, rats were housed individually (isolated) or in cages of 3 with toys (enriched) until postnatal day 42 when conditioned place preference testing began. Following a pretest to determine initial preference, rats were trained with cocaine (3 to 20 mg/kg) for 3 days and one day later, preference was determined. One hr later, rats were sacrificed, brains collected, frozen and later processed for dopamine transporter (DAT) density using quantitative autoradiography.
Results: Cocaine at 30 mg/kg increased preference in both sexes under both housing conditions except in enriched females where little CPP was observed in all prenatal groups at all training doses above 5 mg/kg. DAT density was increased significantly across the caudate putamen and nucleus accumbens (NA) in response to 60 mg/kg prenatal cocaine exposure in males and females compared to vehicle. In addition, there was a pretreatment x sex x housing interaction with an increase in DAT in both NA core and shell in isolated males, but not in females or enriched males after prenatal cocaine exposure.
Conclusions: Male and female adolescent rats responded differently to prenatal cocaine and the effects of environmental enrichment. Enriched females showed little CPP for any dose of cocaine tested regardless of prenatal exposure. Enriched males showed no increase in DAT density in response to prenatal cocaine, while in isolated males there were significant increases in the nucleus accumbens. Thus, enrichment offset some of the neurochemical adaptations that occur in response to prenatal cocaine exposure differentially in males and females.
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EFFECT OF DOPAMINE D1 RECEPTOR BLOCKADE IN THE NUCLEUS ACCUMBENS ON MOTIVATION FOR COCAINE: ROLE OF SEX AND STAGE OF ADDICTION.

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Aims: Although dopaminergic signaling clearly plays an important role in the early stages of cocaine addiction, less is known regarding its role during later stages. Behavioral studies have also revealed sex differences suggesting that the neurobiological mechanisms underlying cocaine addiction may be different between males and females. In this study, we examined the role of dopamine D1 signaling in cocaine reinforcement in both males and females at different stages of cocaine addiction (i.e., from initial exposure following short access (ShA) to extended access (ExA) cocaine self-administration). Specifically, we examined the effect of site specific infusion of the dopamine D1 receptor antagonist SCH 23390 into the nucleus accumbens on motivation for cocaine as assessed under a progressive ratio (PR) schedule.
Methods: Adult male (n=5-11) and female (n=6-7) Sprague-Dawley rats were trained to self-administer cocaine (1.5 mg/kg/infusion) under a fixed ratio 1 schedule with a maximum of 20 infusions. Once cocaine self-administration was acquired (2 consecutive sessions during which all 20 available infusions were obtained) rats were given either ShA to cocaine consisting of 3 more fixed ratio 1 sessions or ExA to cocaine consisting of 10 days of 24h access to cocaine infusions under a discrete trial procedure (4 infusions/hr). Following 14 days of abstinence, cocaine reinforcement was assessed by measuring PR responding, and once stable, the effects of intra-accumbens SCH 23390 infusions were determined.
Results: Although female rats showed higher levels of PR responding for cocaine than did males after ExA cocaine self-administration, no differences were observed following ShA cocaine self-administration. Intra-accumbens D1 receptor blockade produced a greater decrease in PR responding after ShA as compared to ExA cocaine self-administration.
Conclusions: These data suggest that the appearance of sex differences and the role of dopamine D1 receptors in cocaine reinforcement vary as a function of addiction stage.
Financial Support: Supported by NIDA grant R01DA024716 (WJL)

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SEX INFLUENCES ON ALTERATIONS IN IMMUNE FUNCTION AND LEVELS OF THE STRESS-PROTECTIVE HORMONE DHEAS IN COCAINE-DEPENDENT INDIVIDUALS.

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Aims: Cocaine use is associated with sex-specific dysregulation in HPA axis and adrenal medullary stress systems. As these stress pathways also influence the neuroprotective hormone dehydroepiandrosterone sulfate (DHEAS) and immune function, we examined these responses in cocaine abuse.
Methods: 28 abstinent cocaine abusers (12M/16F) and 28 matched healthy volunteers (14M/14F) were exposed to three guided imagery conditions (stress, drug-cues and neutral)one per day, across three days. Plasma DHEAS and inflammatory cytokines (including interleukin -1 receptor antagonist (IL-1)ra, IL-6, IL-10, tumor-necrosis factor-α (TNF-α) and TNF-R1) were assessed at baseline and at various time-points following imagery presentation.
Results: Overall, males demonstrated significantly higher DHEAS values than females (p= .004), but only healthy controls showed increased stress-induced DHEAS levels (p= .0004). For the immune markers, females exhibited higher pro-inflammatory IL-1ra responses to stress compared to neutral($p<0.001$) and to drug-cue (p=.004)conditions. Compared to healthy controls, cocaine patients had greater drug cue-induced IL-1ra levels (p=0.005). Only healthy controls exhibited higher basal and stress-induced levels of the anti-inflammatory cytokine, IL-10 ($p<.04$). For the pro-inflammatory marker TNF-R1, cocaine patients showed a suppressed response of stress relative to neutral(p= .001) and to drug-cue (p = 0.02) exposure.
Conclusions: Increased DHEAS values in males and healthy volunteers suggest a buffering of the stress response in these groups, but lower levels in females and cocaine addicts indicate their greater vulnerability to deleterious stress effects. Suppressed anti-inflammatory responses in cocaine abuse suggest significant sex-specific immune dysfunction, which could make addicts, particularly women, more susceptible to immunological disorders and medical co-morbidity. Such dysfunction may significantly affect relapse risk and result in a more chronic course of cocaine dependence.
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HEPATITIS C KNOWLEDGE AMONG MMT STAFF AND SOCIAL WORKERS IN CHINA.

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Aims: HCV infection becomes a public problem in China as well as in other countries. Medication to treat Hepatitis C is available, however, many HCV positive patient did not reap from this treatment. Drug treatment systems are uniquely situated to educated, counsel, and test drug users for HCV, and facilitate their access to medical treatment. To be optimally supportive of patients concerning HCV, treatment staff needs to know the information about HCV, and then sharing their information to patients. This study examines the HCV knowledge level of MMT staff and social workers in China, and also tries to explore their readiness to provide HCV related information to patients.
Methods: 60 MMT staff and 165 social workers were interviewed. A structured screening questionnaire and HCV Knowledge Scale were used to collect the information regarding HCV knowledge of Hepatitis C,the readiness to provide HCV related information to patients,and activities in providing HCV information during their routine work.
Results: Overall, the score of HCV knowledge was 12.7 (2.1), the averaged scored for social workers was 8.3 (3.2), for MMT staff was13.8 (3.6). Although MMT staff have significant high score of HCV knowledge scale compare to social workers, both of them seldom provided HCV information to patients during their routine work. For Social workers, 75% of them reported never received HCV specific training, 90% reported that HCV –related training should be provided to them. Only about 10% of social workers provided HCV related information to patients. For MMT staff, the scores of HCV knowledge were higher than social worker, but the readiness to provide HCV related information was same to social workers ($p>0.05$). High HCV related knowledge level did not improve their readiness to provide HCV related information to patients.
Conclusions: The results suggested the need for effective HCV-related training for MMT staff and social workers, and increase their readiness to provide HCV information to patients in their work.
Financial Support: This study was supported by Shanghai Health Bureau.
PI Dr. Jiang Du

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TOWARDS EVIDENCE-BASED DISPOSITIONS: A PRELIMINARY EVALUATION OF THE RISK AND NEEDS TRIAGE IN A SAMPLE OF DRUG COURT CANDIDATES.

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Aims: The Risk and Needs Triage (RANT) is a brief tool assessing substance abusing offenders' levels of criminogenic risk and clinical need. It was developed in collaboration with the 4th Judicial District Drug Court in Hennepin County Minnesota to assist in determining offenders' optimal level of criminal justice supervision and community-based treatment. Using evidence-based performance indicators, the RANT determines whether offenders meet criteria for high or low risk and high or low need. In the RANT system, those who score (1) high risk/high need may require more intensive supervision and clinical services (e.g., drug court), (2) low risk/high need may require a lower level of criminal justice supervision and more intensive clinical services, (3) high risk/low need may require more intensive supervision and less intensive clinical services, and (4) low risk/low need may require less intensive supervision and less intensive prevention-based clinical services. The current study evaluated the RANT's psychometric properties and clinical utility.
Methods: The RANT was completed by felony property and drug offenders appearing before the Hennepin County Property Drug Court from March 2007 to February 2008. The internal consistency and factor structure of the RANT were examined in a sample of 627 clients, and its predictive validity and clinical utility was examined in subsample of 459 clients.
Results: Results revealed a 2-factor structure and moderate levels of internal consistency for risk (r = .52) and need (r = .68) items. In addition, risk predicted 1-year criminal recidivism (OR = 3.4, p = .005) with 42% of high risk clients recidivating compared to 19% of low risk clients. High risk/high need clients recidivated at the highest rate (44%).
Conclusions: The results provide support for the reliability, validity, and clinical utility of the RANT.
Financial Support: Minnesota Judicial Branch, 4th Judicial District

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ORAL NICOTINE DISCRIMINATION IN NICOTINE NON-USERS.

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Aims: Nicotine is thought to be the primary agent responsible for tobacco use and dependence. However, nicotine is a relatively weak reinforcer in animals and has not been shown to be reinforcing in human nicotine non-users. This study investigated the discriminative and subjective effects of oral nicotine in nicotine non-users.
Methods: Four healthy volunteers who had less than 20 lifetime exposures to nicotine participated. The study used a double-blind nicotine vs. placebo discrimination procedure. Participants received two sets of capsules daily (one containing placebo and the other nicotine hydrogen tartrate) and completed questionnaires rating 22 subjective effects for two hours after each set of capsules. Discrimination at ascending doses of nicotine was tested.
Results: All four subjects reliably discriminated between nicotine and placebo ($p<.05$, binomial probability distribution). The lowest dose that was discriminated varied between 1.5-4.0 mg/70kg across volunteers. Compared to placebo, nicotine increased ($p<.05$) ratings in one or more volunteers on Drug Strength, Liking, Alert, Urge to do work-related activity, Content/well-being, Concentration, and Stimulated. Nicotine did not significantly increase any other ratings including Disliking, Bad Effects, Lightheaded/dizzy, Headache, or Upset stomach/nauseated.
Conclusions: All four volunteers significantly acquired oral nicotine discrimination and reported increases in positive subjective effects in response to nicotine. A better understanding of the subjective effects of nicotine in nicotine non-users has important implications for understanding both the initiation of nicotine use and the development of addiction to nicotine.
Financial Support: Supported by RO1 DAO3890, T32 DA07209

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EMPLOYMENT-BASED REINFORCEMENT OF ORAL NALTREXONE COMPLIANCE WITHIN UNEMPLOYED INJECTION DRUG USERS.

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Aims: Naltrexone is an opiate antagonist that effectively prevents relapse to opioid use, however rates of compliance are notoriously poor. Reinforcement of naltrexone administration via an employment-based intervention may increase rates of compliance with oral naltrexone.
Methods: Recently-detoxified participants were randomly assigned to a Naltrexone Contingency (NC; n=35) or Work Only (WO; n=32) group for a 6-month period. Participants attended the workplace daily, received access to computer training and educational programs, and could earn up to $6,000 in hourly wages and productivity pay. Urine samples were collected thrice weekly and tested for evidence of opiates and cocaine. Naltrexone urinalysis testing was conducted monthly. Participants in the NC group were required to ingest oral naltrexone thrice weekly to gain entry into the workplace while WO participants received a take-home prescription and could work independently of naltrexone compliance. Outcome measures are naltrexone, opiate and cocaine urinalysis results.
Results: At intake, participants were on average 45 years old, 61% male, 85% African-American and had injected heroin and cocaine for 18 and 13 years, respectively. Data show access to the workplace successfully reinforced compliance with naltrexone. Mean percent naltrexone-positive urine samples were 83% and 34% in the NC and WO groups, respectively. Mean opiate-positive samples were also lower among NC versus WO participants (18% and 31%, respectively); however no effect was observed on cocaine use (41% vs. 39%, respectively).
Conclusions: This study provides evidence that an employment-based behavioral treatment can successfully reinforce compliance with naltrexone and help prevent relapse to opioid abuse. The ability to reinforce compliance of a medication that has a notoriously poor adherence rate in the context of a workplace environment has important implications for dissemination and use with other low-compliance medications.
Financial Support: NIDA R01-DA019386 and T32-DA007209

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RELATIONSHIPS BETWEEN SUBSTANCE USE AND NEUROPSYCHOLOGICAL FUNCTIONING AMONG DRUG USERS IN NOVOSIBIRSK, RUSSIA.

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Aims: To evaluate relationships between frequent opiate and alcohol use and neuropsychological test performance among adult drug users in Novosibirsk, Russia
Methods: Participants were 109 active drug users aged 18 to 40 (X = 26.1; SD = 5.6) and recruited from the Novosibirsk region of Russia with the sample being 100% white and 89% male. The assessment included a urine sample collection to test for recent drug use and neurocognitive test battery comprised of the Trail Making A and B, Stroop Color Word Test, Shipley Institute of Living Scale (SILS), and Wisconsin Card Sorting Task (WCST).
Results: Eighty five percent (N=93) reported lifetime heroin injection and 79% (N=86) reported drinking alcohol in the past month. When compared to infrequent injectors, frequent injectors exhibited significantly higher rates of deficit performance on tests of Trails A (Odds Ratio (OR)=2.6; 95% Confidence Interval (CI), 1.2, 5.8), SILS abstraction scale (OR=2.6; 95% CI, 1.2, 5.8), SILS conceptual quotient (OR=2.8; 95% CI, 1.2, 6.2), WCST % errors (OR=2.3; 95% CI, 1.1, 5.0), WCST Perseverative Responses (OR=2.7; 95% CI, 1.2, 6.1), WCST % Perseverative Errors (OR=2.7; 95% CI, 1.2, 6.1), WCST Conceptual Level Responses (OR=3.8; 95% CI, 1.7, 9.1), WCST % Conceptual Level Responses (OR=3.6; 95% CI, 1.7, 8.7), and WCST Categories Completed (OR=3.2; 95% CI, 1.4, 7.2), adjusting for age, education, years of drug use, and head injury. Compared to infrequent alcohol users, frequent alcohol users exhibited significantly higher rates of deficit performance on the Stroop test (OR=2.4; 95% CI 1.1, 5.3) and Trails B minus A (OR=2.3; 95% CI 1.0, 5.2), adjusting for age, education, years of drug use, and head injury.
Conclusions: Neuropsychological deficits associated with heavy alcohol and opiate use are likely to negatively influence decision-making that may also result in elevated risk behaviors associated with infectious disease.
Financial Support: Supported by the JH Center for AIDS Research and the NIDA Epidemiology Training Program 2T32DA007292

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INTERNALIZATION OF COMPLIMENTARY SEXUAL STEREOTYPES AS A CORRELATE OF RISKY SEXUAL ATTITUDES AMONG AFRICAN-AMERICAN FEMALES.

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Aims: Although standard forms of prejudice and racial discrimination are known to affect physical and mental health in African Americans (e.g., Landrine & Klonoff, 1996), no research has examined the influence of complimentary racial stereotypes on such outcomes. This study examines the relationship between African American women's internalization of complimentary sexual stereotypes (CSS) and their attitudes regarding the acceptability of engaging in risky sexual behaviors.
Methods: Data were gathered from 206 African American women (both drug users and non-drug users) as part of the Black Women in the Study of Epidemics project (B-WISE). A series of multivariate regression models were used to examine associations between women's internalization of CSS and various sex-related attitudes.
Results: The majority of participants were single (89%) and heterosexual (76%) with a mean age of 35 years. Although no significant relationships were found between CSS and measures of drug use, greater internalization of CSS was significantly associated with African American women's beliefs that having sex without protection would strengthen their relationship (B = .37, SE = .19, p = .05), that they could use drugs and always make healthy choices about protection (B = .62, SE = .27, p = .02), and that they knew their partner was safe from HIV by the way he looked (B = .34, SE = .16, p = .03). Marginally significant associations were found for women's beliefs regarding their own levels of HIV risk (B = .41, SE = .22, p = .06) and their willingness to have sex in exchange for money/drugs (B = .29, SE = .19, p = .13).
Conclusions: These results suggest that in addition to distress brought about by the experience of more straightforward types of prejudice and discrimination, the internalization CSS by African American women can lead to increased health risk, particularly in relation to infection with HIV or other sexually transmitted diseases.
Financial Support: This research was supported by the NIDA (R01-DA022967; K01-DA021309).

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PHYSICIAN MENTORING TO FACILITATE BUPRENORPHINE TREATMENT: THE PCSS-BUPRENORPHINE PROJECT.

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Aims: The Physician Clinical Support System-Buprenorphine (PCSS-B) is a CSAT-funded nationwide system of physician-mentors who provide ongoing education and support to facilitate and promote office-based buprenorphine treatment.
Methods: A range of data were collected to assist in the evaluation of the project including electronic surveys and a web-based system for mentors to enter descriptions of each participant contact.
Results: The PCSS-B provides telephone email and in-person support, a website, clinical guidances, and a warmline to providers that participate in the program. There are currently 88 physician-mentors, 5 clinical experts and 4,162 registered participants in the PCSS-B system. Between July 2005 and July 2009, 67 mentors and 4 clinical experts reported providing mentoring services to 632 participants in 48 states, DC and Puerto Rico. A total of 1,455 contacts were provided through email (45%), telephone (34%) and in-person visits (20%). Support has included both clinical issues (76% of contacts) such as dose management, induction procedures, and pain issues and logistical issues (18% of contacts) such as scheduling, payment, availability, paperwork, and medication supply. There were 72,822 visits to the PCSS-B website with 179,678 pages viewed. Seven guidances were downloaded more than 1000 times. The warmline averaged more than 100 calls/month.
Conclusions: We conclude that the PCSS-B model provides support for a mentorship program to assist physicians in the provision of buprenorphine. CSAT has recently funded the PCSS-Methadone (PCSS-M) to assist with the use of methadone in opioid treatment programs and its use for chronic pain.
Financial Support: The PCSS-B is funded by SAMHSA-CSAT.

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SOCIALLY-INDUCED MORPHINE PSEUDO-SENSITIZATION IN ADOLESCENT MICE.

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Aims: Peer influences are among the strongest predictors of adolescents' drug use. In humans, they are commonly thought to be cultural in nature and mediated by cognitive and emotional influences. This study examined whether age-dependent social influences on morphine sensitivity could also be modeled in rodents.
Methods: 140 C57BL/6 mice were used (n=10-26 per group). Adolescent mice were injected during PND 28-33, and tested at PND 42. Adult mice were injected during PND 63-68, and tested at PND 77. Two groups of drug-naïve mice were examined for each age and sex group: 1) saline cage-mates - saline-injected mice housed together with morphine-treated mice (for 6 days, 10-40 mg/kg, s.c.), and 2) saline alone - saline-injected mice housed physically and visually separated from the morphine-treated mice. All mice were physically and visually separated during the locomotion test. Baseline locomotor activity was recorded for 60 minutes. All mice were then injected with 10 mg/kg morphine and recorded for another 60 minutes. Data analysis was conducted using a between-groups ANOVA design followed by Bonferroni's post-hoc comparisons.
Results: Prior interactions with morphine-treated mice resulted in a significantly enhanced hyper-locomotion response to morphine in drug-naïve adolescent male mice (i.e. saline cage mates > saline alone). This was not observed in adults. In adults, there were no significant differences in morphine induced hyper-locomotion between saline alone and saline cage-mates. This phenomenon is also sex-dependent; there was no significant difference in morphine-induced hyper-locomotion between saline cage-mates and saline alone adolescent females.
Conclusions: This study demonstrates age-and sex-dependent differences in the vulnerability to social influences on sensitivity to drugs of abuse. Modeling peer influences in rodents is potentially a key to identifying age-dependent social influences that are not cultural in nature.
Financial Support: NIH grants DA022402 and P50DA05010.

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CLINICAL EFFICACY OF RESIDENTIAL ABSTINENCE-BASED DETOXIFICATION PROGRAM IN HEROIN DEPENDENCE.

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Aims: Besides maintenance treatment programs for opioid dependence with more than 140.000 patients coverage in Iran, short term residential abstinence based programs (RABP)have around 200.000 clients each year. There are serious concerns on long term efficacy of such non medically assisted (but medically supervised) programs.
Methods: 81 heroin dependents, 33.0+6.7 years old, all crystalline heroin smokers at least for last six month, after screening were recruited in a four weeks RABP. Patient were evaluated in the first day in admission center and in 3rd, 10th, 17th, 24th, and 28th (discharge) days in the residential center for medical and psychiatric problems and withdrawal/craving intensities. Successful patients in completing the program were followed up monthly up to three months with urine analysis (UA) and craving checklists.
Results: 78% (62 cases) patients successfully passed the program with negative UA. 50% (41), 45% (37) and 39% (32) of patients returned for one, two and three month follow up with negative UA for opioids in more than 94% of cases. Positive UA for methamphetamine and severity of withdrawal were predictors of residential treatment drop out and higher age of drug abuse onset and Negative UA for benzodiazepines were predictors of three month post treatment abstinence.
Conclusions: There has been a general pessimism about the utility of brief detoxification programs, because many patients soon returned to regular heroin use. But, based on this study, RABP can be effective considerably if enough group and family supports are available by a qualified team and in a prepared atmosphere. Investment in this type of programs can be justified especially when the possibility of reaching drug addicts who would otherwise not have applied for maintenance treatments is considered.
Financial Support: This project has been sponsored by Iranian Drug Control Head Quarter (DCHQ) and Rose Polymer Co.

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PARENTAL CANNABIS USE DURING PREGNANCY AND CHILD BEHAVIOR PROBLEMS AT 18 MONTHS.

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Aims: This study compared the strength of associations between intrauterine cannabis exposure and infant behavioral problems at 18 months of age, with the association between maternal cannabis use only prior to pregnancy, or paternal cannabis use, and these offspring outcomes.
Methods: Within a population-based birth cohort, the Generation R Study, parents reported on their cannabis use habits. Behavioral problems were assessed with the Child Behavior Checklist. In total, information was available in n=3,806 children.
Results: After adjustment for confounders (age and gender of the child, parental education, national origin and alcohol use), maternal cannabis use during pregnancy was associated with more Externalizing Problems in exposed children compared to non-exposed children (odds ratio (OR) 1.86, 95% confidence interval (CI):1.06-3.27). Paternal cannabis use was not associated with a higher risk of offspring behavioral problems when considering confounding factors. Maternal cannabis use during pregnancy was specifically related to Externalizing Problems in girls (OR=3.57, 95%CI: 1.64-7.77), but not in boys. Moreover, after adjustment for maternal psychopathology, the association in girls remained statistically significant (OR=3.07, 95%CI: 1.40-6.79).
Conclusions: Parental cannabis use during pregnancy is associated with problem behavior in children at 18 months of age. Importantly, a gender-specific association was found for maternal cannabis use during pregnancy and child behavior, which may be partially explained by a biological mechanism due to intrauterine cannabis exposure, and partially explained by an unfavorable environment in which these cannabis-exposed children grow up.
Financial Support: The present study was supported by a grant from the Sophia Children's Hospital Foundation, projectnr. 450.

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VALIDATION OF A RAT SELF-ADMINISTRATION DESIGN FOR PRECLINICAL ABUSE LIABILITY ASSESSMENT OF NEW COMPOUNDS.

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Aims: To establish a rat self-administration model for preclinical abuse liability assessment, validated with positive and negative controls.
Methods: Rats were initially under food restriction and trained to lever press for delivery of food pellets on a fixed ratio (FR) 1 schedule of reinforcement. When the behavior was acquired, intravenous catheters were implanted in the jugular vein and food supply was unlimited. Intravenous self-administration was initiated with cocaine (0.5 mg/kg/infusion), available on a FR5 procedure during daily 3-hour sessions. All sessions started with a free priming infusion of the drug available on that particular session. Once stable self-administration behavior was maintained (less than 15% difference from mean in delivered infusions for three consecutive days), cocaine was substituted for vehicle to cause extinction of responding (extinction criteria: maximum 10 delivered infusions per session for three consecutive days). A within subject dose response test was initiated using reference compounds of diverse classes of drugs known to be self-administered by animals and abused by humans, as well as a CNS active negative control. To estimate the rewarding efficacy, the compounds were also tested on a progressive ratio (PR) schedule where the number of lever presses required to receive an infusion was gradually increased within a session until the animal stopped responding.
Results: Reference dose-response curves have been collected for cocaine (0.03-3.0 mg/kg/inf) and nomifensine (0.03-1.0 mg/kg/inf) on the FR5 and PR schedules. Morphine, nicotine, PCP, delta-9-THC and buspirone data is under way. Collected data were analyzed both on group and individual levels.
Conclusions: We have established a rat self-administration model for abuse liability assessment of new compounds. A set of validation data representing different classes of CNS active drugs including negative control data is under way.
Financial Support: AstraZeneca R&D

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ADDING AXIS II PERSONALITY DISORDERS INTO THE MIX: DO THEY INCREASE TREATMENT-SEEKING BEHAVIORS IN MALES AND FEMALES WITH SUBSTANCE USE DISORDERS?

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Aims: The co-morbidity of substance use and Axis II disorders is well-established. Rates of personality disorders (PD) in individuals with substance use disorders (SUD) are high. While the exact relationship between SUD and PD is still debated, the impact of PD on treatment outcomes is well-known. Less is known, however, about the extent to which Axis II disorders influence treatment seeking behavior and if these relationships vary by gender and type(s) of Axis II PD.
Methods: Study participants were 12,707 current or past substance users who were part of the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC). Of these, 3,201 also met criteria for Antisocial, Avoidant, Dependant, Obsessive-Compulsive, Paranoid, Schizoid, or Histrionic personality disorder (PD). Demographically, the participants were primarily Caucasian (67.6%), male (61.9%), and a mean age of 42.6 years. SUD and PD were identified using the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV Version (AUDADIS-IV).
Results: Preliminary analyses found among individuals with alcohol use disorders (AUD), (N=11,748), those with co-morbid Axis II PDs (N=2,943) were nearly twice as likely to seek treatment (22.6%) compared to those with AUDs alone (13.3%) ($p<.001$). Similarly, among individuals with other SUDs (N=4,040), a co-morbid PD increased the probability of treatment seeking more than two-fold (26.2% vs 12.2%; $p<.01$). Subsequent analyses will examine these relationships by gender, and type of PD to determine if different patterns are seen for various subgroups.
Conclusions: Preliminary findings suggest that a co-morbid PD in persons with alcohol and other SUDs is associated with a 2-fold higher rate of treatment seeking. Specific factors that contribute to help seeking (eg, legal problems) are important to explore in future research. Also, specific programming targeting issues more pertinent to men and women with these PD comorbidities also warrant further investigation with a focus on improving outcomes.
Financial Support: NIAAA Grant AA11846

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PRETREATMENT WITH NICOTINE PATCH FACILITATES SMOKING REDUCTION IN ADULT SMOKERS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

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Aims: Individuals with ADHD smoke at rates significantly higher than the general population and few studies have investigated ways to help reduce smoking among those with ADHD. It has been shown in studies of non-ADHD smokers that treatment with nicotine patch prior to the quit date (QD) facilitates subsequent rates of smoking cessation. The purpose of this analysis is to determine whether treatment with nicotine patch prior to QD is related to reductions in post-quit smoking in a sample of ADHD smokers.
Methods: Adult smokers with ADHD (n=15*) enrolled in a smoking cessation study were treated with transdermal nicotine (21 mg/day) for 2 weeks prior to a scheduled QD. On the QD, subjects were randomized to receive either placebo or lisdexamfetamine dimesylate (LDX) for 4 weeks. All subjects continued treatment with nicotine patch following the QD. Carbon monoxide levels were compared at baseline and on the QD. The percent reduction in CO from baseline to QD was used to predict post-quit CO levels two weeks after the QD.
*Data collection ongoing
Results: Following initiation of nicotine patch and prior to the QD, ADHD smokers significantly reduced their expired air CO levels (baseline CO = 25, QD CO = 11.7; $t(14) = 2.9$, $p = 0.01$). Consistent with previous studies of non-ADHD smokers, the percent reduction in CO levels following patch initiation and prior to the QD was a significant predictor of post-quit CO levels, irrespective of treatment assignment** and after controlling for sex and baseline CO levels (= -0.07; $p < 0.01$).
**Because data collection ongoing, treatment assignment is still blinded
Conclusions: These findings have significant implications for the development of effective smoking cessation strategies for individuals with ADHD.
Financial Support: This study was supported by an investigator-initiated research grant from Shire Pharmaceuticals to Duke University Medical Center (PI: Dr. Scott H. Kollins)

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VALPROIC ACID ATTENUATES AMPHETAMINE-INDUCED BEHAVIOR IN MICE.

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Aims: D-Amphetamine increases extracellular dopamine levels by stimulating its release from synaptic terminals. Valproic acid, an anticonvulsant and mood-stabilization agent, increases GABA levels and inhibits glycogen synthase 3 (GSK3). GSK3 has been implicated in the modulation of dopamine-dependent behaviors. We investigated the effect of valproic acid on amphetamine-induced hyperactivity, locomotor sensitization, and conditioned place preference in mice.
Methods: To determine the effect of valproic acid on acute amphetamine-induced activity, adult male CD-1 mice were pretreated with saline or valproic acid (50-300 mg/kg, i.p.) 30 minutes prior to amphetamine (2 mg/kg, i.p.) and activity was measured for 60 minutes. To assess locomotor sensitization, mice were pretreated with saline or valproic acid (300 mg/kg, i.p.) once daily for five days, challenged with amphetamine (1 mg/kg, i.p.) 7 days later, and activity was recorded. To determine the effect of valproic acid on the development of amphetamine conditioned reward, a 4-day unbiased conditioned place preference procedure was used. Mice were administered saline or amphetamine (2 mg/kg, i.p.) and confined to alternate sides of the conditioning chamber for 30 minutes. On day 5, time spent on each side of the chamber in a drug-free state was recorded.
Results: Valproic acid significantly attenuated amphetamine-induced ambulatory and stereotypic activity as compared to saline-pretreated amphetamine controls. Valproic acid also attenuated the development of amphetamine-induced sensitization. Valproic acid did not alter the development of amphetamine-induced place preference.
Conclusions: These data demonstrate that valproic acid attenuated amphetamine-induced hyperactivity and sensitization, however, did not affect amphetamine conditioned reward. Future studies will specifically examine the role of GSK3 in amphetamine-induced behaviors using the selective GSK3 inhibitor, SB 216763.
Financial Support: DA 09580 (EMU), PA Department of Health, Ronald J. Tallarida, PhD Fellowship.

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NON-MEDICAL USE OF PRESCRIPTION ADHD STIMULANTS IS TYPICALLY PART OF A PRE-EXISTING PATTERN OF DRUG ABUSE.

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Aims: Non-medical use of prescription stimulant ADHD medications (NMUPSAM) is frequently reported in the media and published literature, in a manner that implies that such products initiate drug-naïve individuals into drug misuse. However, little is known about the drug use history of those reporting such use.
Methods: This study examined the drug use patterns of those reporting NMUPSAM, based on data from the 2002-2007 National Survey on Drug Use and Health (NSDUH).
Results: Lifetime NMUPSAM was reported by 3.2% of respondents. Of these, 95.5% also reported use of an illicit drug (i.e., marijuana, cocaine/crack, heroin, hallucinogens, inhalants) or non-medical use of another prescription drug (i.e., tranquilizers, pain relievers, or sedatives); and such use preceded NMUPSAM in 77.4% of cases. These respondents reported an average of 2.37 drugs used prior to the first NMUPSAM.
Conclusions: These data suggest that NMUPSAM is uncommonly the initiating factor leading to the abuse of other drugs. Rather, NMUPSAM appears to be adopted by individuals engaged in broader patterns of drug abuse and misuse.
Financial Support: Supported by funding from Shire Development Inc.

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THE P300 EVENT-RELATED BRAIN POTENTIAL AS A NEUROBIOLOGICAL MARKER FOR SUBSTANCE USE DISORDERS: A META-ANALYTIC INVESTIGATION.

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Aims: For decades now, the reduced amplitude of the P300 Event-Related Brain Potential (ERP) has been studied as a possible neurobiological marker for substance use disorders (SUDs). The present meta-analysis integrates the increasing amount of knowledge that is gained from empirical studies that addressed the relationship between the P300 amplitude and current SUD or a family history (FH) of substance use. The primary objective was to compute the overall magnitude of the P300 amplitude differences between high risk (FH+/SUD+) and low risk (FH-/SUD-) groups. A secondary objective was to examine potential variables that might moderate the association between the P300 amplitude and the risk for substance dependence.
Methods: Extensive literature searches were conducted using Pubmed and Scopus, identifying peer-reviewed P300 studies on substance use or a family history of substance use, employing an oddball paradigm. In total, 336 reports were reviewed that yielded 64 separate studies for the present meta-analysis.
Results: Overall, meta-analysis revealed a reduced P300 amplitude at Pz in high risk subjects compared to normal controls, with large effects obtained in the SUD+ group and moderate effects in the FH+ group. The secondary analysis revealed that studies in which subjects were using heroin or cocaine demonstrated larger P300 amplitude effect sizes than studies with alcoholic subject samples. Furthermore, this analysis demonstrated that various sample and task characteristics also affected P300 amplitude effect sizes.
Conclusions: These findings indicate that a reduction of the P300 amplitude is strongly associated with SUDs and to a lesser extent with a FH of substance use. Several variables, such as substance of abuse, task and sample characteristics, were found to moderate the P300 reduction in these samples. It is concluded that the P300 reduction is a useful marker of a substance use disorder and potentially a marker of substance use vulnerability.
Financial Support: ZonMW grant 3116.0002

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THE RELATION BETWEEN HPA AXIS REACTIVITY AND AGE OF ONSET OF ALCOHOL USE.

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Aims: Previous research has shown early onset of alcohol use to be a strong predictor of later alcohol abuse and dependence, as well as of other negative outcomes. In the process of identifying those who are vulnerable to substance use, stress reactivity may prove a viable marker. The purpose of this study was to examine differences in the patterns of hypothalamus-pituitary-adrenal (HPA) axis reactivity to a social stressor in adolescents with varying ages of onset of alcohol use.
Methods: Adolescents who self-reported taking their first drink during early adolescence (12 years and younger), middle adolescence (13-15 years) and late adolescence (16 years and older) and those who reported not having used alcohol by the time of the study were compared on their HPA axis response to a Trier Social Stress Task. Participants were part of a general population study (N=346) in the South Holland province of the Netherlands. Five baseline assessments of salivary cortisol and six assessments taken before, during and after the social stress task were used as indicators of HPA axis reactivity.
Results: Results indicated that those who began drinking at an early age exhibited lower cortisol reactivity in anticipation of the stressor as compared to the middle and late adolescence groups when controlling for age, gender and baseline cortisol levels. Furthermore, the groups differed in their HPA axis response to the social stress task when controlling for age and gender.
Conclusions: An under-arousal of the HPA axis seems to be present in adolescents who begin drinking at an early age. The findings support earlier observations of hypo-activity of the HPA axis in adolescents who begin using substances at an early age and observations of hypo-responsivity in adolescents vulnerable to substance use.
Financial Support: This project is supported by ZonMW grant 3116.0002.

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RECEIPT OF CONTINUING CARE BY PARENTING WOMEN.

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Aims: Drug treatment following an initial episode of intensive care, or "continuing care," is thought to sustain improvements in patient functioning. However, little is known about how many patients typically receive continuing care, who receives such care, and types of continuing care received. We examine 801 parenting women (has children aged <18) initially treated in residential drug treatment settings, and compare those who did (n=190) and did not (n=611) receive continuing care on characteristics at intake and type of continuing care received.
Methods: Patients were recruited at admission to 44 drug treatment programs in 13 California counties. The Addiction Severity Index was administered at treatment entry and administrative data was examined on treatment episodes occurring <31 days from initial discharge.
Results: Mean age was 33, 38% did not complete high school, most were not married(82%), 14% were employed, and most used methamphetamine (44%). Few patients received continuing care (24%). Compared to patients who did not receive continuing care, more continuing care patients were White (74% vs. 61%) and fewer were Hispanic (8% vs. 17%), more received public assistance (32% vs. 23%), more initiated treatment voluntarily (44% vs. 25%) than by court order(16% vs. 33%), and fewer were initially treated in woman-only (vs. mixed-gender) programs (25% vs. 32%). Furthermore, patients in the continuing care group had more severe problems related to substance use, family/social conflict, legal status, and physical/mental health. Notably, most continuing care consisted of additional treatment in residential (66%) instead of outpatient (34%) settings. Future analyses will explore predictors of receipt of continuing care in different settings and longer-term outcomes.
Conclusions: Patients who receive continuing care exhibit severe problems in many key life areas. More research is needed to understand how patient characteristics and other system-level factors, such as type of initial treatment program and treatment referral source, impact pathways to continuing care and associated treatment outcomes.
Financial Support: NIDA R01DA021183, P30DA016383, & K05DA017648

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NEIGHBORHOOD RISK AND PROTECTIVE FACTOR INFLUENCES ON SCHOOL CONDUCT AND PERFORMANCE.

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Aims: Neighborhood disorganization is associated with a range of negative outcomes among urban adolescents. The current study sought to examine the degree which neighborhood-level risk and protective factors are associated with several dimensions of youths' academic functioning and performance.
Methods: Data was collected as part of a NIDA-funded study evaluating the efficacy of a drug abuse prevention intervention among inner city middle school youths. Study analyses focused on 235 youths aged 11 to 16 (X= 13; SD =1.1), with most being black (93%) and 50.2% female. One neighborhood risk index comprised of 5 variables (e.g., kids being beat up/mugged)and one protective neighborhood index comprised of 3 variables (e.g., absence of drug sales and use of drugs in neighborhood) were used. Separate logistic regression models examined relationships between the risk and protective neighborhood indexes and being held back a grade, parents called in for conference, and sent to the principal.
Results: Compared to youth reporting no neighborhood risk, those reporting risk had a significantly higher odds of being sent to the principal (OR = 1.99; 95% CI: 1.00, 3.97), yet no difference in the odds of having parents called in for a conference (OR = 1.32; 95% CI: 0.69, 2.52) or being held back a grade (OR = 0.86; 95% CI: 0.42, 1.74) while adjusting for gender and age. Compared to youth reporting protective factors in their neighborhoods, those reporting no protection had a significantly higher odds of being held back a grade (OR = 2.54; 95% CI: 1.36, 4.74) and having parents called in for a conference (OR = 1.98; 95% CI: 1.12, 3.51) while adjusting for gender and age.
Conclusions: The findings suggest risk and protective neighborhood factors may have differential influences on academic performance and conduct outcomes among youth, and multiple approaches aimed at addressing both types of factors may be needed to promote school performance among youths.
Financial Support: NIDA R01 DA015075 and NIDA Epidemiology Training Program 2T32DA007292

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BRIEF INTERVENTION TO REDUCE CAFFEINE CONSUMPTION IN CAFFEINE-DEPENDENT TREATMENT SEEKERS.

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Aims: Physicians frequently advise caffeine reduction or cessation in individuals who have certain medical conditions. Some daily users are unable to reduce or quit caffeine use, despite a desire to do so. The purpose of this study was to develop a brief manualized treatment to reduce caffeine consumption in caffeine-dependent users.
Methods: Participants were 106 daily caffeine users who were interested in cutting back or quitting their caffeine consumption. Fifty-four participants, who used 200mg or more of caffeine per day and fulfilled DSM-IV criteria for substance dependence applied to caffeine, returned for the treatment session. Participants were randomized to receive a one-hour treatment after an Immediate (return in 1-2 weeks) or Delay (return in 5-6 weeks) condition. Daily caffeine diaries were kept from 1 week before treatment to 5 weeks post-treatment. Timeline follow-back assessments were taken at 6, 12, and 26 weeks.
Results: Mean age was 41.4 years. The majority of the sample was Caucasian (80%) and female (59%). Forty-four percent were married and 72% employed. A repeated measures ANOVA was conducted with Time (Screening, Treatment) and Delay (Delay, Immediate) entered as factors. A separate analysis was conducted with Time (Treatment, Week1, Week2, Week3, Week4, Week5) and Delay (Delay, Immediate) entered as factors. No significant effect of Delay was observed in either analysis. Findings revealed a significant reduction in caffeine consumption across the first 5 weeks of treatment, $F(2.18, 67.52) = 36.98$, $p < .001$, $\eta p2 = .54$. Mean reductions in caffeine from Treatment (468.9mg) to Week5 (159.1) were 66%. Reductions were maintained at 6, (159.7mg), 12 (136.2mg), and 26 weeks (133.6mg).
Conclusions: The study demonstrates that a brief behavioral treatment is efficacious for reducing caffeine intake in caffeine dependent users.
Financial Support: Supported by NIDA R01 DA03890

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THE INFLUENCE OF NEURO-COGNITIVE IMPAIRMENT ON INTERVENTION OUTCOMES AMONG INJECTION DRUG USERS LIVING WITH HIV/AIDS.

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Aims: Drug- and sex-related HIV risk behaviors and sub-optimal adherence to HIV medication regimens can jeopardize the health of HIV–infected injection drug users (IDUs) and threaten community health. Findings to date indicate that it is feasible to deliver a brief behavioral risk reduction/medication adherence group intervention to HIV-infected IDUs in a community-based setting. Being adherent to HAART or being able to successfully participate in behavioral interventions targeting adherence and harm reduction often requires a relatively high level of cognitive abilities. HIV infection and substance abuse are known to independently affect the central nervous system and this can result in neuro-cognitive impairment. In combination, their effects can be even more profound and this is directly relevant to intervention development because a significant number of people living with HIV/AIDS have a positive history of substance abuse. We aimed to examine the impact of cognitive impairment on outcomes among HIV-infected IDUs participating in our CHRP+ intervention.
Conclusions: We evaluated the extent to which changes in Information, Motivation, and Behavioral skills (IMB) with respect to medication adherence and sex- and drug-risk behavior outcomes are predicted by cognitive impairment following the brief 4-session Community-Friendly Health Recovery Program for HIV-infected Drug Users (CHRP+). Findings suggest that it may be helpful to specifically tailor such behavioral interventions to accommodate cognitive impairment. Implications for the design of future interventions are discussed.
Financial Support: Funding provided by NIH/NIDA K23 DA17015 (Copenhaver PI), Optimizing HIV prevention for HIV-positive Injection Drug Users.

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COMPARING HEROIN USERS AND PRESCRIPTION OPIOID USERS SEEKING SUBOXONE® TREATMENT FOR OPIOID DEPENDENCE.

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Aims: The number of Americans receiving treatment for abuse of pain medications increased 167% from 360,000 to 601,000 persons between 2002 and 2008 (SAMHSA, 2009), and treatment providers are likely treating a growing percentage of prescription opioid (PO) users. Research has compared heroin and PO users in both opioid treatment program (OTP) and office-based settings (Banta-Green et al., 2009; Torrington et al., 2007), and the current study expands study findings to include opioid-dependent participants receiving Suboxone® in a research clinic setting.
Methods: In an ongoing NIDA-funded trial comparing the effectiveness of combined pharmacotherapy and behavioral therapy for opioid dependence, the first 177 treatment-seeking participants self-reported being primarily heroin users (n = 113) or PO users (n = 64).
Results: Baseline analyses show that the heroin and PO groups did not vary by gender, education level, age at first opioid use, or recent poly-substance use. Preliminary analyses indicate differences between the two groups, including mean number of lifetime drug treatment episodes [heroin = 6.13(8.49); PO = 2.12(2.38)], and pain as the main reason for seeking treatment (5.3% of heroin users compared to 16.9% of PO users). Interestingly, a greater percentage of the heroin group reported using other opioids (96.4%), whereas less than half of the PO group (49.2%) reported past heroin use. Also presented are findings on group differences in HIV risk behavior, medical and psychiatric problems, and treatment retention.
Conclusions: Findings from this study have important implications for treatment providers, who may use the information to adapt treatment plans for either heroin- or PO-dependent patients presenting for treatment with Suboxone®.
Financial Support: NIDA Grant DA020210

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ESTIMATED CANNABIS-ASSOCIATED RISK OF DEVELOPING A NEWLY INCIDENT DEPRESSION SPELL: FOCUS ON EARLY-ONSET CANNABIS USE.

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Aims: In recent studies, there has been focus on suspected mood disturbances due to early-onset cannabis use (EOCU with onset < 18 years). We seek to estimate suspected EOCU-associated excess risk of experiencing a depression spell in adulthood.
Methods: Data are from the 2005-2007 United States National Surveys on Drug Use and Health for non-institutionalized community-dwelling residents aged 12 or older (n=103,432 after exclusion of 54,719 persons 12-17 years old at survey, 8,169 with pre-adult depression spell, and 299 missing on crucial data). Logistic regression was used to estimate relative risk (RR) while taking into account sampling weights and the complex sample structure.
Results: An estimated 31% of adult onset depression spell cases had used cannabis before 18 compared to 22% of non-cases (unadjusted RR = 1.7; 95% Confidence Interval, CI = 1.6, 1.8; $p<0.001$). With controls for sex, age, race/ethnicity, and early-onset cigarette/alcohol use, the estimate was 1.3 (95% CI = 1.2, 1.4; $p<0.001$). EOCU-associated risk of depression spell did not vary between the sexes, but increased across the 26-34, 35-49, 50-64, and 65+ age strata (from 1.2 to 4.9; all $p<0.012$). Non-Hispanic Whites, Blacks, and Hispanics also had modestly elevated EOCU-depression associations (stratum-specific adjusted RR = 1.2, 1.5, and 1.7 respectively; all $p<0.001$).
Conclusions: When cannabis smoking starts in adolescence, there is a modest but statistically robust excess risk of developing a depression spell in the adult years, even with controls for suspected confounding variables.
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ASSOCIATION BETWEEN PSYCHIATRIC DISORDERS, ALCOHOL AND OTHER SUBSTANCES USE IN BRAZILIAN DRIVERS.

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Aims: Due to geographical and financial difficulties, there are no studies estimating the association between DUI and psychiatric disorders in Brazil, difficulting the development of programs that address the drivers need. This study aims to ascertain this association and compare drivers with positive BAC and previous use of other substances, through telephone interviews.
Methods: A cross-sectional sample of 1,147 individuals driving in federal highways in 23 Brazilian cities was breathalyzed and tested for drugs with saliva kits. After this, they provided phone contacts and were interviewed via telephone using a Rolling Consent model to collect questions from the MINI. Data were analyzed using Fisher's exact test.
Results: The sample is comprised of 95% of males, with a mean age of 35.8 ± 11.1 years. 8% had a positive alcohol reading or substance finding in saliva, and reported a higher prevalence of psychiatric diagnoses like depression (22.8%, p<0.00), mania (5.5%, p=0.01) hypomania (6.8%, p=0.04), post traumatic stress disorder (10.5%, p<0.00) and antisocial personality (8.9%, p<0.00) when compared to other drivers (3.8%, 1.0%, 2.7%, 0,5% and 1.3% respectively).
Conclusions: This is the first study with Brazilian drivers through telephone interviews, which allows to access drivers from different regions of the country, decreasing costs. The form of consent used to that data are not completely discarded if the participant decides to give up and prevents him feel compelled to answer questions until the end of the interview. Our results point to the association between DUI and psychiatric disorders in this sample. Therefore, individuals who drive under the influence need assessments and interventions targeted to specific psychiatric disorders. Brazil still does not have public policies designed to minimize the problem.
Financial Support: This study was supported by National Secreteriat for Drug Policy (SENAD)

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COMPARISON OF THE EUROPEAN AND US APPROACHES TO THE EVALUATION OF ABUSE LIABILITY AND DRUG SCHEDULING FOR NEW CHEMICAL ENTITIES.

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Aims: Evaluation of abuse liability is an important aspect of safety testing for the development of centrally-active new drugs or new chemical entities (NCEs). Recent guidance and experience reveals a growing divergence between the testing procedures recommended by the European Medicines Agency (EMEA) and the U.S. Food and Drug Administration (FDA); these agencies also have different roles in setting product labelling. The regulatory requirements are now so divergent that one abuse evaluation package is no longer guaranteed to satisfy both EMEA and FDA.
Conclusions: Preclinical testing
Assessing the subjective effects (drug-discrimination), reinforcement (self administration) and tolerance/dependence potential of NCEs is required by FDA and EMEA. However in Europe, rodents are the recommended species, GLP is recommended with testing to be completed before Phase 1. In USA, there is a greater reliance on primates with data from primate self-administration experiments weighted heavily. The FDA does not demand GLP, although its value is appreciated. US preclinical abuse testing often also takes place later in clinical development
Clinical testing
In Europe, all evaluations of abuse, tolerance, dependence and withdrawal for NCEs are collected from the Phase 1 and Phase 2/3 clinical trials' databases using appropriate MedDRA search terms. There is no specific EMEA guideline clinical testing for abuse/dependence and no requirement for a trial in drug experienced human volunteers. In contrast, although FDA cannot legally mandate a drug experienced volunteer study, evidence from such trials is often a key factor in the decision-making and failure to to obtain such data might complicate and delay scheduling decisions.
Product Label and Scheduling
Although EMEA evaluates abuse/dependence as part of the approval of NCEs, Controlled Drug status and Scheduling is a national decision in the EU and scheduling varies widely across EU countries, and the US.
Financial Support: Supported by RenaSci and Pinney Associates.

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GENDER DIFFERENCES IN THE PHARMACOKINETICS AND EFFECTS OF 3,4-METHYLENEDIOXYMETHAMPHETAMINE IN HUMANS.

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Aims: There are few data about the pharmacokinetics and acute pharmacological effects of MDMA in women. The aims were to compare the concentrations of MDMA and metabolites in plasma and its pharmacological effects between women and men.
Methods: A non-controlled clinical trial was conducted in 12 healthy female and 15 healthy male recreational users of MDMA. Only extensive metabolizers for CYP2D6 activity (phenotyped using dextromethorphan as probe drug) were selected. Subjects received a single oral dose of MDMA (1,4 mg/kg; mean dose for males and females 95 and 80 mg, respectively). Females were administered during follicular phase. Blood samples were obtained at different times until 72 hours for determination of MDMA and metabolites using GC/MS. Pharmacological evaluations included physiological parameters (BP, HR, T, PD) and subjective effects (visual analogue scales of positive and negative effects, ARCI and VESSPA questionnaires).
Results: Plasma concentrations of MDMA (Cmax and AUC) were significantly higher in men, but concentrations of MDA (Cmax) were significantly higher in women. In the case of the pharmacological effects, females presented higher increases in systolic blood pressure, heart rate and temperature in comparison to males. Females showed higher scores than males in subjective scales related to negative effects and/or adverse effects of MDMA (bad effects, dizziness, depression, and psychotic symptoms), but males scored higher in scales related to changes in perceptions.
Conclusions: Females present higher physiological and negative effects of MDMA than males with lower plasma concentration. Our results indicate that females could be more sensitive to the effects of MDMA than males.
Financial Support: Acknowledgements: NIDA Grant 5R01BA017987-01, FIS RTA RD06/0001/1009, 2005SGR00032 and MICINN FI09/00355. R. Pardo is recipient of a fellowship Rio Hortega, FIS no. CM08/00051.

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NORMATIVE DATA ON CLIENTS SEEKING TREATMENT ASSESSED WITH THE FRENCH MODIFIED ADDICTION SEVERITY INDEX. MULTIDIMENSIONAL COMPARISON OF SUBSTANCE AND NON-SUBSTANCE DEPENDENT PATIENTS.

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Aims: The ASI is nearly 30 years old and is used since 1992 in France. Since 2006, the French modified ASI includes items regarding tobacco and non-substance addictive behaviors. Previous studies showed the validity of the added sections.
Objective: To provide data on the ASI from a sample of patients admitted to treatment in addiction clinics in South-West of France regardless of type of addiction.
Methods: The 780 included patients were divided into groups according to their answers to question D14 of the Drug / Alcohol section of the ASI. Six groups of patients were defined according to whether the main problem was alcohol, opiates, cannabis, tobacco, non-substance addictive disorders or polydrug.
Results: The length of the ASI interview is dependent of the level of impairment. Polydrug users presented the higher level of impairment and varied substances used. The tobacco group and non-substance addictive behavior group presented less other substance use. The non-substance addictive behaviors were mainly retrieved in the non-substance addictive behavior group. The alcohol group presented higher alcohol-related scores, the tobacco group higher tobacco-related scores and the drug-related scores were higher for the opiate and polydrug groups. All addictions shared psychiatric impairment, as severity scores were high for all groups. Subjects with non-substance addictive behaviors also used substances mainly alcohol and tobacco. The prevalence of ISR scores higher than 4 ranged from 3% to 33% in areas other than the one they sought treatment for.
Conclusions: The results showed the feasibility of the French adaptation of the ASI regardless of the addiction. A significant proportion of clients seeking treatment for one addiction qualified for treatment for an other and the modified ASI may allow to identify these clinical situations regardless of the patients awareness when seeking help.
Financial Support: PHRC 2006, MILDT-INSERM 2004

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GENDER DIFFERENCES IN ACCEPTABILITY OF A THERAPEUTIC TELEPHONE SYSTEM IN PRIMARY-CARE BUPRENORPHINE MAINTENANCE.

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Aims: Compared to men, women face substantial barriers to successful substance abuse treatment including greater child care responsibilities, stigmatization, and higher rates of psychosocial problems. Computer-based automated systems provide an alternative to traditional counselor-based treatment and may address these barriers, yet women may be less comfortable than men with these systems. We predicted that male patients would provide higher usability ratings of an automated phone system.
Methods: The Recovery Line is an automated cognitive behavioral-based therapeutic telephone system that allows patients to learn about and practice skills in vivo. It helps patients identify problems, suggests solutions, and includes sections providing inspirational messages and immediate assistance. 10 male and 7 female patients currently prescribed buprenorphine completed a brief demographic and technology use questionnaire and expected likability and helpfulness. Patients were provided access to the Recovery Line for a week and asked to call the system daily. They returned the following week to provide system ratings and detailed feedback via personal interview.
Results: Women were younger than men (p=.01), but did not differ on other demographic or patient characteristics. There were no gender differences in time using the system or number of modules reviewed. Analysis of Covariance (ANCOVA) was used to control for differences in expected likability/helpfulness and age. Ratings of the system were high for both men and women, but women rated the system significantly higher than men in likeability (p=.01, 4.6 vs. 3.3), and helpfulness (p=.02, 4.6 vs. 3.7).
Conclusions: Findings suggest that therapeutic telephone-based automated systems may be more acceptable and interesting for women. Such systems may also be efficacious since patients can use the system in their own environment at any time and thus whenever patients are at risk of relapsing.
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PAIN DURING HEROIN SELF-ADMINISTRATION ENHANCES RELAPSE OF HEROIN-SEEKING IN RATS.

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Aims: Opiates, including heroin and OxyContin, can be highly addictive. Despite having both reinforcing and analgesic properties, little is known about how these factors interact to affect ongoing opiate self-administration and relapse. Experimentally, relapse can be studied using the extinction-reinstatement model in animals, whereby exposure to previously drug-paired cues, stress, or a drug priming injection 'reinstates' extinguished drug-seeking behavior, operationally defined as responding on a previously drug-paired operandum in the absence of primary reinforcement. Thus, the current study examined whether heroin self-administration and subsequent relapse would be affected by inflammatory pain during the self-administration phase.
Methods: Twenty-four hr after an intraplantar injection of the inflammatory agent Complete Freund's Adjuvant (CFA, n=16) or sham injection (n=12), male Sprague-Dawley rats pressed a lever for heroin (0.25 ug/50 ul/infusion, IV) paired with a light+tone stimulus during 14 daily, 2 hr sessions. Following extinction of responding, the ability of heroin-paired cues, the anxiogenic α2-noradrenergic receptor antagonist, yohimbine (2.5 mg/kg, IP), and a priming injection of heroin (0.25 mg/kg, SC) were examined for their ability to reinstate heroin-seeking.
Results: Although no differences were noted during self-administration, CFA animals showed significant enhancement in conditioned-cued and stress-induced, but not heroin-primed, reinstatement (ps<0.05). Separate electrophysiological and microdialysis data also demonstrated that pain not only produced a long-lasting enhancement in ventral tegmental area dopamine (DA) cell firing, but also potentiated cocaine-evoked DA release in the nucleus accumbens.
Conclusions: Overall, these data demonstrate that pain during opiate administration may increase the ability of stimuli to promote relapse in individuals abstinent from opiate use via activation of mesolimbic DA pathways.
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PSYCHIATRIC COMORBIDITY AND THE PERSISTENCE OF DRUG USE DISORDERS.

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Aims: Drug use disorders are a major public health problem, yet little is known about their persistence when studied prospectively in the general population. Using representative, longitudinal data, the present study aimed to obtain estimates of the persistence of DSM-IV drug use disorders and identify psychiatric risk factors for persistence throughout a 3 year period.
Methods: Data came from Waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. This analysis included subjects with past-year DSM-IV drug abuse or dependence at Wave 1 who participated in Wave 2 (N=615). The Alcohol Use Disorder and Associated Disabilities Interview Schedule, a structured diagnostic interview, was used to obtain psychiatric diagnoses. Adjusted Odds Ratios (ORs) estimating the association between Axis I and II comorbidity and drug use disorder persistence were derived from weighted logistic regression models.
Results: Drug use disorders persisted in 33.34% of respondents. Of the Axis I disorders, major depression significantly predicted persistence, an effect that remained after adjusting for Axis I comorbidity (OR, 1.94). Of the Axis II disorders, antisocial, borderline, narcissistic and schizotypal personality disorders significantly predicted persistence, controlling for Axis I comorbidity (ORs, 2.36-3.68). Antisocial and schizotypal personality disorders remained significant when adjusting for Axis II comorbidity, treatment and psychiatric family history (ORs 2.52-2.74).
Conclusions: Persistence of drug use disorders was significantly predicted by major depression, antisocial and schizotypal personality disorders. These findings suggest the potential clinical utility of assessing and treating comorbid depression and personality disorders in patients with drug use disorders. Future research should focus on understanding the role of specific comorbid psychiatric symptoms in the course of drug use disorders, and the genetic and environmental influences on these associations.
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THE CASE FOR CASH: CONTINGENCY MANAGEMENT FOR COCAINE DEPENDENCE.

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Aims: Despite strong empirical support for contingency management (CM), concerns about its cost and safety have hindered its transfer to real-world practice. Unsupported negative assumptions about the use of cash with substance abusers have led to the almost exclusive use of non-cash incentives in CM protocols. However, prior research has found cash to be as safe as non-cash incentives. Moreover, cash has been shown to be more effective and less time and cost intensive than other incentives. This study is among the first to empirically examine the efficacy and ethics of a cash-based CM procedure.
Methods: The 3-group randomized study compared the efficacy and ethics of a (1) voucher-based CM intervention, (2) cash-based CM intervention, and (3) non-CM intervention in a sample of 99 cocaine-dependent clients attending an outpatient treatment program. Outcomes included: UDS-confirmed abstinence, clinic attendance, and participants' self-reported use of incentive payments.
Results: Preliminary analyses on clients who completed the 12-week intervention revealed that rates of abstinence were approximately 82% in the cash condition, compared to 69% (d = .41) in the voucher condition, and 65% (d = .51) in the control condition (p = .001). A similar pattern was observed for clinic attendance with attendance rates of approximately 80% in the cash condition, compared to 75% (d = .19) in the voucher condition, and 64% (d = .55) in the control condition, p = .06. In addition, there were no differences between the three groups in the extent to which they engaged in risky behaviors including gambling, paying money for sex, and drinking alcohol to intoxication, p's = .31 to .80.
Conclusions: These findings provide preliminary support for the greater clinical utility of cash incentives in behavioral substance abuse treatment.
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PHYSICIAN MANAGEMENT WITH AND WITHOUT COGNITIVE BEHAVIORAL THERAPY IN PRIMARY-CARE-BASED BUPRENORPHINE/NALOXONE.

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Aims: To determine if cognitive behavioral therapy(CBT) added to physician management (PM) improves outcomes in patients receiving primary care-based buprenorphine/naloxone(BUP).
Methods: 135 opioid dependent patients were randomized to receive BUP for 24 weeks and either PM or PM and CBT(PM+CBT). PM was provided 20 minutes monthly. CBT was provided for 50 minutes weekly for 12 weeks. Self-report data and urine tests were obtained weekly. We used repeated-measures ANOVA to compare the treatments on opioid-negative urine samples during the two 12 week time periods and weeks of continuous opioid-negative samples. We tested the overall model including time, treatment condition, and the interaction of treatment by time. Retention was evaluated using Kaplan-Meier product limit method.
Results: 69 patients were randomized to PM and 66 to PM+CBT. Patients were predominately male (73%) and white (90%), mean age of 34. Treatment conditions did not differ on gender (p = .67), race (p = .57), age (p = .62), or primary type of opioid used (.76). Based on urine tests, illicit opioid use during the trial did not differ by treatment, $F(1,133)=0.52$, p=.47, and there was no interaction of treatment condition by time, $F(1,133)= 2.77$, p=.099. Treatment means for the first 12 weeks (CBT=6.3, PM=6.1, p=.85,ES=.03) and the second 12 weeks were not significant(CBT=5.1, PM=4.1, p=.25, ES=.20). Treatment and time interacted for continuous weeks of opioid negative urines, $F(1,133)=4.41$, p=.04. Mean continuous weeks of opioid negative urines for PM patients decreased from the first 12 weeks (4.8) to the second 12 weeks (3.0), $F(1,133)=24.18$, p<.01. PM+CBT patients did not decrease, $F(1,133)=3.50$, p=.07(4.7 to 4.0). Self-report of illicit opioid use did not differ by treatment, p =.66, and there was no interaction of treatment by time p=.65. Retention did not differ by treatment, $X2 = .22$, p=.64.
Conclusions: When added to PM in primary care-based BUP, CBT does not decrease illicit opioid use or increase treatment retention.
Financial Support: NIDA RO1 DA019511

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CROSS-NATIONAL RESEARCH ON EARLY-ONSET CANNABIS USE AND FAILURE TO COMPLETE EDUCATIONAL MILESTONES.

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Aims: Studying community survey participants in 16 countries, we estimate the strength of association linking early-onset cannabis smoking (< age 17 years) with later failure to complete educational milestones.
Methods: Data are from the World Mental Health Surveys Initiative (WMHS), with probability samples from the Americas (Mexico, Colombia, U.S.), Europe (Belgium, France, Germany, Italy, Netherlands, Spain, Ukraine), Middle East and Africa (Israel, Lebanon, Nigeria, South Africa) and Asia (Japan, People's Republic of China). A standardized interview schedule was used to assess drug involvement and educational attainment, with calibration for a cross-country standardized definition of each educational milestone under study. A meta-analytic approach is used to complement estimates for each country.
Results: In these WMHS data, early-onset cannabis use (EOCU) is associated with failure to finish secondary school by age 18 in the three countries of the Americas and in Israel ($p<0.05$) but not in the 12 other countries. Nonetheless, the meta-analysis summary estimate is statistically robust. There is EOCU-associated failure to enter into college by age 21 in the U.S. and Ukraine; this association is inverse for South Africa (all $p<0.05$). EOCU is not associated with failure to finish tertiary school.
Conclusions: EOCU is a marker of risk for failing to achieve key educational milestones beyond primary school in some parts of the world, but the available evidence does not yet support a cause-effect interpretation.
Financial Support: SUPPORT FROM NIDA: D43TW05819, R01DA016558, K05DA015799.

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PRELIMINARY EVALUATION OF EXTENDED-RELEASE NALTREXONE IN MICHIGAN AND MISSOURI DRUG COURTS.

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Aims: Drug courts are designed for offenders who commit crimes while under the influence of drugs or alcohol. Extended-release naltrexone (XR-NTX) was designed to be a once-monthly injection, which theoretically, might facilitate treatment for alcohol dependence in criminal justice. This pilot study examined the feasibility and effectiveness of treatment with XR-NTX in the drug court setting.
Methods: Data were collected on clients treated with XR-NTX and a similar number of matched controls (i.e., no XR-NTX) from 4 courts in Michigan (2 drug courts; 2 DUI-specific courts; combined annual clients, 3,789) and 3 courts in Missouri (1 drug court; 2 DUI-specific courts); combined annual clients, 382). Treatment with XR-NTX was open-label, voluntary and was combined with psychosocial treatment. Referral was primarily for treatment of alcohol dependence, with some cases of concurrent alcohol dependence and other drug use disorders. Referrals came from judges, probation officers, court coordinators and treatment providers. All of the clients were considered by the courts to be the most difficult cases, and typically had been charged with previous DUI offenses.
Results: An initial sample of 51 clients were identified. Compared to the control group, treatment with XR-NTX was associated with a reduction in new arrests while under drug court supervision (OR=0.224) and in the number of new arrests per month (OR=0.327). Treatment with XR-NTX was also associated with a reduction in the average proportion of positive alcohol screening tests per month (OR=0.242) and a reduction in the number of missed drug court sessions (OR=0.388).
Conclusions: The current pilot sample was difficult to obtain suggesting why effectiveness research in this setting is so rare. Nonetheless, treatment with XR-NTX appeared to be feasible and was associated with a consistently large treatment effect across multiple outcomes relevant to the drug court setting.
Financial Support: Treatment of the Missouri clients was funded by a grant from the State of Missouri. Drug court evaluation sponsored by Alkermes, Inc. under a contract with Northwest Professional Consortium, Inc.

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SELF-REPORTED STIMULANT USE, ADHD SYMPTOMS AND KNOWLEDGE OF ADHD DIAGNOSIS AMONG A NATIONAL SAMPLE OF YOUTH.

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Aims: This analysis identifies an association between self-reported symptoms of ADHD and knowledge of ADHD diagnosis; it also describes the prevalence of stimulant use by ADHD diagnosis among a sample of 10 to 15 year olds (n=1447).
Methods: Data came from the National Monitoring of Adolescent Prescription Stimulant Study (N-MAPSS, LB Cottler PI), a study of use and misuse of prescription stimulants. Participants were recruited through an entertainment venue-intercept method from 10 US cities in late 2008. Participants aged 10-15 were grouped based on knowledge of ADHD diagnosis (Yes, No, DK) and self-reported ADHD symptoms (0-3 Sx vs. 4-5 Sx).
Results: Lifetime stimulant use did not differ among youth with knowledge of ADHD diagnosis (ADHD Dx) regardless of symptoms (65% 0-3 Sx vs. 58% 4-5 Sx; NS). While some youth were unsure of ADHD status (DK Dx; n=156), if they reported 4-5 Sx they were more likely to report stimulant use compared to those reporting 0-3 Sx (25% vs. 9%; p=0.01). Among those reporting No ADHD diagnosis (No Dx), stimulant use was also more prevalent in those reporting 4-5 Sx (15%) vs. those with 0-3 Sx (8%) (p=0.002). Over half (62%) of stimulant users (n=219) reported either 4-5 Sx or ADHD Dx; 34% had 0-3 Sx and No Dx. For nearly three quarters of the youth (71%), self-reported symptoms and diagnosis agreed. As expected, the ADHD Dx group had the highest proportion reporting 4-5 Sx (45%) vs. 15% of No Dx and 28% of DK Dx (p<.0001).
Conclusions: Stimulant use was associated with knowledge of ADHD diagnosis. Those without knowledge of an ADHD diagnosis were more likely to use prescription stimulants if a larger number of symptoms (4 or 5) were endorsed compared to those who endorsed fewer or zero symptoms. Stimulant users with negative ADHD status remain a concern.
Financial Support: N-MAPSS is implemented by Washington University in St. Louis under contract from Pinney Associates, Inc., with funding provided by Shire Pharmaceuticals.

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USING PILL PHOTOS TAKEN WITH A CELL PHONE TO ASSESS ADHERENCE IN A CLINICAL TRIAL.

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Aims: Medication non-adherence is a common and serious problem that compromises clinical trials, reduces therapeutic efficacy and increases costs. Determining adherence can be difficult. Clinical trials often use MEMS (Medication Event Monitoring System) to assess adherence, though this technology often produces apparent over-adherence. Photos taken on cell phones (CP) are time-stamped and easily emailed. This study compared adherence measured by pill counts (PC), MEMS and cell phone pill photos (CPPP).
Methods: CPs with cameras were provided to 20 subjects enrolled in an 8 week clinical trial of modafinil for methamphetamine addiction. Participants documented every modafinil administration by placing the pill in their hand and photographing it immediately prior to ingestion, with a $3 compensation for each photo sent to the lab. A 10-day supply of medication was dispensed weekly; pills remaining in returned MEMS devices were counted manually. PCs were compared to MEMS and CPPP estimates of adherence.
Results: Overall adherence estimated by PC was (94.9 ± 13.5 %), for MEMS (93.6 ± 15.0%), and for CPPP (76.9 ± 14.6%). For individual weeks, CPPP and MEMS agreed with PC with similar frequency (Fisher's Exact Test, 2 tailed (FET 2T): OR 1.11, p= .79). When measures disagreed with PC, MEMS over-reported adherence more than CPPP (FET 2T: OR 3.88, p<0.001) and PP underreported adherence more than MEMS (FET 2T: OR 3.48, p<0.001).
Conclusions: Adherence assessed by CPPPs is as accurate as adherence assessed by MEMS. When compared to PC, MEMS overestimates adherence and CPPP underestimate adherence. In contrast to MEMS, CPs are widely available and relatively inexpensive. Although not done in this study, CPs can also be used to prompt adherence and collect outcome and AE data. Clinical trialists and practicing physicians can easily employ CPPP to assess adherence.
Financial Support: Supported by DA 018179

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DIFFERENCES IN RISKY BEHAVIORS AND MALE PARTNER CHARACTERISTICS AS AN EXPLANATION FOR RACE DISPARITIES IN STIS.

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Aims: There is a differential burden of STI seropositivity among black drug users. The purpose of this study is to determine whether the association between race and STI status is eliminated after controlling for high risk behaviors and male partner characteristics of female drug users.
Methods: The present sample includes 238 female participants enrolled in the NEURO-HIV Epidemiologic Study. The sample was 65% black (mean age = 31.6). The odds of reporting an STI were estimated using multiple logistic regression models to determine the influence of groups of covariates on the association between race and STI. Covariates included (1) demograhic factors;(2) risk taking behaviors; and (3) male partner characteristic.
Results: In the unadjusted model, black females were 2 times more likely to report having an STI (OR=2.3;95%CI =1.31-4.18). After adjusting for demographic factors, the relationship between race and STI status was no longer significant (OR=1.6;95%CI=0.85-3.22). Opiate use was associated with STI status (OR=2.1;95%CI=1.12-3.92) and including substance use in the model further reduced the odds ratio of race and STI (OR=1.3;95%CI=0.64-2.60). After the variables drug use with a casual partner and sex with a male who used crack were added to the equation, the odds ratio for race and STI increased (OR=2.1;95%CI=0.96-4.43). Females who had sex with males who smoked crack were more likely to report ever having an STI (OR=3.5;95%CI=1.78-7.00). No relationship emerged between drug use with a casual partner and STI status.
Conclusions: In addition to demographic factors, accounting for substance use reduced race disparities in STIs. Also, male partner characteristics emerged as a significant covariate of STI status. Accounting for individual risk taking behaviors and partner characteristics may reduce race disparities among substance using females. Researchers are encouraged to take a second look at differences in individual behaviors and partner characteristics as plausible contributors to STI disparities among high risk females.
Financial Support: NIDA grants R03DA024981 and T32DA007292

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IS THE ASSOCIATION OF THERAPEUTIC ALLIANCE WITH DAYS OF USE ALWAYS NEGATIVE?

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Aims: Therapeutic alliance, representing the quality of the therapeutic relationship, has been correlated with positive treatment outcomes regardless of treatment modality. This study tested whether participants' and therapists' perceptions of therapeutic alliance were associated with total days of use across participants in three MI/MET trials in the CTN.
Methods: Identical measures were obtained in three CTN trials of MET/MI. Across all studies, participants completed the Helping Alliance Questionnaire (HAQ) and other identical measures as part of a larger assessment battery. Therapists also completed a parallel version of the HAQ form. We focused on patient (n=867) and therapist (n=883) HAQ scores at 4 weeks and outcome defined as patients' self-reported substance use across 4 weeks of treatment.
Results: Linear regression analyses were conducted to determine whether patient and therapist HAQ scores at 4 weeks were associated with patients' self reported substance use across 4 weeks of treatment. For participants assigned to the MET/MI condition, higher patient HAQ scores were associated with fewer (b= -0.073) days of self-reported substance use, and for participants assigned to TAU, higher scores were associated with more (b=0.025) days of self-reported substance use (p=0.13 for treatment x patient HAQ interaction). Higher therapist HAQ scores were associated with more (b=0.057) days of use for participants assigned to the MI/MET condition, whereas for participants assigned to TAU, higher therapist HAQ scores were associated with fewer (b= -0.074) days of use (p=0.095 for treatment x therapist HAQ interaction).
Conclusions: While these findings were not statistically significant, these trends counter previous research describing a clear relationship between therapeutic alliance and positive treatment outcomes regardless of treatment modality. Potential reasons for the differential relationship of therapeutic alliance and days of use between treatment conditions are discussed.
Financial Support: NIDA CTN

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STAFF PERSPECTIVES ON INNOVATION ADOPTION: LESSONS LEARNED FROM NIATX 200.

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Aims: NIATx 200 examined 201 treatment agencies participating in a process improvement collaborative focused on increased adoption of business practices. Research questions: (1) What business practices are being used to improve access and retention? (2) Which business practices are more likely to be implemented? (3) What differences in perceived use exist based on job function?
Methods: NIATx 200 encouraged agencies to adopt business practices to improve treatment access and retention. Surveys at baseline, 9, and 18 months presented a new group of business practices associated with improving access, engagement, and transitions between levels of care. Staff perceptions were sought about the degree to which each practice was implemented. Example practices included reminder calls, walk-in appointments, and orienting clients to outpatient treatment. Chi-Square tests measured changes in perceived adoption over time for each practice and examined differences by job function.
Results: Results indicate that practice adoption varies and may be affected by ease of implementation. For example, agencies are more likely to orient clients to outpatient treatment (45.6%) than hold joint staff meetings with referral sources (17%) to improve transitions between levels of care. Similar differences exist for other practices. Practice adoption improves when process improvement techniques are used. For example, staff perceptions about reducing excess paperwork improved from 35.5% to 48.2% (chi-square = 43.24). Differences in opinions on practice implementation exist across job function.
Conclusions: NIATx 200 assesses adoption rates of business practices designed to improve treatment access and retention. It highlights the role of process improvement in enhancing practice adoption rates. Results may help researchers understand the degree to which business practices have been adopted and may indicate future research opportunities for enhancing adoption.
Financial Support: Supported by the National Institute on Drug Abuse (R01 DA020832)

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SELECTIVE ACTIVATION OF THE 5-HT$_{2C}$ RECEPTOR REDUCES COCAINE SELF-ADMINISTRATION AND CUE-INDUCED REINSTATEMENT.

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Aims: Nonselective agonists at the serotonin 5-HT$_{2C}$ receptor (5-HT$_{2C}$R) have previously been shown to decrease cocaine self-administration and lever pressing for cues associated with cocaine self-administration. A recently developed compound, WAY 163909, exhibits high affinity and efficacy as a 5-HT$_{2C}$R agonist with an antipsychotic and antidepressant-like profile *in vivo*. Here, we hypothesized WAY 163909 would reduce cocaine self-administration (SA) and cue-induced reinstatement.
Methods: Male Sprague-Dawley rats (n=14) were trained to self-administer cocaine (0.25 mg/kg/inf; 1hr/day; FR1-5). Rats were pretreated with WAY 163909 (0, 0.5, 1, or 2 mg/kg; IP) 15 min prior to daily sessions, with a minimum of two intervening training sessions. A separate cohort of rats (n=36) was trained to SA cocaine (0.75 mg/kg/inf) during daily 3 hr sessions (FR1-5) for 14 days. Rats underwent daily extinction sessions and, upon reaching extinction criteria (<15 lever presses for 3 days), were tested for cue reinstatement following pretreatment with WAY 163909 (0, 0.3, 0.5, or 1 mg/kg; IP) in a between subject design.
Results: Pretreatment with WAY 163909 dose-dependently reduced rates of operant responding for cocaine infusions; mean active lever presses (± SEM) were significantly suppressed at a dose of 2 mg/kg of WAY 163909 (9.2 ± 5) vs. vehicle (25±2.3; p=0.017). WAY 163909 also dose-dependently suppressed cue-induced reinstatement of cocaine-seeking following extinction; cue-evoked lever presses (± SEM) were significantly suppressed after 1 mg/kg of WAY 163909 (14.1 ± 4.4) vs. vehicle (28.7±3.4; p=0.024).
Conclusions: These data indicate that the novel, selective 5-HT$_{2C}$R agonist WAY 163909 attenuates the reinforcing effects of cocaine as well as the incentive-motivational effects of cocaine-paired cues. The present findings suggest that WAY 163909 may be therapeutically useful to curtail withdrawal and craving.
Financial Support: DA 06511, DA 020087, WAY 163909 was a generous gift from Wyeth

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THE BRAIN SUBSTRATE UNDERLYING VARENICLINE'S ACTIONS IN REDUCING SMOKING SATISFACTION.

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Aims: Varenicline (Chantix) is the most effective smoking cessation agent to date, and animal studies suggest that it reduces the degree of reinforcement received from nicotine, through indirect actions on brain reward systems. The animal data are supported by treatment trials demonstrating reductions in the degree of reinforcement received from smoking in varenicline- compared to placebo-treated smokers, as assessed by the modified Cigarette Evaluation Questionnaire (mCEQ). Here, we tested whether the brain's characteristic response during smoking cue exposure (increased activity in ventral striatum (VS), medial orbitofrontal cortex (mOFC; amygdala, insula, etc.) would correlate with varenicline-induced reductions in reinforcement.
Methods: Using perfusion MRI in 21 subjects, we examined the effects of varenicline (vs placebo) in nonabstinent smokers during smoking cue exposure. Smokers were imaged during cue exposure, before and following a 3-week medication regimen. The mCEQ was administered at both time points. We observed that varenicline, but not placebo, eliminated craving and reversed pre-randomization reward-related brain activity in VS and mOFC during cue exposure (ACNP 2009). Next, we regressed the mCEQ item 'smoking satisfaction' against the smoking cue reactivity brain data after the medication regimen.
Results: We observed a robust correlation between varenicline-induced decreases in brain activity in bilateral VS and superior frontal and reduced satisfaction received from smoking (uncorrected at the cluster level at p = 0.000, 20 cont voxels, t val range from 3.7–6.2).
Conclusions: These data show that smokers with a greater varenicline-induced activation of lateral OFC in the brain at rest, and who had decreased limbic responses to cues, also had greater reductions in smoking satisfaction. This study reveals a previously unknown mechanism underlying the clinical effectiveness of varenicline.
Financial Support: R21DA025882-02, 5-P60-DA-005186; Alexander Funds;Pfizer Pharma

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THE CHOICE BETWEEN COCAINE-REMIFENTANIL MIXTURES AND EITHER DRUG ALONE: INCREASING MIXTURE DOSE.

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Aims: Among drug abusers, the cocaine-opioid combination is often preferred to either drug alone. Laboratory research with this combination has been ambiguous as to whether the combination is, at maximum, a stronger reinforcer than either of the component drugs. The present study was designed to examine this possibility in monkeys given a choice between mixtures and the component drugs.
Methods: Using a two-lever discrete-trials choice paradigm, three male rhesus monkeys were allowed to choose between a fixed dose of cocaine (100 μg/kg) and other doses of cocaine (10-300 μg/kg) or remifentanil (0.03-3.0 μg/kg). Previously we have reported that a combination of half the ED50 of cocaine with half the ED50 of remifentanil was superadditive in two of the monkeys but was not a stronger reinforcer than either drug alone. The goal of the current experiment was to examine the generality of this finding with higher doses of cocaine and remifentanil in the mixture. To do this, the doses in the mixture were doubled and the monkeys were allowed to choose between the higher mixture and higher doses of cocaine (560 μg/kg) or remifentanil (1.7 μg/kg) alone. Finally, the mixture doses were doubled again (i.e., quadruple the doses of the original mixture) and the same choice was offered in two monkeys, one given cocaine (560 μg/kg) as an alternative and the other remifentanil (1.7 μg/kg).
Results: When the mixture doses were doubled, choice was approximately equal for the mixture and the component drugs in all monkeys. Quadrupling the mixture doses resulted in a mixture preference over cocaine in the monkey tested under this condition. However, choice was roughly equivalent for the quadruple mixture and remifentanil in the other monkey.
Conclusions: These data extend previous findings by demonstrating that in sufficient doses a mixture of cocaine and remifentanil can be an equivalent or stronger reinforcer than cocaine alone. There was no indication that the mixture was a stronger reinforcer than remifentanil.
Financial Support: Support for this research was provided through a NIDA grant R01-DA019471 to WLW.

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COLLABORATIVE BEHAVIORAL MANAGEMENT REDUCES CRIME, DRUG USE AMONG DRUG-INVOLVED PAROLEES.

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Aims: Collaborative behavioral management (CBM) integrated the roles of parole officers and treatment counselors to provide role induction counseling, contract for pro-social behavior, and contingent reinforcement of contracted behaviors. The Step'n Out study of the Criminal Justice-Drug Abuse Treatment Studies (CJ-DATS) aimed to examine the effect of CBM versus standard parole (SP) on crime, drug use and rearrest over nine month follow-up.
Methods: From 2005 to 2007, a six-site clinical trial randomized 486 parolees to CBM or SP for 12 weeks. Eligible subjects volunteered, had a treatment mandate and a minimum of 3 months of parole. Crime and drug use were assessed at 3- and 9-months after parole initiation using a calendar method. Arrests were obtained from criminal justice records. Logistic and zero-inflated Poisson regression analyses assessed effects on rearrest, crime and drug use.
Results: Follow-up rates were 92% at 3 months and 82% at 9 months. Over 9 months, parolees who self-reported criminal involvement committed fewer crimes in the CBM condition (risk ratio [RR] .79; 95% CI .74, .86) than in the SP condition. Reductions were seen in violent (RR .01; 95% CI .002, .08), property (RR .13; 95% CI .06, .27) and drug-related (RR .79; 95% CI .73, .85) crimes. The CBM group had greater reductions in opiate (RR .80; 95% CI .74, .86) and marijuana (RR .74; 95% CI .69, .80) use. The CBM group had greater reductions in use of the primary problem drug (RR .67, 95% CI .63, .72), in particular for methamphetamine (RR .07; 95% CI .01, .31), opiates (RR .84; 95% CI .76, .91), or marijuana (RR .54; 95% CI .49, .61). The CBM group also had a greater non-significant reduction in rearrest (OR .84; 95% CI .56, 1.25).
Conclusions: Collaborative behavioral management reduced criminal involvement and drug use over 9 months among drug-involved parolees.
Financial Support: CJ-DATS was funded under a cooperative agreement from NIDA/NIH, with support from the CSAT/SAMHSA, CDC, NIAAA/NIH and the Bureau of Justice Assistance.

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SOCIAL INTERACTION PREVENTS COCAINE RELAPSE IN A RAT MODEL: FUNCTIONAL BRAIN MAPPING.

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Aims: While the worsening of drug abuse during social interaction is a well known phenomenon, the effects of social interaction, if offered as a mutually exclusive choice to drugs of abuse, are much less well investigated.
Methods: After cocaine CPP had been established, subjects (Sprague Dawley rats; N=58) were divided into two groups. One group received i.p. saline extinction training, i.e. saline injections in both chambers. The other group was also given the opportunity to have social interaction in the saline-paired chamber with a conspecific of the same weight and gender on the other day. On the third day, all animals were tested for CPP. This cycle was repeated three more times. Immunohistochemistry was used for functual brain mapping and qRT-PCR was employed for the detection of changes at the receptor level. Intergroup comparisons were performed with ANOVA followed by the Newman-Keuls test (StatView®).
Results: A single 15 min social interaction proved sufficient for the reallocation of the rat's behavior away from a drug-paired context toward the social interaction context. Four such brief episodes of social interaction (1) produced preference for the social interaction-associated chamber even if cocaine exposure was continued and (2) were able to inhibit reacquisition of cocaine CPP, a model of relapse. This behavioral change was paralleled by a reversal of cocaine-induced activation of the immediate early gene zif268 in several brain areas that are well known for modulating drug reward.
Conclusions: Social interaction, if offered in a context that is clearly distinct from the previously drug-associated ones, may profoundly speed up the recovery process in addicts.
Financial Support: This research was supported by the Austrian Science Fund (FWF) through grant P18787-B05 and a Lise-Meitner-Fellowship to R.E, by the MFF grant 154, and the VEPPP.

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A SLOW-ONSET, LONG-DURATION METHYLPHENIDATE ANALOG IS NOT SELF-ADMINISTERED IN COCAINE-NAïVE RATS.

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Aims: In an effort to develop a non-abusable medication for treating cocaine abuse, we synthesized a series of methylphenidate analogs with slow onsets and long durations of action. We previously reported that 32,476, an analog with selectivity for the dopamine transporter, has an onset of 20-30 min and a long duration of action on rodent locomotor, microdialysis, and electrical brain stimulation assays with intraperitoneal injection. In rats that have been trained to self-administer intravenous cocaine, a) an intraperitoneal injection of the compound reduces the self-administration of cocaine, and b) substitution of 32,476 for the cocaine produces lower rates of self-administration that appear to be trending toward extinction of the behavior. On a progressive ratio schedule, the compound has a lower break point than cocaine suggesting a lower abuse potential. We have now determined whether the compound will have abuse potential in cocaine-naïve rats.
Methods: Intravenous self-administration studies were performed with fixed-ratio reinforcement schedules. Data was analyzed by ANOVA, individual group comparisons, and t-tests.
Results: We now report that 32,476 is not self administered at significantly higher than saline rates in cocaine-naïve rats (n=8).
Conclusions: These results suggest that 32,476 may be suitable as an agonist substitution therapy for treating cocaine abuse and provide evidence for the hypothesis that a dopamine reuptake inhibitor with slow-onset, long-duration pharmacokinetics will have reduced abuse potential.
Financial Support: Supported by grant DA015795 from the National Institute on Drug Abuse

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THE ASSOCIATION BETWEEN INDIVIDUAL SOCIAL FACTORS AND NEIGHBORHOOD SOCIAL CONTEXT ON FREQUENT HIV TESTING AMONG NEW YORK CITY DRUG USERS.

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Aims: Frequent HIV testing is necessary for early detection of HIV, subsequent treatment and HIV prevention. Therefore, we examined individual (sexual practices, social networks), neighborhood social context (%high school education, %< poverty, and social cohesion) associated with frequent HIV testing (>4 times in lifetime) among 653 newly initiated injection drug users (IDUs) and non-IDUs (heroin/crack/cocaine users) recruited by respondent driven sampling and targeted street outreach enrolled in the "Social Ties Associated with Risk of Transition in Injection Drug Use" (START) study.
Methods: We combined START baseline data with NYC census data and neighborhood social cohesion data taken from an ancillary NYC resident study. PROC-GLIMMIX was used to account for the hierarchical-level data.
Results: Individual (sexual orientation, lifetime STD testing, ≥3 social networks) and neighborhood (social cohesion, awareness of proximity to a syringe exchange program, negative belief of drug/ alcohol hospitalization, job training improvement for previously incarcerated belief, ≥50% high school education and disadvantage measured by Townsend scale) factors were bivariately associated with frequent HIV testing. In the final model, individuals who lived in neighborhoods that believed drug/alcohol hospitalization was negative (OR:0.36;95%CI:0.13-1.02) were marginally less likely to report frequent HIV testing. Those reporting history of herpes, chlamydia, gonorrhea or syhpillis testing (OR:1.67;95%CI:1.02-2.74), having 3 or more drug-using network members (OR:1.58;95%CI:1.01-2.45) and higher neighborhood-level education (OR:1.81;95%CI:1.01-3.25) were significantly more likely to frequently test for HIV.
Conclusions: These data suggest that negative attitudes about drug use may affect HIV testing behavior. However, additionally, social network based interventions may be an optimal approach to increase HIV testing behavior and should be explored, particularly in lower SES neighborhoods.
Financial Support: NIDA

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THE GROWTH OF NEIGHBORHOOD HAZARDS AND YOUTHFUL DRUG INVOLVEMENT.

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Aims: The Neighborhood Inventory for Environmental Typology (NIfETy) is an objective, contextual, and structured inventory designed to assess the incidence and prevalence of environmental indicators theorized to be linked with resident exposure to violence, alcohol and other drug (VAOD) activity in urban communities. This block-level inventory was constructed to delineate the contexts in which youth live and experience deleterious community-level exposures, the frequency and severity of exposure, and the factors which promote or sustain elevated levels of VAOD exposure within neighborhoods. This current research examines how urban environmental hazards over time influence youthful drug involvement.
Methods: The youth data are derived from the second generation of randomized preventive intervention trials at the Baltimore Prevention Program (BPP) at Johns Hopkins. This is an epidemiologically defined population of 799 predominantly African American urban first graders who were randomly assigned to either a standard setting (i.e., control) classroom or to a classroom featuring one of two theory-based, developmental preventive interventions. The data are rich in repeated measures documenting psychological well-being, social adaptation, substance use and misuse, achievement and school performance, as well as family characteristics. Data collection began in 1993 as participants entered first grade (age 6) and continues through the present. The current research uses Generalized Growth Mixture Modeling to identify distinct developmental trajectories of neighborhood environment that were used to predict subsequent illicit drug use.
Results: Four distinct neighborhood classes were identified, including a low hazard, moderate hazard, chronically hazardous and increasingly hazardous neighborhood. The odds of drug use were highest among youth in the chronically hazardous (OR=1.3, p=0.03). This estimate was adjusted for prior drug illicit drug involvement.
Conclusions: This research is a first step toward understanding how neighborhood environment is related to illicit drug use.
Financial Support: R01AA015196,R01DA11796,and 1U49CE000728.

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BRAIN POTENTIAL INDICES OF REWARD VARY WITH BEHAVIORAL CONTROL.

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Aims: A low level of behavioral control is a risk factor for alcohol and drug abuse. This may result, in part, from an association between control and the valuation of rewards and penalties. The purpose of this study was to evaluate reward processing in groups of individuals with distinct levels of behavioral control.
Methods: Using the Control scale of the Multidimensional Personality Questionnaire, two groups were identified (High Control: n=17 men, 11 women; Low Control: n=12 men, 11 women). On separate days, event-related brain potentials were recorded 3 hours after placebo or 10 mg d-amphetamine, while participants performed a gambling task. Participants were asked to select between cards whose color was associated with large or small monetary amounts; their choices were unpredictably associated with wins and losses. P300 elicited by the outcome of their choices reflects processing of rewards and penalties.
Results: Overall, P300 elicited by wins was larger than that elicited by losses ($p<.0001$). There was also a three-way interaction for P300 amplitude (Control x Sex x Valence; $p=.0316$). In men, the effect of valence differed in the two Control groups ($p=.0138$): In Low-Control men, P300 amplitude was affected by valence (win > loss) ($p=.0054$); in High-Control men, there was no difference in P300 elicited by wins and losses ($p=.4235$). In women, the Control x Valence interaction was not significant ($p=.6788$). Although d-amphetamine increased P300 amplitude overall, it did not alter this pattern of effects.
Conclusions: As reflected by P300 elicited in a gambling task, the salience of winning and losing depends on the level of behavioral control in men but not women. Such valuations may affect decisions in laboratory gambling tasks, as well as in life situations that involve gains and losses. As such, these findings address cognitive processes associated with behavioral control, an important risk factor for alcohol and drug abuse, as well as sex differences in that relationship.
Financial Support: Supported by a grant from the National Institute on Drug Abuse (DA018674).

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ENHANCED DOPAMINE RELEASE IN THE DORSOLATERAL CAUDATE PUTAMEN DURING RELAPSE AS A FUNCTION OF PREVIOUS COCAINE SELF-ADMINISTRATION HISTORY.

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Aims: Growing evidence suggests that persisting neuroadaptive changes occur with prolonged cocaine use, whereby the dorsal striatum comes to exert greater control over cocaine-seeking behavior. The current study investigated striatal dopamine (DA) release in the dorsolateral caudate putamen (dlCPu) at the time of relapse following abstinence in rats that experienced short or long daily access to cocaine self-administration. We hypothesized that animals receiving long access cocaine self-administration would show enhanced striatal DA release at the time of relapse.
Methods: Male Sprague-Dawley rats (n= 20) were trained to self-administer i.v. cocaine (0.2 mg/50 ul infusion) for 6 days (2 hr sessions). Animals were then switched to one of two access conditions: short access (2 hr/5 days) or long access (6 hr/15 days). Following completion of self-administration, animals underwent two relapse tests and concurrent microdialysis in the self-administration context after 24 hr and 14 days of abstinence. Microdialysis probes (2 mm) were inserted into the dlCPu and basal samples were collected at 20 min intervals for 1 hr prior to testing and throughout the 2 hr context relapse session. Samples were analyzed for extracellular DA levels using HPLC and electrochemical detection.
Results: Results indicate increased DA release in the dlCPu at relapse in animals that received long access cocaine as compared to short access cocaine ($p<0.05$).
Conclusions: Enhanced DA release in the dlCPu at relapse occurred in an intake-dependent manner, supporting a progressive change in the dlCPu with prolonged cocaine self-administration. Enhanced DA release in the dlCPu may contribute to heightened stimulus-response (i.e., habit) learning relevant to cocaine addiction.
Financial Support: (Supported by NIH Grant DA10462)

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VIGABATRIN AS A TREATMENT FOR METHAMPHETAMINE DEPENDENCE.

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Aims: Vigabatrin is a GABA transaminase inhibitor that is approved for the treatment of epilepsy and that has shown promise as a treatment for stimulant dependence. We conducted a trial to assess the safety and efficacy of vigabatrin as a treatment for methamphetamine (MA) dependence.
Methods: MA dependent outpatients at 8 trial sites were randomized to oral vigabatrin (VGB) or matching placebo (PBO) tablets for 12 weeks. The VGB dose was escalated over two weeks to 1.5 g bid; the dose was tapered during week 12. Randomization was stratified partially based on frequency of MA use in the 30 days prior to screening (≤18 days v. >18 days). Adverse events, self-report of MA use, and urine toxicology for MA were assessed three times per week. Visual fields were assessed before VGB was started and at the completion of the trial. Success was defined a priori as abstinence in the last two weeks of the trial based on both self-report and urine toxicology.
Results: Target enrollment was 180 subjects. The trial was halted after 29 subjects were randomized to VGB and 28 subjects were randomized to PBO due to financial reasons, not safety or efficacy. There were no serious adverse events and no visual field defects. Five subjects (17%) in the VGB group met criteria for success v. two (7%) in the PBO group ($p=0.23$). In the more frequent users, success rates were 2/16 (13%) and 0/15 (0%) in the VGB and PBO groups, respectively, and the greatest number of consecutive MA-negative urine samples were 3.1 (6.5) and 0.7 (1.8) ($p=0.15$).
Conclusions: Definitive conclusions cannot be drawn from this trial due to the small N. Although statistically significant differences in efficacy were not seen, decreased MA use and lack of toxicity support additional testing of vigabatrin in MA dependence.
Financial Support: Supported by Catalyst Pharmaceutical Partners, Inc

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INTERACTIVE ROLE OF HIV-1 CLADE SPECIFIC TAT PROTEIN AND COCAINE IN BLOOD-BRAIN BARRIER DYSFUNCTION: IMPLICATIONS FOR NEUROAIDS.

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Aims: In recent years, increasing interest has emerged to assess the HIV-1 clade C viral pathogenesis due to its anticipated spread in the US and other western countries. Previous studies suggest that clade C is less neuropathogenic than clade B; however, the underlying mechanism is poorly understood. Additionally, the interactive role of drugs of abuse such as cocaine on clade associated neuropathogenesis has not been reported. In the current study, we hypothesize that HIV-1 clade specific Tat proteins exert differential effects on blood-brain barrier (BBB) integrity and cocaine further differentially aggravates the BBB dysfunction.
Methods: We evaluated the effect of Tat B and Tat C and/or cocaine on the BBB integrity using an in vitro model constructed with primary human brain microvascular endothelial cells (HBMEC) and astrocytes. Further, we analysed tight junction proteins (ZO-1 and JAM-2) expression in response to Tat B and Tat C and/or cocaine treatment.
Results: Our results show a decrease in BBB membrane integrity as measured by transendothelial electrical resistance (TEER) across the BBB on treatment with Tat B, Tat C and/or cocaine and concomitant increase in paracellular permeability of propidium iodide and transmigration of monocytes across the BBB. However, the observed effects were significantly higher with combined treatment of Tat B plus cocaine compared to Tat C plus cocaine. This BBB dysfunction was associated with altered expression of tight junction protein ZO-1 and JAM-2.
Conclusions: Our results for the first time delineate the differential role of Tat B and Tat C and the synergistic role of cocaine in BBB dysfunction, which may be correlated with the clade specific differences observed in neuroAIDS manifestations.
Financial Support: This work was supported in part by National Institute on Drug Abuse grant R37DA025576, R01DA012366 and R01DA021537.

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CHANGES IN BRAIN ACTIVATION PATTERN DURING CUE REACTIVITY AFTER ONE MONTH ABSTINENCE IN HEROIN DEPENDENTS.

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Aims: Drug related cues provoke changes in behavior, self-report craving and brain function and these reactions may serve as markers or predictors of treatment outcome. Previous research has identified a network of brain regions that sub serve cue reactivity. The effects of drug treatment on activation of this network are not well established.
Methods: 25 opioid-dependents, currently heroin smokers were selected from the waiting list of a residential abstinence-based treatment center. Prior to treatment, subjects underwent a fMRI session during which they viewed heroin-related cues presented in a block-design. Cue induced craving (CIC) was measured before, during and after imaging. 23 subjects were abstinence at the one month time-point and completed a post abstinence imaging session.
Results: Subjects showed significant reduction in CIC report from 48% (SD: 28%) to 07% (SD:11%), $t(22)=7.35$, $p<0.001$. Viewing heroin cues resulted in significant activation during both the pre and post treatment scans in regions identified in previous studies. Greater activation was observed pre- and compared to post-abstinence in the left temporal fusiform gyrus, right hippocampus and right thalamus (pulvinar); whereas greater activation was observed in post- compared to pre-abstinence in left middle frontal gyrus and right superior frontal gyrus.
Conclusions: One month of heroin abstinence results in a shift of brain cue-reactivity from subcortical and limbic areas to more frontal regions. These findings may suggest that reactivity to cues changes from relatively bottom-up to top-down processing following prolonged abstinence. Future analyses will determine whether pre or post-abstinence measures are predictive of longer-term treatment outcomes.
Financial Support: This study has been sponsored by Tehran University of Medical Sciences and Rose Polymer Co.

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NEUROPSYCHOLOGICAL PERFORMANCE OF COCAINE ADDICTS DURING TREATMENT.

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Aims: A great number of studies have observed impairments on executive functions of cocaine addicts. However, it remains unclear whether these neuropsychological deficits persist in abstinent patients. The aims of the present study were (1) to explore the course and persistence of neuropsychological deficits of cocaine dependent outpatients over a 12 month period, and (2) to examine whether neuropsychological performance at treatment entry predicts treatment outcome (treatment retention and cocaine abstinence) among cocaine addicts.
Methods: Fifty cocaine addicts enrolled in an outpatient program for cocaine dependence in Spain were randomly recruited. A neuropsychological test battery including different executive functioning measures was administered at treatment entry and twelve months later. Urine specimens were collected throughout the treatment to monitor abstinence.
Results: Results showed a trend towards improvement in the neuropsychological measures at twelve months after treatment entry. Neuropsychological performance improved in attention and fluency tests, remained stable in inhibitory control tasks and worsened in mental flexibility tests. Finally, there were no significant differences regarding neuropsychological scores at baseline between abstainers and relapsers or completers and dropouts.
Conclusions: There was an overall improvement on neuropsychological performance, which suggests that executive functioning impairments might be reversible in patients addicted to cocaine. Knowledge of neuropsychological impairment may be clinically useful, but future studies should examine the presence of any specific effects and their persistence. Finally, neuropsychological measures were not a significant predictor of treatment outcome at 12 months after treatment entry.
Financial Support: Spanish National Plan on Drugs (Ref. MSC-06-01) and the University of Oviedo.

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PRODUCING SMOKING CRAVING BY USING IMMERSIVE VIRTUAL ENVIRONMENTS.

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Aims: Cue Exposure Treatment, CET, consist of controlled and repeated exposure to stimuli associated with substance use in order to reduce associated craving. Virtual reality has shown its efficacy as a exposure tool in several psychopathological disorders. The aim of this study was to assess the validity of 7 immersive virtual reality environments to produce smoking craving.
Methods: Participants were 45 smokers and 40 non-smokers. Subjects were exposed to 7 complex virtual scenes with smoking related cues that reproduce typical situations where people smokes (being in a pub, having lunch and having breakfast at home, drinking coffee in a cafe, after having lunch at a restaurant, waiting in the street and watching TV at night) and to a neutral virtual environment (a museum). Environments were presented with a Head Mounted Display with tracking sensors. Subjective craving (measure with a visual analogical scale) and psychophysiological measures (heart rate, temperature and skin resistance) were registered during the exposure.
Results: In the smokers group, subjective craving were significantly higher in the virtual environments with smoking craving cues than in the neutral environment. As expected, the non-smokers group referred no desire of smoking during the exposure to the scenes. Some psychophysiological variables were also related with smoking status and subjective craving.
Conclusions: This results suggest that complex virtual reality environments that simulate real situations are able to elicit craving. This technology could be useful in the improvement of CET for substance use disorders and more specifically for smoking cessation programs. Nevertheless, it is necessary to have a minimal number of situations that enhance the probability of generalization of extinction in real life.
Financial Support: This work was supported by one grant of the Ministry of Science and Innovation (MICIIN) of the Spanish Government, Ref. PSI2008-05938/PSIC.

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BLOCKADE OF DOPAMINE D3 RECEPTORS BY SB-277011A INHIBITS INCUBATION OF CRAVING FOR COCAINE IN RATS.

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Aims: The dopamine (DA) D3 receptor has been suggested to be a promising target for anti-addiction medications. Previous studies from our laboratory have shown that SB-277011A, a selective DA D3 receptor antagonist, inhibits cocaine's rewarding effects and reinstatement of drug-seeking behavior triggered by cocaine, cocaine-associated cues, or foot-shock stress. The present study sought to determine whether SB-277011A also inhibits incubation of craving for cocaine in cocaine-withdrawn rats.
Methods: Long-Evans rats (n=50) were allowed to self-administer cocaine (0.5 mg/kg/infusion, 3-hr/session). Each cocaine infusion was associated with a light-and-tone cue. After stable cocaine self-administration (~ 2 weeks) was achieved, all animals underwent withdrawal (in home cages) from cocaine self-administration. Resumption of cocaine-seeking behavior was assessed at 2, 10, 30 or 60 days after cocaine withdrawal. Resumption was tested under extinction conditions during which lever pressing did not produce either cocaine infusion or presentation of cocaine-associated cues.
Results: We found that: 1) there was a progressive increase in extinction responding over 30 days following cocaine withdrawal (which did not continue to 60 days), suggesting development or incubation of craving over the first 30 days after cocaine withdrawal under the present experimental conditions; 2) extinction responding was inhibited by SB-277011A (24 mg/kg, i.p., 30 min prior to testing) at all withdrawal time points; 3) SB-277011A (6-24 mg/kg) produced a dose-dependent inhibition of extinction responding at 30 days after cocaine withdrawal; and 4) SB-277011A (24 mg/kg) had no effect on extinction responding at 30 days after withdrawal from sucrose self-administration.
Conclusions: These findings, combined with previous data, suggest that DA D3-selective receptor antagonists merit further investigation as potential anti-cocaine medications.
Financial Support: Intramural Research Program, NIDA/NIH.

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ILLICIT DRUG USE AND EXTRACURRICULAR INVOLVEMENT DURING COLLEGE.

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Aims: Little data is available on the relationship between college extracurricular involvement and drug use. Possible mechanisms like self-selection, exposure to drug-using peers and limits on time suggest drug use might vary by type of extracurricular activity involvement. This study examined associations between persistent marijuana use and ten types of extracurricular activities in college. Involvement in extracurricular activities will be associated with illicit drug use even at the college level.
Methods: From a larger sample of 1253 college students in a longitudinal study, two groups were selected based on drug use patterns during four years of college: persistent marijuana users (n=416) and consistent non-users of illicit drugs (n=204). Data on regular involvement in ten extracurricular activities (volunteering, religious groups, athletics, Greek life, academic clubs, government/leadership, arts, activity-based clubs, advocacy groups and job/internship) were collected during face-to-face interviews. Logistic regression models controlling for sex, race and SES tested associations between each extracurricular activity and drug group membership.
Results: Involvement in religious and academic groups was associated with a decreased likelihood of being a persistent marijuana user (OR=.28, p<.001 and OR=.36, p=.005). Greek life was associated with increased likelihood for persistent marijuana use (OR=3.62, p<.001). Subanalyses revealed that when non-users were compared to a subset of persistent marijuana users who also used another drug persistently, results differed, with the academic association falling out and art involvement attaining significance.
Conclusions: Results confirm prior findings that Greek involvement is associated with greater risk for illicit drug use and add to literature on possible protective mechanisms of other activities. Associations between drug involvement and extracurricular activities may differ by type and extent of drug use.
Financial Support: R01-DA14845, A. Arria, PI

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MDMA–INDUCED FEELINGS OF SOCIABILITY IN HUMANS MAY HAVE A SEROTONERGIC MECHANISM.

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Aims: MDMA (3, 4-methylenedioxymethamphetamine, 'Ecstasy') is a widely used illicit drug that can induce feelings of sociability and closeness to others. MDMA induces serotonin release by entering the neuron through the serotonin transporter (SERT) and subsequently causing neurotransmitter storage vesicles to release their contents. Blocking the SERT with a selective serotonin reuptake inhibitor (SSRI) interferes with the ability of MDMA to release serotonin and decreases many of its effects in humans and animals. However, it is not clear if the MDMA-induced serotonin release affects sociability.
Methods: We are comparing the effects of MDMA (1.5 mg/kg oral) alone and when given after approximately one week of the SSRI citalopram (20mg/day oral) using a 5-session, double-blind, placebo-controlled, within-subject design. Sociability is measured with the Interpersonal Adjective Scales - Revised (IAS-R) and visual analog (VAS) item "closeness to others"
Results: A planned interim analysis showed main effects of dosing condition on VAS "closeness to others" ($F_{4,44}$=13.82, p<0.001) and IAS-R gregariousness-extraversion ($F_{4,44}$=7.81, p<0.001). MDMA increases both measures compared to placebo (p=0.006 and p<0.001) and citalopram pretreatment significantly attenuates these effects (p=0.032 and p<0.001).
Conclusions: The effects of MDMA on sociability and feelings of closeness to others in humans may be mediated by MDMA interactions with SERT.
Financial Support: Supported by R01 DA017716 and DA016776

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BEHAVIORAL EFFECTS OF THE NOVEL HALLUCINOGEN 2C-C.

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Aims: 4-Chloro-2,5-dimethoxyphenethylamine (2C-C) is a hallucinogenic compound structurally related to the classic hallucinogen 2,5-dimethoxy-4-methylamphetamine
(DOM) and to other phenethylamine hallucinogens. There have been some reports of recreational use, but very little controlled examination of the behavioral and pharmacological effects of 2C-C.
Methods: The effects of 2C-C on locomotor activity was tested in mice. 2C-C was tested in rats trained to discriminate a number of hallucinogenic and psychostimulant compounds which cover a range of mechanisms including dopamine, norepinephrine and serotonin receptors. The training compounds included methamphetamine, 3,4-methylenedioxymethylamphetamine (MDMA), lysergic acid diethylamine (LSD), (-)-2,5-dimethoxy-4-methylamphetamine (DOM), and dimethyltryptamine (DMT).
Results: 2C-C produced a time- and dose-dependent depression of locomotor activity following 30 and 100 mg/kg within 10 minutes following injection and lasted 30 to 120 minutes. Convulsions were observed in 2/8 mice and tremors in 6/8 mice at 30 minutes following 100 mg/kg 2C-C. Lethality occurred in 1/8 mice within 120 minutes following 100 mg/kg. 2C-C fully substituted for the discriminative stimulus effects of DOM (ED50=0.80 mg/kg) and MDMA (ED50=0.80 mg/kg). 2C-C partially substituted for the discriminative stimulus effects of LSD and DMT (maximum drug-appropriate responding of 75%) in the dose range of 2.5-10 mg/kg. Dose-dependent suppression of responding was observed from 5 to 25 mg/kg. Adverse effects were observed following 25 mg/kg 2C-C, including reddening of the extremities (3/3 rats) and excessive salivation (1/3 rats).
Conclusions: C-C produces discriminative stimulus effects similar to those of other hallucinogens, particularly DOM and MDMA, the two most structurally related compounds. This implies that 2C-C may have comparable abuse liability. In addition, the dangerous adverse effects may also contribute to decisions about scheduling of 2C-C.
Financial Support: Supported by NIH N01DA-2-8822 and NIH N01DA-7-8872.

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USING THE GELBERG-ANDERSEN BEHAVIORAL MODEL FOR VULNERABLE POPULATIONS TO PREDICT HEALTH SERVICES UTILIZATION AMONG HOMELESS ADULTS, BY HEPATITIS B OR C SEROSTATUS.

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Aims: Homeless people have high rates of illness and death, including hepatitis (HBV and HCV). Health care is essential to identify persons with hepatitis. Using the Gelberg-Andersen Model and structural equation modeling, we sought to understand health care access among this high-risk group and assessed whether HBV or HCV disproportionately affected access. Models identified predictors of HBV or HCV and associations between these infections and health care utilization.
Methods: Population-based probability sample of 534 homeless adults in 41 shelters and meal programs in Los Angeles was interviewed and tested for HBV and HCV. Structural models assessed the impact of predisposing, enabling, and need variables on utilization in the past 12 months (emergency department (ED), hospitals, and ambulatory visits).
Results: HBV or HCV positivity (43%) was positively associated with injection drug use, competing needs, older age, less education, and jail or prison history. ED use was predicted by regular source of care, insurance, younger age, alcohol abuse, perceived bad health, fewer competing needs and more medical conditions; ED use was less likely among HBV- or HCV-positive adults. Hospitalizations were predicted by female gender, more medical conditions, and greater percentage of life homeless; hospitalizations were less likely among African-Americans. Ambulatory office visits were predicted by regular source of care, case management, more education, and perceived bad health; # of visits were lower among HBV- or HCV-positive adults than others (<1 vs. 2 visits).
Conclusions: Homelessness severity and alcohol abuse places homeless adults at risk for needing ED care. Having a medical home and a supportive relationship are key facilitators of access. HBV- or HCV-positive adults used less ambulatory services despite their need. Ambulatory services targeting HBV-and HCV-positive homeless adults are needed.
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CHARACTERIZATION OF USERS IN A POPULATION OF DRUG ADDICTS.

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Aims: The French Monitoring Centre for Drugs and Drug Addiction, Observatoire Français des Drogues et Toxicomanies (OFDT) has among other goals the characterization of drug addict populations. A more precise knowledge of users groups, defined by their "key" substances or specific modes of use would allow targeted actions toward prevention. The aim of the study was to characterize pattern of use in a population of drug addicts: sharing drugs and/or drug equipment, using crack and alcohol heavily.
Methods: Cross-sectional evaluation of 1018 subjects from the 2006 PRELUD survey to determine characteristics associated with each pattern of use. A multivariate logistic regression was performed for variables, considered as evaluation criteria.
Results: Sharing drugs/drug equipment was statistically associated with female gender, having been to at least ten rave parties, having used alcohol during the month and having health problems linked to the injection of substances during the month. Crack or free base cocaine use during the preceding month was statistically associated with being less than 25 years old, absence of long-term housing and with having been to at least ten rave parties lifetime. Heavy alcohol use was statistically associated with male gender, the 25-35 years age group, a lower level of education and having snorted drugs at least once.
Conclusions: These results show that some characteristics are significantly associated with the use of psychoactive substances. Some prevention strategies could target subgroups, such as protecting women from sharing drug use equipment.
Financial Support: Non applicable

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TREATNET II: WORKING TOWARDS EVIDENCE-BASED DRUG DEPENDENCE TREATMENT AND CARE: CAPACITY BUILDING CASCADE.

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Aims: The United Nations Office on Drugs and Crime (UNODC) initiated Treatnet II in 2008, building on Treatnet I. The project aims at improving the technical capacity for the provision of evidence-based drug treatment and care services, including their capacity to support HIV and AIDS prevention. Treatnet II advocates for the concept of drug dependence as a multifactorial disease, to be treated with the same quality as any other health disorder.
Methods: The strategy to achieve its goal includes three lines of action: Advocacy, Capacity Building and Service Improvement (development and strengthening of drug dependence treatment services). Treatnet II is currently active in 20 low-and middle income countries in Africa, Central Asia, Latin America and South East Asia. The poster will focus on the Capacity Building Component of Treatnet II. The project is following a cascaded Train the Trainer Approach. During the second half of 2009, 24 "Master Trainers" trained more than 120 trainers from all Treatnet regions on the delivery of a specific volume of the Treatnet Capacity Building package, so that these can train staff in their countries and hence contribute to the development of a well qualified workforce delivering evidence-based drug dependence treatment and care.
Results: The cascaded Train the Trainers approach guarantees sustainability of knowledge and skills transfer while reaching a high number of professionals working in the field of drug dependence treatment.
Conclusions: By the end of 2011 more than 21000 practioners will have been trained on a) Screening, Assessment and Treatment Planning b) Psychosocial Treatment c) Pharmacological Treatment at national level. To ensure cultural relevance the training package has been translated into the national languages and the trainers take a leading role regarding the cultural adaptation and the ongoing scientific review and updating of the training package.
Financial Support: Canada, Spain, Sweden, United States of America, and the OPEC Fund for International Development.

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NIDA'S CLINICAL TRIALS NETWORK CAN FACILITATE COMPARATIVE EFFECTIVENESS RESEARCH ON ADDICTION TREATMENTS.

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Aims: Recent Congressionally-mandated reports on Comparative Effectiveness Research (CER) define CER as "the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care," in order to "assist patients, clinicians, purchasers, policy makers, and the public to make informed decisions that will improve health care at both the individual and population levels." The purposes of CER are congruent with the mission of NIDA's Clinical Trials Network: To ensure the transfer of promising research results to physicians, clinicians, providers, and patients by conducting studies of behavioral, pharmacological and integrated treatments in rigorous, multi-site clinical trials to determine effectiveness across a broad range of community-based treatment settings and diversified patient populations.
Conclusions: The CTN's research infrastructure includes clinical expertise centered in major universities and local community-based addiction treatment programs studying patient care in real-world settings. The CTN will enhance its ability to conduct addiction CER by: 1) incorporating clinical settings that frequently see patients with co-morbid substance use disorders, 2) routinely integrating the use of health information technology into its studies, and 3) developing new research methods for evidence generation (studies and trials), evidence synthesis (systematic reviews and modeling studies), and evidence translation. There are FDA approved pharmacological intervention options to treat addictions to opioids (methadone, buprenorphine and naltrexone), alcohol (disulfiram, acamprosate, and naltrexone), and nicotine (nicotine replacement therapy, bupropion, and varenicline), but CER evidence indicating which options work best for whom, when, and in what circumstances is lacking. There is an urgent need to conduct these CER studies, and the CTN is the ideal platform for this endeavor.
Financial Support: NIDA/NIH/HHS

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ACETYLCHOLINE ESTERASE INHIBITOR TACRINE REDUCES EXTINCTION RESPONDING FOR AMPHETAMINE.

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Aims: Acethylcholine esterase inhibitors (AChE-I) enhance central levels of synaptic acetylcholine (ACh). Increasing ACh level in ventral tegmental area or in nucleus accumbens could however have opposite effects to dopaminergic transmission, so that the net effect of cholinomimetic drugs on drugs of abuse-induced dopamine release, and related addictive behaviour, has not been clarified yet. Moreover, the potential drug-drug interactions that might occur for Alzheimer's patients receiving AChE-Is are relatively unknown. We aimed to study the effects of systemic treatment with an AChE-I, tacrine, on amphetamine stimulus discrimination, self-administration and within-extinction responding.
Methods: Six Sprague Dawley rats were trained to discriminate between d-amphetamine (0.6 mg/kg SC, 15 min prior session) and saline up to final FR10:Sd. Different doses of tacrine (0.625, 1.25, 2.5 mg/Kg/mL, IP, 60 min prior session) were tested for generalisation to amphetamine training dose. The effect of tacrine pre-treatment (0.32 mg/Kg IV, 20 min prior session) on amphetamine self-administration was studied in a group of 6 rats trained to a schedule of FR2:d-amphetamine (0.1 mg/kg/infusion) IV self administration (1-h session). Finally, tacrine (0.32 mg/Kg IV) effect during a within-session extinction 24-hrs later an amphetamine IV self-administration session was tested.
Results: Tacrine discriminative stimulus did not generalize with amphetamine and tacrine pre-treatment did not have any effects on amphetamine self-administration. However, when given before the within-session extinction, tacrine induced a decreased in amphetamine-paired (- 50.36%, P=0.02) lever responding vs. vehicle.
Conclusions: These results suggest that tacrine can have a potential improvement effect on learning within-session extinction responding. Further studies are needed in order to understand which brain processes (motivational or cognitive?) underlie these tacrine effects on extinction responding.
Financial Support: This project has been founded by Joint Project 2007 University of Verona.

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CHRONIC METHYLPHENIDATE TREATMENT DOES NOT AFFECT THE COURSE OF DOPAMINERGIC DEVELOPMENT IN JUVENILE RHESUS MONKEYS.

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Aims: Millions of children are medicated with stimulant drugs, such as methylphenidate (MPH), to treat ADHD. The potential for chronic MPH treatment to have long term effects on the developing brain is of great concern. MPH exerts its actions on the dopamine (DA) system by blocking the DA transporter (DAT), elevating DA levels in the striatum. This study examined the effects of chronic MPH treatment on D2 receptors and DAT, as measured by positron emission tomography (PET), in juvenile rhesus monkeys.
Methods: PET scans were conducted in 16 monkeys using [18F] FCP to quantify D2s and [18F] FCT to quantify DAT at baseline and post-treatment. An extended release formulation of MPH was administered orally daily for 12 months at therapeutically relevant doses to 8 monkeys, while 8 monkeys received placebo. Distribution volume ratios (DVRs) were calculated for specific binding in three striatal regions of interest: caudate, putamen and ventral striatum. Analysis of variance and appropriate t-tests were conducted to examine changes in D2 and DAT DVRs within and between groups.
Results: DA D2 receptor availability declined significantly over a 12 month period in the putamen and caudate, but not the ventral striatum, of both the placebo and MPH treated groups. There were no differences in the magnitude of the decrease between the groups. DAT availability did not change over time in any of the brain regions examined in either group. There were no differences in DAT binding between the MPH and placebo groups.
Conclusions: During development, D2 receptor availability declines in the putamen and caudate of juvenile monkeys. This decrease may reflect reductions in D2 receptor number or increases in basal levels of synaptic DA. Unlike the D2, DAT binding did not change over time. The key finding of this study is that MPH treatment did not alter binding to D2 or DAT. These findings suggest that chronic MPH treatment may not cause long term alterations in dopaminergic development, even during a dynamic period of brain development.
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AN ANIMAL MODEL OF NEGATIVE URGENCY AND THE EFFECT OF D-AMPHETAMINE ON BEHAVIORAL OUTCOMES OF UNEXPECTED NONREWARD.

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Aims: Urgency is one of four distinct facets of impulsivity. It is the tendency to engage in risky behavior due to extreme positive or negative affect, such as what occurs when an unexpected reward is received (positive urgency) or an expected reward is not received (negative urgency). Urgency has been found to predict problem drinking as well as stimulant use among college students. The current study was designed to determine if behavioral invigoration occurs following food reward omission as a model of negative urgency in rats.
Methods: Rats were trained with a Pavlovian association in an initial component in which a cue light served as the conditioned stimulus (CS), and always led to an unconditioned stimulus (US), a sucrose pellet delivery. Following this initial component, rats were allowed to complete a response requirement for sucrose pellets in a second operant component. After extensive training, omission trials were inserted every fifth session to determine if nonreward during the Pavlovian component altered responding during the operant component. On reward omission trials, the light in the initial component did not lead to a sucrose pellet. To determine the role of motivation in the urgency effect, rats were give free access to food and tested in the same procedure to determine if the unexpected nonreward would enhance the difference between reward and test sessions. Following one test session with free access to food, rats were subsequently administered d-amphetamine (0.0, 0.03, 0.1, 0.3, and 1.0 mg/kg, subcutaneously).
Results: Rats showed significantly higher rates of responding during test sessions with occasional reward omission trials than during baseline sessions when all trials contained expected reward when food restricted. Access to free feed enhanced the urgency effect, whereas d-amphetamine administration did not eliminate the urgency effect.
Conclusions: A behavioral measure to quantify mood-based rash action may help us understand the neurobehavioral causes of urgency, and reduce risk of substance use and misuse in a more effective way.
Financial Support: NIH grants T32 DA007304 and P50 DA05312

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COMPARISON OF BASELINE AND IN-TREATMENT MEASURES OF MOTIVATION AND DISTRESS IN PREDICTING TREATMENT RETENTION.

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Aims: To examine measures of motivation and distress, administered at baseline and one- and three-months in-treatment, as predictors of treatment retention to one-, three-, and six-months.
Methods: Participants were 240 (45% female; 96% African American) opioid-dependent entrants to a 30-day buprenorphine detoxification program linked to long-term outpatient drug-free treatment. Participants had consented to be involved in a study of early treatment engagement strategies. Motivation for treatment was assessed using the TCU Motivation scales and distress was assessed using the Beck Hopelessness Scale. Measures were administered at baseline and at one- and three-months in-treatment. Retention was assessed with regard to whether the participant was still in treatment (yes *vs.* no) at one-, three-, and six-months post-baseline.
Results: Binary logistic regression analysis revealed that baseline measures of neither motivation nor distress were significantly associated with retention to 1-month. In contrast, both motivation (OR = 1.8; 95%CI = 1.1, 3.1) and distress (OR = .81; 95%CI = .69, .96) at 1 month predicted retention to 3 months; lower motivation and higher distress were associated with an increased likelihood of premature treatment termination. While baseline measures of motivation and distress were unrelated to treatment retention to six months, distress at 3 months predicted retention to 6 months (OR = .62; 95%CI = .38, .99).
Conclusions: Results suggest that premature drop-out is best predicted by in-treatment rather than baseline measures of motivation and distress. The implication of our findings is that by assessing patient motivation and distress at regular intervals, it may be possible for staff to intervene at appropriate points to reduce the possibility of premature termination.
Financial Support: NIDA Grant # 11402

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TREATMENT OUTCOMES OF METHAMPHETAMINE-DEPENDENT ADULTS WITH ANXIETY DISORDERS.

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Aims: Although anxiety is one of the most prominent psychiatric complaints of methamphetamine (MA) users, little is known about the association between anxiety disorders and treatment outcomes in this population. In a longitudinal follow-up study of 526 treatment-seeking MA dependent adults, this investigation examined the association of post-treatment anxiety disorder diagnoses with psychiatric, substance use, and functional outcomes.
Methods: Participants received psychosocial treatment for MA dependence as part of the Methamphetamine Treatment Project and were reassessed for psychiatric symptoms, psychosocial functioning and 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: Of the 526 participants, 26.2% (N=138) met criteria for a current or past anxiety disorder at 3-year follow-up. Relative to those without an anxiety disorder, the presence of an anxiety disorder was associated with poorer MA use outcomes over the 3-year follow-up period, increased risk of hospitalization (Odds Ratio [OR]=1.8, 95% Confidence Interval [C.I.], 1.1-3.4), and higher levels of psychiatric-and substance-related functional impairment over time.
Conclusions: MA users with co-occurring anxiety disorders may therefore benefit from early psychosocial and/or pharmacologic interventions to address psychiatric symptoms.
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SEX DIFFERENCES IN THE RELATIONS BETWEEN YOUTH PSYCHOPATHOLOGY AND SUBSTANCE USE.

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Aims: Previous research suggests an association between psychopathology and substance use for adolescents. The current research seeks to examine how this relation varies by gender. We hypothesize that psychosocial problems will vary by gender when predicting youths' substance use.
Methods: Data were from two randomized trial studies evaluating the efficacy of cognitive-behavioral and family systems drug abuse prevention and treatment for middle and high schoolers. The present study included 287 youth aged 11 to 22. The sample was 56% male and was 82% black. Psychosocial problems (e.g., anxiety, attention problems, and rule breaking) were assessed using the Youth Self Report. Lifetime frequency of substance use (i.e., alcohol, cigarettes, marijuana) was measured using self-report. Psychosocial problems were entered into a linear regression, stratified by gender, predicting lifetime frequency of substance use, while controlling for age.
Results: Rule breaking was a gender invariant predictor of substance use (for females: $\beta = 0.54$, $p < 0.001$; for males $\beta = 0.42$, $p < 0.001$). However, other predictors varied by gender. For females, substance use was negatively related to attention problems ($\beta = -0.44$, $p < 0.05$) and social problems ($\beta = -0.39$, $p < 0.05$). Alternately, for males, substance use was positively related to age ($\beta = 0.28$, $p < 0.001$) and negatively related to anxiety ($\beta = -1.57$, $p < 0.01$).
Conclusions: The negative relations between psychosocial problems and substance use suggest a coping mechanism at play. Specifically, females may use substances as a way to gain acceptance from their peers (reduce social problems) and males may use substances as a way to reduce anxiety. That rule breaking was a predictor for both males and females highlights the strong, reinforcing link between externalizing problems and substance use. Taken together, findings suggest that intervention should take a dynamic approach: focusing on the more common externalizing link and social/internalizing issues that may serve to maintain substance use.
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EXECUTIVE FUNCTION CLUSTERS PREDICT PATTERNS OF DRUG DEPENDENCE AND USE.

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Aims: A link has been made between substance dependence and deficits in executive function (EF). However, the majority of research focuses on dependent samples, and examines deficits on individual EF tasks. This study examined clusters of EF deficits and their relationship to dependence and use.
Methods: Eligible participants (n = 101) were HIV negative men reporting ≥ 5 days of drug use in the last 90. Subjects completed five EF tasks (IGT, IGT-variant, WCST, Go-nogo, counting span), a timeline follow-back interview of recent substance use, and the SCID substance abuse module to assess current abuse and dependence. K-means cluster analysis was conducted to examine patterns of EF performance. Logistic regression and $\chi 2$ were used to examine the association between clusters and drug use/dependence.
Results: A 3-cluster solution fit best and identified clusters that differed quantitatively and qualitatively. Cluster A (n = 32, 32%) performed poorly on all five EF tasks (Globally Impaired). Cluster B (n = 31, 31%) performed well on all tasks (Unimpaired). Cluster C (n = 38, 37%) performed poorly only on the IGT and variant (Impaired Decision-Making). Heterogeneity was observed among clusters in both amount of use and dependence. Overall drug use was highest in Cluster A, with over 50% reporting 17 or more instances of drug use in the past 30 days, compared to only 16% in the other two clusters ($p < .01$). Over 65% of participants in Cluster A met criteria for dependence, compared to 29% in Cluster B. Participants in Cluster C were more evenly divided, with 47% dependent. In Cluster C, dependence was associated with low socioeconomic status ($p < .05$).
Conclusions: EF deficits among substance users can be classified into qualitatively and quantitatively distinct clusters, which predict different patterns of use and dependence. These findings underscore the importance of understanding patterns of EF deficits among high-risk substance users.
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LOWER DIFFUSION IN PARIETAL WHITE MATTER OF ADOLESCENT DRUG USERS.

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Aims: Methamphetamine (METH) and marijuana (THC) abuse is prevalent in the United States. In 2005, METH-users comprised 4.3%, and THC-users were 40.1%, of the population aged 12 and older. Diffusion tensor imaging (DTI) uses water diffusion to detect microstructural changes in brain white matter (WM). While DTI studies of WM in adult METH-users report decreased integrity of the frontal lobe, results in adult THC-users are conflicting, including changes in the frontal and parietal WM. These WM regions are responsible for executive function and sensory-motor integration, respectively. The objective of this study is to investigate whether brain development is altered in adolescent METH- and THC-users compared to age-matched controls.
Methods: After securing informed consent, DTI scans were acquired on a 3T MR scanner. There were 11 METH-users (age: 19.3+2.3 years), 15 THC-users (age: 19.4+1.6 years), and 15 non-drug using controls (age: 19.4+2.2 years). Fractional anisotropy (FA), axial and radial diffusivities, and apparent diffusion coefficient (ADC) values for each voxel were calculated using DTIStudio. Regions of interest (ROIs) included the frontal and parietal WM.
Results: Overall, no group differences were observed. However, there are trends towards lower ADC ($F=2.095, p=0.137$), axial ($F=1.428, p=0.252$) and radial diffusivities ($F=1.848, p=0.171$) within the right parietal WM of drug-users.
Conclusions: Lower diffusion in drug-users may reflect more densely packed axons due to smaller axonal diameter or more myelination. This increase in regional density within parietal WM may affect the psychomotor function of drug-users. A larger sample size and more ROIs are needed to further analyze the effects of METH and THC on normal brain maturation.
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PERFORMANCE MEASURES AS PREDICTORS OF CLIENT OUTCOME AMONG A METHAMPHETAMINE-DEPENDENT SAMPLE AT 24- AND 36-MONTH FOLLOW-UP.

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Aims: This study examines the utility of several treatment performance measures - initiation, engagement, retention, monitoring participant drug use during treatment through urinalysis testing, and continuity of care as predictors of methamphetamine (MA) use outcomes at 12- and 36-month follow-ups.
Methods: This study included 1,016 MA-dependent individuals who participated in a randomized, controlled trial of outpatient psychosocial treatment for MA dependence called the Methamphetamine Treatment Project (MTP) between 1999 and 2002. Treatment performance was monitored on all MTP participants via an in-treatment tracking form. Follow-up MA use data collection was completed with approximately 875 at the 12-month follow-up and 587 at the 36-month follow-up.
Results: Correlation analyses indicate a significant association between treatment engagement and retention with documented MA abstinence at the 12-month follow-up. A mixed logistic regression analyses indicated that of the performance measures examined, sustained abstinence from MA during treatment (three consecutive negative urine samples during treatment) was the strongest predictor of testing negative for MA at the 12-month ($OR = 2.82$, $p < 0.001$) and 36-month ($OR = 2.17$, $p < 0.01$)) follow up points.
Conclusions: The development of robust performance measures is an important step to increase the accountability and effectiveness of addiction treatment systems. Study results suggest that sustained abstinence during outpatient treatment may be a useful performance measure. Furthermore, these findings suggest the utility of treatment performance measures in the development of appropriate treatment plans for MA dependence.
Financial Support: Data from this study is based on a larger project entitled "the Methamphetamine Treatment Project – MTP," which was funded by grant 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.

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LEVETIRACETAM TREATMENT FOR COCAINE-DEPENDENT METHADONE-MAINTAINED PATIENTS.

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Aims: The aim of this pilot study was to examine the efficacy of levetiracetam 3 grams/day in modifying cocaine-using behavior among methadone-maintained patients.
Methods: 28 treatment seeking cocaine and opioid dependent subjects who were predominately Caucasian (92%), males (57%) and unemployed (50%) with an average age of 34 years were inducted onto methadone treatment that was adjusted until clinically indicated (range 40-150 mg). Levetiracetam was started on week 2 and was increased until the target dose of 3000mg/day was achieved by week 4. Initial assessments included Severity of Dependence Scale (SDS), SCID, and ASI. Weekly assessments included self-reported drug use, 3 fixed scheduled urine samples per week for drug testing, vital signs, and side effect questionnaire. All subjects received weekly cognitive behavioral therapy. The primary outcome measure was thrice-weekly drug free urine samples. The main data analyses were performed using mixed-effects regression models.
Results: The subjects had been dependent on cocaine for an average of 8 years and 20% smoked crack cocaine. Treatment retention was over 70% and did not differ between groups (Log Rank = 0.14, p =0.7). Treatment with levetiracetam (n=16) reduced cocaine use as indicated by 63% of subjects achieving three or more weeks of abstinence with a mean proportion of BE-free urines of 38%. This was compared to the placebo group (n=12) that achieved 36% of three or more weeks of abstinence with a mean proportion of BE-free urines of 35%. Mixed-effects ordinal regression models showed a trend of levetiracetam by time interaction compared to placebo (Z = 1.68, df= 1, p = 0.09).
Conclusions: Levetiracetam along with methadone treatment for this dual dependent population in this pilot study was well tolerated and there appears to be a trend in reducing cocaine use that warrants further evaluation with a larger RCT.
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WITHDRAWN

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CHILDREN BORN FROM MOTHERS TREATED WITH SUBSTITUTION (BUPRENORPHINE OR METHADONE): LONG-TERM OUTCOMES ?

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Aims: Between 1994 and 2008, 38 children borned from 32 mothers when they were treated with substitution prescribed by the the same practitionner, in Paris, France. Goal: to summarize what happened to them, years after birth (mean age during study : 8,3).
Methods: 3 groups of items were focused. 1st was studied the way they were living with their parents : with both, only mother, in the family or with foster parents. 2nd Health status of children : comparative status in regard to HIV/HepC infection of the parents, late post natal consequences and development. 3rd came their educational status : type of school, time to achieve the earliest cursus, attention and other disorders.
Results: Upon 38 children, we observed 1 sudden infant death syndrom (SIDS). 1 kid borned with a spastic paresia of ankles. 0 were infected with HIV and 1 still had a positive PCR for HCV at the age of 3. Focusing on the family life, a majority of children lived with their parents (30/37). 5 of them lived in family, with frequent visits of their parents. 1 lived with foster parents whitout any contact with the mother after a court statement. All of the 37 children were going to a regular school, including the one with a paresia. Surprisingly, during their first 15 years, 2 children lost their mother. 1 deceased with a terminal liver failure and the other had a sudden death postmortem diagnosis.
Conclusions: Substitution treatments help opiate dependent mothers and parents to efficiently bring up children. It seems beneficial to every single protagonist of health. A special vulnerability of those mothers and parents could, if confirmed by further studies, need more protection. The future of these children appears linked to the way their parents are treated.
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11 rue Baylet, 75011 PARIS FRANCE
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FACTORS ASSOCIATED WITH BACKLOADING AMONG INJECTION DRUG USERS IN BALTIMORE, MARYLAND: THE ROLE OF EXECUTIVE FUNCTIONING.

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Aims: This study tested the hypothesis that impaired impulse control is associated with higher risk to backload even while controlling for intellectual functioning among current injection drug users (IDU) living in Baltimore, MD.
Methods: Associations of demographics, frequency of injection, duration of drug use, injecting speedball, intellectual functioning and impulse control with backloading were analyzed using logistic regression on cross-sectional data from 397 IDU from Baltimore, Maryland.
Results: Injectors scoring in the top quartile of standardized commission errors of the Test of Variation in Attention (TOVA) had almost twice the odds of backloading (AOR=1.95; 95% CI: 1.04 – 3.65) compared to those who scored in the lower three quartiles of TOVA commission errors. African American participants had half the odds of backloading (AOR=0.50; 95% CI: 0.27 – 0.93) compared to participants of other race/ethnicity; and those who reported injecting speedball (mixture of heroin and cocaine) had more than 5 times the odds (AOR=5.26; CI: 2.37 – 11.7) of backloading compared to those who did not report injecting speedball.
Conclusions: Study findings suggest poor impulse control as measured by the TOVA is associated with backloading, even after adjusting for intellectual functioning, duration of drug use, frequency of use and type of drug injected. Since backloading is a known and persistent high-risk behavior for bloodborne infectious diseases including hepatitis C and HIV, such findings may impact a renewed shift in prevention interventions to focus on cognitive remediation, delayed gratification, and problem-solving among IDUs.
Financial Support: This research was supported by RO1 DA010777 to William W. Latimer, PhD, MPH and the Drug Dependence Epidemiology Training Program T32 DA007292 (PI: William W. Latimer, PhD, MPH).

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REVERSIBLE AND PERSISTENT DECREASES IN COCAINE SELF-ADMINISTRATION AFTER TREATMENT WITH THE CHOLINESTERASE INHIBITORS RIVASTIGMINE AND DONEPEZIL.

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Aims: We recently observed that pretreatment with the cholinesterase inhibitor tacrine can produce long-lasting reductions in cocaine-reinforced behavior, described as persistent attenuation. This effect occurred at an increased rate in rats genetically modified to self-administer cocaine at high levels (the HS line). In addition to inhibiting both acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE), tacrine can potentiate actions of dopamine (DA). The present study was conducted to evaluate effects donepezil (which selectively inhibits AChE) and rivastigmine (which inhibits both AChE and BuChE) on cocaine self-administration.
Methods: HS rats self-administered different doses of cocaine under a fixed-ratio-5 (FR-5) schedule. Over a four-day period, vehicle, donepezil, or rivastigmine was infused as animals were maintained in home cages (21 hours per day).
Results: Both compounds dose-dependently decreased cocaine self-administration, but differed in the potency and temporal pattern of their effects. Self-administration of low-dose cocaine was decreased to a greater degree by rivastigmine than donepezil (50% effective doses of 2.33 and 6.21 mg/kg-day, respectively), but this early effect did not continue beyond sessions immediately following treatment with rivastigmine. Group means for cocaine self-administration were decreased at some time points occurring between 1 and 3 days after treatment with 10 mg/kg-day of donepezil (late effects), with decreases of more than 80% observed in some individual rats that persisted for one week or longer. Early, but not late, effects were correlated with signs of cholinergic stimulation.
Conclusions: In summary, reversible and persistent effects on cocaine self-administration differ between cholinesterase inhibitors, with persistent effects being less directly related to cholinergic actions.
Financial Support: This work was supported by a grant to KG from the Medical Research Service, Department of Veterans Affairs.

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THE 5-HT2C RECEPTOR INVERSE AGONIST SB 206553 DECREASES METHAMPHETAMINE-SEEKING IN RATS.

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Aims: Methamphetamine (Meth) dependence is a significant societal problem, with no FDA-approved pharmacotherapy. The antidepressant mirtazapine attenuates Meth-seeking in rats (Graves & Napier, Soc for Neurosci Abstract #62.20 2008). Mirtazapine historically considered as a 5-HT2C receptor (R) antagonist, also exhibits inverse agonist properties (Chanrion et al Mol Pharmacol 73:748 2008). Reducing constitutive activity of 5-HT2CR may offer a unique target to alter Meth-seeking. AIM: To assess the effects of a 5-HT2CR inverse agonist vs. an antagonist on Meth-seeking and motor activity.
Methods: Rats self-administering Meth were tested for Meth-seeking via cue reactivity (CR) assessments wherein rats lever pressed for cues contingently presented in the absence of Meth. CR was repeatedly tested with 2 days of self-administration between each CR test. Dose-response assessments were made with the 5-HT2CR inverse agonist SB 206553 (SB) at 1, 5, or 10mg/kg and the antagonist SDZ Ser 082 (SDZ) at 0.1, 0.3, or 1mg/kg; doses were tested in a random order. Rats then underwent abstinence for 5 days and tested for spontaneous and Meth-evoked motor activity in the presence of 10mg/kg SB, 1mg/kg SDZ or corresponding vehicles.
Results: SB at 5 and 10mg/kg decreased Meth-seeking; SDZ had no effect. SB at 10mg/kg had no effect on spontaneous motor activity, but it decreased Meth-evoked vertical activity. SDZ (1mg/kg) had no effect on spontaneous or Meth-evoked motor.
Conclusions: Our results indicate the potential for 5-HT2CR inverse agonists in the pharmacotherapy of Meth abuse. Further studies are needed to fully elucidate the possible role of 5-HT2CR constitutive activity in Meth-induced maladaptive behaviors such as drug-seeking and relapse
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BODY COMPOSITION AND METABOLIC CHANGES IN WOMEN SMOKERS DURING A CESSATION ATTEMPT.

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Aims: The potential for weight gain poses a significant barrier to smoking cessation, particularly among women. However, little is known about specific changes in body composition and metabolic indices during a cessation attempt.
Methods: As part of an ongoing parent study exploring menstrual cycle effects on smoking cessation, 23 women underwent an evaluation of body composition (BOD POD air displacement plethysmography) before and after a one month randomized trial of varenicline versus nicotine patch.
Results: Participants reduced smoking from 15.4 ± 1.2 (mean ± SE) to 1.4 ± 0.6 cigarettes per day (90% change). Over the course of the one-month cessation attempt, participants gained 1.1 ± 0.6 kg total mass (1.6% change), including 0.7 ± 0.6 kg fat mass (4.2% change) and 0.4 ± 0.5 kg fat free mass (1.1% change). However, resting metabolic rate increased by 14.0 ± 10.3 kcal/day (1.2% change). Within this small sample, body composition and metabolic indices did not correlate significantly with change in cigarettes per day.
Conclusions: This preliminary investigation demonstrates the feasibility of incorporating detailed body composition measurement to elucidate important variables involving weight change during a smoking cessation attempt. This method may be employed with a larger sample to explore potential correlations with treatment assignment, cessation status, and other variables.
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NON-FATAL OVERDOSE AMONG PEOPLE WHO ABUSE PRESCRIPTION OPIOIDS.

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Aims: Non-fatal overdose is a common morbid event experienced by heroin users and risk factors for its occurrence are well established. Prescription opioid abuse is an emerging public health concern in the United States with implications for overdose prevention efforts. We conducted an analysis to better understand the prevalence and risk factors for non-fatal overdose in this population.
Methods: We analyzed responses from 6,920 patients in treatment for substance abuse or dependence who self-reported past month abuse of a prescription opioid, collected by the Addiction Severity Index-Multimedia Version® (ASI-MV®) Connect, a national database for real-time prescription opioid abuse surveillance. Data were obtained from November 2005 through December 2008. Bivariate followed by binary logistic regression analyses were conducted to uncover risk factors for lifetime occurrence of non-fatal overdose.
Results: Among the 38.3% of prescription opioid abusers reporting a history of overdose, the median number of overdoses was 2 (interquartile range 1-4). Controlling for important demographic confounding variables, risk factors independently associated with history of nonfatal overdose included history of incarceration; history of emotional, physical, and sexual abuse; lifetime suicide attempts; prescribed psychiatric medications in past month; primary problem drug: heroin; being unemployed; not living with one's children; past month injection of heroin, cocaine, and any prescription opioid; snorting any prescription opioid; past month use of benzodiazepines, drinking to intoxication, and polydrug use; having a chronic, persistent pain problem; and recent visits to the emergency room.
Conclusions: Lifetime prevalence of non-fatal overdose is similar to rates found among heroin users but several factors differentiate risk of non-fatal overdose among prescription opioid abusers. The extent to which prescription opioid abusers are being reached by overdose prevention and response efforts such as naloxone distribution should be assessed.
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A QUALITATIVE ANALYSIS OF WOMEN'S EXPERIENCES IN EMPIRICALLY SUPPORTED SINGLE-GENDER VS. MIXED-GENDER SUBSTANCE ABUSE GROUP THERAPY.

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Aims: Little is known about women's attitudes and experiences with empirically supported single-gender vs mixed-gender substance abuse group therapy. The aim of this qualitative study is to compare women's self-reported experiences and satisfaction in these two treatments.

Methods: Semi-structured exit interviews were conducted with women (N=28)who participated in a Stage I trial comparing single-gender Women's Recovery Group(WRG)(N=22)versus the mixed-gender control condition,Group Drug Counseling(GDC)(N=6). Interviews focused on women's experiences and satisfaction with the 12 week group therapies and were taped and transcribed for analysis. As part of grounded theory analysis, the research team created open, selective/axial, and theoretical codes.Codes were compared with each other to develop an inductive and data-based conceptual model that describes participants'experiences in single vs. mixed–gender group therapy.

Results: Participants identified their sense of self,relationship with the therapist,and interaction with other group members as key elements of their group therapy experience. Responses regarding these elements clustered into 4 categories: self-presentation in the group, perceptions of the atmosphere in the group, discussion topics, and characteristics of communication. Women in the WRG group more frequently endorsed feeling safe, being able to be all aspects of oneself, having their needs met, feeling support and intimacy, and experiencing empathy, honesty, and comfort. In contrast, women in the GDC group reported the need for women to motivate men to speak in group, irrelevant talk in group, feelings of judgment and constraint, and differences between women's and men's recovery.

Conclusions: Women in single-gender treatment report enhanced comfort, intimacy, social bonding, and having their needs met. Further study is necessary to examine whether these types of group process differences mediate substance abuse treatment outcomes.

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YOHIMBINE INCREASES OPIOID-SEEKING BEHAVIOR IN BUPRENORPHINE-STABILIZED, HEROIN-DEPENDENT VOLUNTEERS.

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Aims: Human laboratory models have examined effects of acute stressors on drug craving but not drug seeking. Yohimbine (YOH; alpha2-noradrenergic [NE] autoreceptor antagonist) precipitates reinstatement of extinguished drug seeking in laboratory animals. The aim of this human study is to test whether YOH increases opioid seeking and 'stress'-like psychophysiological effects.

Methods: A within-subject, double-blind, randomized crossover design is used to test whether YOH (0, 16.2 and 32.4 mg, PO) pretreatment will dose-dependently increase hydromorphone (HYD, IM) vs. money seeking on a choice progressive ratio schedule, and induce 'stress'-like effects. Heroin dependent subjects, stabilized on buprenorphine 8 mg/day to attenuate opioid withdrawal distress, sample HYD 12- and 24-mg bolus doses (sess. 1-2), and can work for units of HYD (1 or 2 mg) or money ($2) on a 3-hr task (1000–1300) after YOH pretreatments (0930 in sess. 3-8).

Results: Preliminary analyses (n=7 completed of n=12) indicate that HYD 2- vs. 1-mg units generate higher breakpoints, $F(1,12)=6.72$, $p<.05$. Relative to placebo, YOH is increasing HYD breakpoints (Ms=2143, 3487 and 3521), $F(2,12)=2.52$, $p=.15$. Behavioral economic analysis shows that, relative to placebo, YOH 16.2 and 32.4 mg both significantly increase HYD demand inelasticity (Pmax=2578, 5088 and 4295), $F(2,59)=8.30$, $p<.001$. YOH significantly increases blood pressure (SBP ≈15 and DBP ≈10 mmHg), YOH x Time Fs(14,84)=6.23 and 3.41, ps<.01, but not heart rate. YOH modestly increases ratings of opioid withdrawal symptoms, YOH $F(1,12)=5.52$, $p<.03$, and anxiety (POMS), YOH [linear] x Time [quadratic] $F(1,6)=6.07$, $p<.05$, but not heroin craving. Saliva cortisol data are forthcoming.

Conclusions: These preliminary data show that YOH, a pharmacological agent with a longer duration of action than cognitive stressors, which can be repeatedly administered under double-blind conditions, increases opioid seeking and alpha2-NE-mediated physiological response (blood pressure) in the absence of craving or clinically significant distress.

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CHARACTERISTICS OF PARTICIPANTS WITH CO-OCCURRING DISORDERS IN CALIFORNIA'S PROP 36 AND THEIR CRIMINAL JUSTICE AND TREATMENT OUTCOMES.

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Aims: This study compares participants with and without co-occurring substance use and mental health disorders (COD) who were referred to substance abuse treatment through "Prop 36" in California, which allows non-violent drug offenders to go to treatment instead of prison.

Methods: Administrative data on mental health diagnoses of Prop 36 participants were linked with data on their treatment participation and arrests within 12 months of their eligibility for participation. Participants with COD (N=2,526, 15.9%) and without (N=13,385; 84.1%) in 2001-02 were compared on their background characteristics, treatment participation, and criminal justice outcomes.

Results: : Primary diagnoses of participants with COD were 42% mood disorder, 31% psychotic disorder, 6% anxiety disorder, 13% drug use disorder, and 9% other type of disorder. Less than one-fifth of these participants were identified with COD in the substance abuse treatment system. Among participants with COD there were higher proportions of Whites (54% vs. 49%), women (36% vs. 23%), heroin users (16% vs. 12%), homeless individuals (19% vs. 12%), and individuals not in the labor force (50% vs. 37%), and fewer Hispanics (24% vs. 30%). There were no differences in treatment completion rates, although participants with COD were less likely to stay in treatment for 90 days or more (40% vs. 46%). A higher proportion of participants with COD than those without were arrested within 12 months of eligibility for treatment (64% vs. 60%) and they averaged more arrests (1.43 vs. 1.21). [all differences: $p < .01$]

Conclusions: Individuals with COD who are referred to substance abuse treatment through the criminal justice system are unlikely to be assessed with mental health disorders. Improved diagnostic assessment and service delivery to this population may improve their treatment retention and criminal justice outcomes.

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PSILOCYBIN DOSE-EFFECTS IN HEALTHY VOLUNTEERS: MYSTICAL-TYPE EXPERIENCE, FEAR, AND HEADACHE.

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Aims: In a prior study in healthy volunteers, a high dose of psilocybin (30 mg/70 kg) occasioned mystical-type experiences and anxiety when administered under supportive conditions. This study characterized the effects of a range of psilocybin doses.

Methods: This double-blind study evaluated psilocybin (0, 5, 10, 20, 30 mg/70 kg, p.o.) administered under supportive conditions. Participants were 18 adults (17 hallucinogen-naïve). Five 8-hr sessions were conducted individually at about 4-week intervals. The sequence of psilocybin doses was ascending in half of the participants and descending in the others, with placebo scheduled quasi-randomly. During sessions volunteers used eyeshades and directed their attention inward.

Results: On volunteer-completed post-session questionnaires assessing psychological and somatic effects (Hallucinogen Rating Scale) and mystical experience (M scale, States of Consciousness Questionnaire), and on monitor ratings of overall drug effect, psilocybin effects were generally a monotonically increasing function of dose, with no effect of dose sequence. 39% of volunteers (7 of 18) rated extreme fear or feeling trapped sometime during the session; such episodes occurred in 6 of 7 of these volunteers after the 30 mg/70 kg dose and in 1 of 7 after 20 mg/70 kg. After 30 mg/70 kg, monitor ratings of anxiety/fear across the session showed an unpredictable time-course. The incidence and intensity of post-session headache was an increasing function of dose, with 89% of participants reporting post-session headache after the highest dose.

Conclusions: Psilocybin produced dose-related increases in hallucinogen psychological and somatic effects, mystical experience, anxiety, and post-session headache. The headache effect might be related to clinical reports that psilocybin exposure prevents cluster headaches. Despite careful screening, preparation, and interpersonal support, a significant proportion of participants experienced anxiety/fear sometime during the session.

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MARIJUANA: AGE OF ONSET AND FRONTAL INHIBITORY TASKS USING FMRI.

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Aims: Chronic, heavy MJ smokers have demonstrated alterations on cognitive tasks and patterns of cortical activity (fMRI), yet few studies have examined the neurobiologic impact of age of onset of MJ use. We recently found that during the Multi Source Interference Test (MSIT), which incorporates elements of cognitive interference and inhibitory control, healthy controls demonstrated focal midcingulate activation while chronic, heavy MJ smokers had a larger, more diffuse area of activation in a more anterior cingulate region.
Methods: To test the hypothesis that age of onset of MJ use is related to BOLD activity, we split this group of 12 chronic, heavy MJ smoking subjects into those who began smoking prior to age 16 (early onset, N=5) and those who started at age 16 or later (late onset; N=7). A random effects model was used to examine their fMRI data in SPM.
Results: Early onset MJ smokers demonstrated significantly greater midcingulate activation during the MSIT relative to those who began using MJ after the age of 16. In contrast, late onset MJ smokers demonstrated robust activation in a more anterior region of the anterior cingulate. These findings are particularly striking, as despite similar task accuracy, late onset MJ smokers took significantly longer to complete the interference condition (x=881.6 msec) relative to the early onset MJ smokers (x=798.4 msec; p=.03).
Conclusions: Data from this pilot study underscores the importance of examining age of MJ onset, as the neural circuitry that facilitates the completion of complex inhibitory tasks may be differentially impacted by early MJ use. Early onset MJ smokers appear to demonstrate a similar pattern to controls on the MSIT, while late onset MJ smokers exhibit a pattern more similar to chronic MJ smokers as a group. This data may represent a neuroadaptation of neural circuitry in the early onset MJ smokers as a result of early exposure to marijuana during a vulnerable neurodevelopmental period. Further investigation is warranted, as early exposure to MJ may result in reorganization of critical brain regions.
Financial Support: NIDA R21 and R03 to Dr. Gruber

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COGNITIVE IMPAIRMENT DURING ALCOHOL INTOXICATION IN HIV POSITIVE DRINKERS.

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Aims: Heavy drinking is twice as common among HIV positive people as in the general population and contributes to cognitive impairment. This subanalysis of a larger study on the interaction of alcohol and antiretroviral medications (ARV) examines the acute effect of alcohol on cognitive functioning among HIV positive drinkers.
Methods: HIV positive drinkers eligible for, but not yet on ARV, were randomly administered either 1g/kg alcohol (oral), calculated to obtain a peak blood alcohol concentration (BAC) of 100-130 mg/dL or alcohol placebo, then were monitored over 8 hours. Cognitive measures included a multiple-form, 2-minute, WAIS-III Digit Symbol Substitution Test (DSST), and a Time Estimation Task (TET), which involved reproducing stimulus durations.
Results: Subjects (n=6) were 2 Caucasian, 3 African-American, and 1 Latino men; 2 had less than high school education. Mean age was 45 (range: 33-58), mean CD4 270 (range: 195-361 mm3); none had advanced liver disease; 5 had alcohol dependence or abuse (none with current physical dependence), 1 methamphetamine dependence. BAC was 0 mg/dL at baseline, 137 mg/dL (26) (mean (SD)) at 1.5 hours (peak) and 94 (31) at 4 hours. DSST number correct was 57 (11) at baseline, 47 (19) at 1.5 hours, and 52 (15) at 4 hours. For placebo these were 54 (8), 52 (10), and 54 (9). Post-alcohol values indicated very low level of function relative to WAIS-III norms (for mean age 45y), lower than values at baseline and for alcohol placebo, although this did not reach statistical significance in this small sample. Inaccurate reproduction of the TET 20-second stimulus averaged 6 (7) seconds at baseline, 9 (9) at 1.5 hours, and 7 (7) at 4 hours. Post-alcohol values were significantly larger than corresponding placebo values ($p < .05$), which were 3 (5), 0.9 (1), and 0.8 (1).
Conclusions: The DSST and TET reveal impaired concentration and memory with moderate BAC, underscoring the potential for high risk behavior for HIV transmission even with moderate alcohol use in this population. Additional data from this ongoing study will be presented.
Financial Support: NIAAA R01AA018001 (EMK)

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METHADONE MAINTENANCE TREATMENT FOR PROBATIONERS: PREDICTORS AND OUTCOMES.

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Aims: Methadone maintenance is effective in reducing heroin use and crime but remains underutilized within the US criminal justice system. Increased provision of methadone treatment for individuals on parole or probation could have high public health impact.
Methods: The current study examined predictors of treatment outcomes among 181 heroin-addicted probationers newly enrolled in methadone maintenance in four treatment programs in Baltimore. Participants were assessed with the Addiction Severity Index, the TCU motivation scales, and a supplemental questionnaire at baseline and at 3-, 6-, and 12-month follow-ups. A urine sample was collected at each follow-up point.
Results: The 12-month treatment retention rate was 49%. Greater compliance with the requirements of probation was associated with both longer treatment tenure and fewer days of income-generating crime at 12-month follow-up. Women, those with higher levels of pretreatment cocaine use, and individuals with lower motivation (desire for help) at baseline were more likely to report higher levels of cocaine use at 12-month follow-up.
Conclusions: Probationers and parolees are a unique subpopulation that may benefit from increased availability of methadone treatment.
Financial Support: Center for Substance Abuse Treatment KD1 T1 12315

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SEX-RELATED HIV RISK BEHAVIORS AMONG INJECTION DRUG USERS.

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Aims: HIV incidence studies indicate that injection drug users (IDUs) are at elevated risk for HIV infection through sexual risk (Kral et al. 2001; Strathdee et al., 2001). In this analysis, we assessed factors associated with condom use with steady and casual sex partners among IDUs in four California communities.
Methods: We used two sub-samples of respondents from the OP-SEP who reported having a steady sex partner (n=392) and a casual sex partner (n=241). We used bivariate analysis and multivariate logistic regression to determine variables independently associated with consistent condom use with steady and casual sex partners. We considered such variables as demographics, income, drug use, injection frequency, injection risk, and SEP use among others.
Results: Only 14.4% reported consistent condom use with a steady sex partner and 44.4% reported consistent condom use with a casual sex partner. Being Black predicted consistent condom use for steady partner (Adjusted odds ratio [AOR] = 3.12; 95% confidence interval [CI] = 1.72, 5.67) and casual partner (AOR=3.74, 95% CI=2.05, 6.80) as did SEP use for steady partner (AOR= 1.98; 95% CI = 1.04, 3.77 and for casual partner (AOR=3.86, 95% CI=2.09, 7.09). Participants who reported sharing a cooker in the last 30 days (AOR=0.52, p<.037) and injected by another person (AOR=0.40, p<.026) were significantly less likely to report consistent condom use with a steady sex partner. Participants that reported backloading to split or mix drugs (AOR=0.40, p<.003) were significantly less likely to report consistent condom use with casual sex partners.
Conclusions: SEP use is associated with consistent condom use as are injection behaviors such as backloading and sharing cookers. Efforts to reduce sex-related risk among IDUs are still urgently needed.
Financial Support: NIDA grant #R01-DA1420

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THE EFFECTS OF METYRAPONE AND OXAZEPAM ON COCAINE SELF-ADMINISTRATION FOLLOWING ADRENALECTOMY IN RATS.

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Aims: Previous research has shown that the hypothalamic-pituitary-adrenal (HPA) axis is involved in psychostimulant reinforcement. Specifically, we have found that bilateral adrenalectomy (ADX) completely abolishes the acquisition of IV cocaine self-administration (SA) without affecting food-maintained responding. This suppression of SA was partially reversed by adding corticosterone to the rats' drinking water. In another experiment, pretreatment with metyrapone (MET), which blocks the synthesis of corticosterone, resulted in dose-related decreases in ongoing cocaine SA. Additionally, we have shown that ADX reduces cocaine SA by approximately 25%, but does not abolish it. Oxazepam (OX), a benzodiazepine, also dose-dependently decreases ongoing cocaine SA either when delivered alone or in combination with MET, and then at doses that produced no effects by themselves. The current experiment was designed to determine if MET and OX would still decrease cocaine SA following adrenalectomy.
Methods: Adult male Wistar rats were trained to respond under a 2-hour multiple, alternating schedule of cocaine SA and food reinforcement (fixed-ratio 4) during alternating 15-min periods. After responding stabilized, the rats were tested with MET (50 mg/kg, ip), OX (5 and 10 mg/kg, ip) and combinations of the two drugs (MET 50/OX 5 and MET 50/OX 10). Animals were then adrenalectomized and allowed to recover for one week before continuing SA. The rats were then retested using the same drug doses and combinations. Plasma corticosterone was measured to verify the adrenalectomy.
Results: We report that bilateral adrenalectomy does not block the effects of MET, OX or their combinations on cocaine SA. The decreases, depending on the treatment, ranged from 5-95% both before and after ADX.
Conclusions: These data suggest that these drugs are affecting the HPA axis on a level other than the adrenal glands (which produce corticosterone), possibly through CRF-related mechanisms or ACTH, or they could produce their effects through the GABAA receptor complex.
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DOES THE WAY OF DRINKING (BINGE DRINKING) AFFECT THE EVOLUTION OF HEPATITIS C AMONG ALCOHOL ABUSERS?

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Aims: Aim: The quantity of alcohol drunk per day obviously agrees with the evolution of hepatitis C. But little is known on this correlates with different ways of drinking.
Methods: Study: In 693 patients met in the addiction medicine unit of a general hospital in Saint Dizier, Champagne-Ardennes, France, from 2003 until 2005, 34 tested positive for HCV and among them, 2 were infected by sharing drug consumption material. Focusing on the way of drinking, we find a group B of "binge drinkers" (n=14) and a group R of "regular daily drinkers" (n=11)
Results: Results: Both groups seem similar in terms of sex ratio, age, duration of HCV disease and mean level of alcohol consumption. In the group B the mean Metavir score was 2.7 in comparison to 1.5 in the group R, which seems highly significant.
($p< 0.01$)
Conclusions: Conclusion: The way of drinking seems to play a major role in the evolution of hepatitis C. More work is needed to determine how therapy can deal with it
Financial Support: none

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UNOBSERVED VERSUS OFFICE BUPRENORPHINE/NALOXONE INDUCTION: A PILOT RANDOMIZED CLINICAL TRIAL.

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Aims: Physician adoption of buprenorphine treatment of opioid dependence is limited by time and logistical concerns about observed induction recommended by national guidelines. Unobserved induction may mitigate this barrier. We sought to assess preliminary safety and effectiveness of unobserved vs. office buprenorphine/naloxone (BUP/NX) induction.
Methods: Twenty DSM-IV opioid dependent patients entering a 12-week primary care BUP/NX maintenance study were randomized to unobserved or office induction, stratifying by past BUP use. All patients received verbal and written instructions with physician phone support as needed. A withdrawal scale was used to initiate and monitor treatment. Clinic visits occurred weekly for 4 weeks then monthly. The primary outcome, successful induction 1 week after the initial clinic visit, was defined as retained in treatment and withdrawal free on BUP/NX. Secondary outcomes included prolonged withdrawal beyond 2 days after BUP/NX initiation, and week 4 stabilization, defined as being in treatment and illicit opioid free for the 2 prior weeks.
Results: Patient characteristics and outcomes were similar between groups: 6/10 (60%) successfully inducted in each group, 3/10 (30%) experienced prolonged withdrawal, and 4/10 (40%) stabilized by week 4. One unobserved patient experienced precipitated withdrawal but stabilized by week 1. There was a trend toward higher Day 1 mean (SD) buprenorphine dose in the home induction group (14 (5) mg vs. 10 (5) mg, p=.08). The number of physician phone contacts and call length during week 1 did not differ between groups, with an overall mean (SD) of 5 (4) calls lasting 4 (1) minutes.
Conclusions: The pilot study enabled operational assessment of unobserved and office induction and suggests comparable safety and effectiveness, which points toward utilization of non-inferiority design during future definitive protocol development.
Financial Support: Supported by K23 DA02000 (EWG), K02 DA00465 (FRL), and R01 DA025991, DA020576-01A1, DA019511-03 (DAF).

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ORGANIZATIONAL CHANGE TO ADDRESS TOBACCO DEPENDENCE: PRE, POST AND FOLLOW-UP RESULTS.

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Aims: This study tested a manualized organizational change intervention designed to integrate drug abuse and tobacco dependence treatments.
Methods: The intervention was implemented in three residential treatment sites. Surveys were administered to staff and clients at pre and post-intervention and at six month follow-up.
Results: At pretest, staff (n=114) were 75% female, 68% white, 23% African American. 42% were current smokers. At pretest, clients (n=150) were 58% female, 76% Caucasian, 15% African-American, and 85% current smokers.
Mean scale scores were calculated for for knowledge, beliefes, barriers, efficacy in regards to cessation services, and practices to address smoking. Scores were compared using 2-way ANOVA with factors for clinic, time, and their interaction. There was significant change pre to post-intervention in staff beliefs, counselor self-efficacy and smoking-related practices, and changeswere maintained at follow-up for counselor beliefs and practices ($p<.05$). Client mean scores shalso owed significant improvement for beliefs about smoking cessation and services received while in treatment, and these chanes were maintained at follow-up.
Conclusions: Results suggest that the organizatinal change intervention was associated with changes in smoking-related beliefs and practices, for both staff and clients, from pre to post intervention. These changes were maintained 6 months after the intervention ended. Observed changes varied by clinic and suggest differential implementation of the intervention among sites. While organizational change occured and was maintained through the intervention we suggest additional pro-active policy support (local, state, nation) for tobacco dependence may be needed to maintain change in the programs.
Financial Support: NIDA R01DA020705, P50DA09253, U10 DA15815

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THEORIES OF ADDICTION: COCAINE USERS' EXPLANATION FOR CONTINUING DRUG USE AND RELAPSE.

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Aims: In the current study we administered the same survey to non-treatment seeking cocaine-dependent volunteers (N=40) to better understand why they used cocaine and relapsed after a period of abstinence.
Methods: All volunteers met DSM-IV criteria for cocaine abuse or dependence but not other Axis I psychiatric disorders or dependence on other drugs of abuse except for nicotine. The survey consisted of questions regarding drug use answered using a scale from 1-7 (1 'not at all', 7 'very much'). Answer extremes (1-2 and 6-7) were grouped and compared.
Results: Results show that 63% (vs. 8%) affirmed that they used cocaine due to its PR properties ("pleasure seeking") (P<0.001). Fifty-five percent (vs.13%) also endorsed they relapsed because they wanted to "get high". Percentage of answers volunteers felt 'very much' vs. 'not at all' applied to them for each question per category included: NR ("pain avoidance") 35% vs. 23%, IS ("craving") 33% vs.18%, SRL ("habits") 33% vs. 33%, and ICD ("impulsivity") 28% vs. 23% were not significantly different. Except for PR, answers from each category were significantly correlated with BDI depression scores (range r=.36-.47). PR was positively correlated with number of years of cocaine use (r=.42).
Conclusions: Results are in general agreement with that obtained from METH-dependent users and support the notion that PR is the prime motivator for psychostimulant use. Data suggest therapy focused on reducing the PR effects of cocaine may be efficacious for cocaine dependence. This notion is consistent with recent data showing sustained-release amphetamine and methamphetamine formulations significantly block cocaine's positive reinforcing effects and significantly decrease cocaine use.
Financial Support: DA017754

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POLYSUBSTANCE USERS IN THE CRIMINAL JUSTICE SYSTEM – A COMPARISON WITH HEROIN AND AMPHETAMINE USERS.

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Aims: This study in criminal justice clients aims to describe polysubstance users, compared to primary heroin and amphetamine users, and to compare polysubstance users with and without opioid use.
Methods: In a database containing Addiction Severity Index assessments of 7,085 clients, we compared clients with a dominating problem of polysubstance use (n=1183), heroin (n=391) or amphetamine (n=1396). Polysubstance users with (n=408) and without (n=775) recent opioid use were compared in logistic regression.
Results: Compared to heroin users, polysubstance users were less likely to be non-Nordic immigrants (12 vs 31%) or to live in major cities (43 vs 61%). They had lower frequency of heroin, methadone and injections, equal frequency of other opioids, and higher frequency of binge drinking, tranquillisers, amphetamine, cannabis, hallucinogenic drugs, history of psychiatric medication, depression, suicide attempt, cognitive symptoms, difficulty controlling violent behaviour, and parental substance use. Compared to amphetamine users, polysubstance users were younger (31.9 vs 37.4 yrs), more often male, and reported more psychiatric symptoms, overdoses, and higher frequency of binge drinking, all opioids, tranquillisers, cocaine, cannabis, and hallucinogenic drugs, but less injections. In logistic regression, polysubstance use including opioids, compared to polysubstance use without opioids, was associated with younger age (31.1 vs 32.4 yrs), less binge drinking (4.9 vs 7.3/30 days), more tranquillisers (14.2 vs 7.1/30 days) and injections (16.3 vs 9.2/30 days), overdose (65 vs 32%) and current somatic medication (56 vs 51%).
Conclusions: Clients with dominating polysubstance use had a more severe picture and demographic differences, compared to primary heroin and amphetamine users. Polysubstance users with opioid use appear to be more problematic and more closely connected to tranquillisers, rather than to alcohol. Other opioids than heroin/methadone were common both among polysubstance and heroin users.
Financial Support: University hospital, Malmö, Sweden.
Swedish Research Council.

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A RANDOMIZED CONTROL TRIAL USING BURPRENORPHINE FOR OPIATE ADDICTION: A DESCRIPTIVE ANALYSIS OF FEMALE OFFENDERS.

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Aims: Buprenorphine has demonstrated efficacy in treating opiate dependence by reducing cravings and retaining patients in treatment. This ongoing study is the first to compare buprenorphine to placebo in combination with medication management in a sample of female offenders. The study began with a single-arm trial in which all women received buprenorphine and is currently in the double-blind randomized control trial phase. The specific aim of this preliminary project was to provide a description of the sample of women who completed baseline assessments to enroll in this study.
Methods: Thirty-five women in the criminal justice system receiving inpatient detoxification and drug rehabilitation completed baseline assessments. Baseline information included demographics, criminal history, substance use history, medical history, and psychiatric history.
Results: Participants were young (31.9 ± 9.0 years), primarily Caucasian (89%), divorced or separated (51.4%) women with at least a high school diploma/GED (74.4%). Most women were unemployed (85.7%) with several receiving government assistance (26%) and/or obtaining money illegally (34.5%). In addition to opiates, participants met dependence criteria for cocaine (44.4%), benzodiazepines (36.4%), alcohol (25.7%), and cannabis (9.1%). Many also met criteria for other psychiatric disorders, primarily MDD (50%), panic disorder (40%), and GAD (37.1%). Primary opiates of choice were Dilaudid (25%), Oxycontin (22.3%), and Heroin (16.7%). Participants also endorsed HIV risk behaviors such as needle use (70.6%), sharing needles (38.2%), exchanging sex for drugs (35.2%), and inconsistent use of condoms (88.3%).
Conclusions: Female offenders presenting for enrollment in this buprenorphine trial were largely young, White, educated women addicted to various opiates and were engaging in multiple HIV risk behaviors. Future analyses are needed to assess treatment outcomes among this special population using medication-assisted therapies.
Financial Support: Support was provided by R21DA0119838 and Reckitt-Benkheiser.

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SUBTYPES OF ADOLESCENT SEDATIVE/ANXIOLYTIC MISUSERS: A LATENT PROFILE ANALYSIS.

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Aims: Few empirically-based taxonomies of nonmedical prescription drug misusers have been published. This study used latent profile analysis (LPA) to identify classes of adolescent sedative/anxiolytic misusers.
Methods: Sedative/anxiolytic misusers (N = 247) averaged 15.8 (S.D. = 1.1) years of age; a majority were male (83.8%), White (70.0%), and resided in rural/small town areas (53.8%).
Results: LPA yielded a three-class solution. Class 1 (59.1%) was comprised of youth with significantly lower levels of currently distressing psychiatric symptoms, fewer lifetime traumatic experiences, less problematic substance use histories, less frequent antisocial behavior, and less impulsivity than youth in Classes 2 and 3. Class 2 (11.3%) youth had high levels of currently distressing psychiatric symptoms and more frequent antisocial behavior compared to youth in Classes 1 and 3. Class 3 (29.5%) youth evidenced levels of psychiatric and behavioral problems that were intermediate to those of Class 1 and 2 youth. Compared to youth in Class 1, Class 2 and 3 youth misused sedatives/anxiolytics more frequently and had higher levels of the psychiatric symptoms for which these drugs are prescribed. Significant differences between classes were observed across a range of health and behavioral variables.
Conclusions: Adolescents who misused prescription sedatives/anxiolytics evidenced significant heterogeneity across measures of psychiatric and behavioral dysfunction. Youth with comparatively high levels of anxiety and depression reported significantly more intensive sedative/anxiolytic misuse than their counterparts and may be at high risk for sedative/anxiolytic abuse and dependence.
Financial Support: This study was supported by NIDA grants DA021405 (Natural History, Comorbid Mental Disorders, and Consequences of Inhalant Abuse, M.O. Howard, PI), DA15929 (Neuropsychiatric Impairment in Adolescent Inhalant Abusers, M.O. Howard, PI), and T32 DA007304 (M.T. Hall).

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HAIR ANALYSIS VS. CONVENTIONAL METHODS OF DRUG TESTING IN PRE-TRANSPLANT PATIENTS.

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Aims: Transplant programs require 6 months abstinence before surgery. Variable drug testing procedures may impact findings, potentially biasing the candidate selection process. Our AIM was to compare results of conventional ETOH/drug tests with those of hair toxicology.

Methods: 42 patients donated 443 samples. 2X2 tables of frequency counts compared results from hair testing with other methods. Sensitivity, specificity, and kappa values were calculated.

Results: Participants were middle aged (47.9), mostly minority (66%)males(81%); 71.4% needed a new liver, the rest a kidney. At BL, 35.7% self-reported using ETOH, 28.6% cocaine and 21.4% opiates in the past 30 days. Sensitivity was fair for self-report (.34), but low for BAL (0.12); specificity was high (0.85 and 1.0, respectively). Kappa values showed only slight agreement (0.18 and 0.12)compared to hair. For cocaine, sensitivity was moderate for self-report and urine (.48 and .42)and specificity was high (1.0 and 0.98). Kappa values were moderate (0.55 and 0.47). For opiates, sensitivity was moderate for self-report and urine (.58 and .52), with specificity high (.93 and .95). Kappa showed moderate agreement for self-report (.56) and urine (.52) compared to hair.

Conclusions: While negative hair tests were complemented by negative findings on other tests, positive hair tests were only inconsistently associated with other positive results. Hair testing identified more users across testing methods and substances. Only 34% of ETOH+ hair tests were self-reported, with 12% detected by BAL. For cocaine and opioids, 48% and 58% of positive hair samples were self-reported, with 42% and 52% detected in urine. Hair testing helps overcomes self-report bias and short detection windows, making it a viable alternative for transplant patients with addiction problems.

Financial Support: Supported by NIH/NIDA (R01DA015772)

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STRESS-INDUCED CHANGES IN MOOD AND CORTISOL RELEASE PREDICT STIMULANT EFFECTS OF AMPHETAMINE.

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Aims: Stress is thought to contribute to both the initiation and relapse to drug abuse. However, the mechanisms by which stress influences drug use are unclear. Interestingly, responses to acute administration of stimulant drugs are similar to certain neuronal and hormonal responses to acute stress, and there is accumulating evidence that individual variation in the positive reinforcing or euphorigenic effects of a drug are related to individual differences in responsivity to acute stress. In this study we evaluated relationships between physiological and subjective responses to a stressful task and amphetamine in a sample of healthy adult volunteers.

Methods: Individuals (N=34) participated in four experimental sessions; two behavioral sessions involving a stressful task (i.e. public speech) or a non-stressful control task, and two drug sessions involving oral administration of amphetamine (20mg) or a placebo. The dependent measures included salivary cortisol, heart rate, mean arterial pressure, and subjective ratings of mood.

Results: As expected, both stress and d-amphetamine increased cortisol, heart rate and blood pressure. Stress increased negative mood, whereas d-amphetamine induced stimulant and drug liking effects. Analyses revealed that increases in negative mood states after stress were positively correlated with positive mood responses to amphetamine. In addition, we found significant positive correlations between cortisol responses to stress and positive mood responses to amphetamine. Finally, stress-induced increase in cortisol and heart rate were positively correlated with mean arterial pressure following amphetamine administration, although these did not remain statistically significant following correction for multiple comparisons.

Conclusions: These results support and extend previous observations that subjective, hormonal and cardiovascular responses of stress and amphetamine are related.

Financial Support: NIDA (F32 DA024920, DA02812, T32DA07255), University of Chicago Hospital's GCRC (USPHS MO1RR000555), NCI Cancer Center (P30-CA14599).

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LIFE TRAJECTORIES OF WOMEN METHAMPHETAMINE USERS WITH CHILD SEXUAL ABUSE HISTORIES.

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Aims: Childhood sexual abuse (CSA) has numerous effects on women's life experiences, behaviors, and bodies. Women with CSA histories are especially vulnerable to substance abuse, depression, other mental illnesses, retraumatization, violence, sexual risk, suicidality, and physical health problems. The aim of this study was to explore the life trajectories of women methamphetamine (meth) users with CSA histories in order to elucidate how meth use and CSA histories were connected phenomenologicallly.

Methods: Thirty meth-dependent women in residential treatment completed life history interviews. The average age of the participants was 28 years and 56% were Latina, 30% white, 7% Native American, and 7% mixed. Participants started using meth at an average age of 15, and most (67%) were poly-drug/alcohol users.

Results: Out of the 30 participants, 13 (43%) described their histories of childhood sexual abuse, by a variety of perpetrators, for varying lengths of time (from one time to several years). All 13 women described engaging in multiple sexual risk behaviors which they attributed to their meth use and their CSA histories. All 13 women reported being victims of adult violence, and 10/13 (77%) reported perpetrating violence as adults, representing 59% of the subgroup (n=17) who perpetrated violence. Three of the 13 women described suicidal thoughts or attempts related to their CSA experiences.

Conclusions: In this study, women meth users associated the combination of their CSA histories and their meth use with numerous risky behaviors and mental health problems. A substantial body of evidence indicates that childhood trauma has long-lasting behavioral and neurobiological effects, as does meth use. Considering the prevalence of childhood trauma among women meth users and the pronounced neurobiological effects of chronic meth use, more research needs to be done on the biopsychosocial, combined impact of childhood trauma and chronic meth use among women users.

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QUETIAPINE INCREASES MARIJUANA CRAVING AND RELAPSE IN THE HUMAN LABORATORY.

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Aims: Only a small percentage of individuals seeking treatment for their marijuana use achieves sustained abstinence. Marijuana withdrawal, which produces anxiety, irritability and insomnia, likely contributes to these high relapse rates. Because the atypical antipsychotic, quetiapine, reduces these symptoms in a variety of psychiatric conditions, this study assessed whether quetiapine decreases marijuana's direct effects, marijuana withdrawal and marijuana relapse using a human laboratory design.

Methods: Nontreatment-seeking, marijuana smokers were maintained on placebo and quetiapine (200 mg/day) in this counter-balanced, within-subject study. Each dose was administered for 7 days prior to a 9-day inpatient phase. On the first inpatient day, participants repeatedly smoked active marijuana (6.2% THC) under controlled conditions. For the following 3 days, they only had access to inactive marijuana (0.0% THC: abstinence). On the subsequent 4 days, active marijuana (6.2% THC) was available for self-administration (relapse). Participants had to pay for self-administered marijuana using study earnings.

Results: Male (n=12) and female (n=2) volunteers who smoked an average of 10 marijuana cigarettes/day, 7 days/week completed the study. Compared to placebo, quetiapine maintenance (1) increased marijuana craving during active marijuana administration, (2) decreased certain physical symptoms of marijuana withdrawal (muscle pain, upset stomach, difficulty falling asleep), and (3) increased ratings of marijuana craving during withdrawal and (4) increased relapse to marijuana: quetiapine nearly doubled the number of puffs of active marijuana self-administered after 3 days of abstinence. Quetiapine also worsened performance on cognitive tasks, regardless of marijuana condition.

Conclusions: Maintenance on quetiapine (200 mg) increased marijuana craving, increased marijuana relapse and worsened cognitive performance. These data suggest that this dose of quetiapine would not be likely to improve marijuana treatment outcome.

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BEHAVIORAL AND FUNCTIONAL EVIDENCE OF MGLU2/3 AND MGLU5 METABOTROPIC GLUTAMATE RECEPTOR DYSREGULATION IN COCAINE-ESCALATED RATS: FACTOR IN THE TRANSITION TO DEPENDENCE.

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Aims: Rats with extended daily access to cocaine show escalating cocaine self-administration and behavioral signs of dependence. Regulation of glutamatergic transmission by metabotropic glutamate receptors (mGluR) has emerged as a mechanism in the addictive actions of drugs of abuse. We examine here whether neuroadaptive dysregulation of mGluR function is a factor in escalating cocaine self-administration.
Methods: Rats with daily access to cocaine for 1h (short access, ShA) vs. 6h (long access, LgA) were tested for differences in the effects of an mGlu2/3 agonist (LY379268) and an mGlu5 antagonist (MTEP) on cocaine-reinforced progressive-ratio (PR) responding, as well as expression levels and functional activity of mGlu2/3 and mGlu5 receptors.
Results: LgA history was associated with higher break points on the PR schedule than ShA history. LY379268 dose-dependently lowered breakpoints on the PR schedule in the LgA group but reduced breakpoints only at the highest dose in the ShA group. Consistent with this behavioral effect, mGlu2/3 functional activity was significantly elevated following LgA cocaine self-administration, without concomitant changes in receptor protein expression. Conversely, MTEP reduced PR performance in the ShA group and failed to alter breakpoints in the LgA group. LgA history was associated with decreased mGlu5 expression, accompanied by reduced mGlu5 functional activity in the nucleus accumbens.
Conclusions: Functional upregulation of mGlu2/3 and downregulation of mGlu5 receptors is a likely factor in the transition to cocaine dependence. Moreover, the differential behavioral effects of LY379268 and MTEP in rats with an LgA cocaine history have important implications for the treatment target potential of mGlu2/3 vs. mGlu5 receptors.
Financial Support: This work was supported by NIH/NIDA grants DA017097 and DA07348 (FW).

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EXAMINING THE RELATIONSHIP BETWEEN SOCIAL SUPPORT AND CRACK AND COCAINE USE IN AN INCARCERATED POPULATION OF MOTHERS AND NON-MOTHERS.

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Aims: Limited research has shown that the correlates of substance use differ for mothers and non-mothers and, specifically, that substance-using mothers are more dependent on social support than non-mothers given their greater number of obligations and limited financial resources. This study aims to compare the life circumstances of mothers and non-mothers and to examine the relationship between perceived social support and frequency of crack/cocaine use for both groups of women.
Methods: Data from 307 female prison inmates collected during the CJ-DATS Reducing Risky Relationships for HIV protocol were used in this analysis to examine the relationship between perceptions of social support and crack/cocaine use. This relationship was examined separately for mothers of minor children and non-mothers using ordinary least squares regression. Race and employment status were included as control variables.
Results: The majority of women in this sample were mothers of at least one child under 18 (68.1%, N=209). Mothers in this sample were significantly younger ($p<.01$), scored higher on the General Victimization Inventory ($p<.05$), and were more likely to have engaged in prostitution in their lifetime and to have had a financial crisis in the six months prior to incarceration ($p<.05$) than non-mothers. Having more social support ($p<.05$) and being employed ($p<.01$) were significantly associated with less frequent crack/cocaine use for mothers but not for non-mothers.
Conclusions: Findings demonstrate that the life circumstances of substance-using women who are mothers tend to be more severe than non-mothers and that social support and employment are particularly important for mothers and may be effective routes for intervention to reduce crack/cocaine use.
Financial Support: This research was supported by the National Institute on Drug Abuse (U01-DA016205; PI: Carl Leukefeld).

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COLLEGIATE RECOVERY COMMUNITIES: FACILITATING AND INVESTIGATING RECOVERY IN THE YOUNG ADULT DEMOGRAPHIC.

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Aims: The prevalence of alcohol and drug abuse/dependency on college campuses is well documented (CASA, 2007; Wechsler & Wuetrich, 2002). Two common approaches to addressing collegiate substance abuse/dependency, prevention and harm reduction, show minimal effectiveness. Arguably, the inclusion of initiatives to facilitate and support recovery (i.e. social support communities) is a necessary, yet missing, component of campus efforts. Preliminary studies reveal the importance of social support for collegiates, ages 18 to 25, in their recovery efforts (Cleveland & Groenendyk, in press). Unfortunately the literature is silent concerning campus initiatives to target students with alcohol/substance dependency disorders and/or collegiates in recovery. The Collegiate Recovery Community (CRC) model is a promising effort toward addressing gaps in services for the collegiate population as well as investigating the phenomena of addiction and recovery in young adult populations. The aim of this presentation is to describe the CRC model and to increase awareness of preliminary evidence of successes of recovering collegiates enrolled in CRCs.
Conclusions: Students in recovery from alcohol/substance dependency in CRC programs demonstrate a relapse rate of 4% while enrolled in CRC programs (Cleveland, Harris, Baker, Herbert, & Dean, 2007). Additional anecdotal evidence shows positive outcomes in educational and occupational attainment for collegiates participating in a CRC. Replication of the CRC model is currently supported by Congressionally-directed funds. Six institutions of higher education are using this model to provide recovery support on campus. The replication of this model, and preliminary evidence of its effectiveness, suggests the need for further evaluation and outcome assessment.
Financial Support: United States Department of Education- P116Z090320

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DEVELOPMENT OF ANIMAL MODELS OF TOBACCO DEPENDENCE USING CIGARETTE SMOKE EXPOSURE.

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Aims: Animal models of tobacco dependence typically rely on injection or infusion of pure nicotine. Models using cigarette smoke inhalation would more accurately simulate nicotine exposure in smokers.
Methods: The primary goal of this study was to validate methods for administering cigarette smoke to rats using either nose-only exposure (NSE) or whole-body exposure (WBE). A secondary goal was to begin examining whether this type of smoke exposure can elicit behavioral effects relevant to the study of tobacco addiction.
Results: Administration of smoke via NSE (10- or 45-min) or WBE (1-4 hr) produced nicotine serum levels similar to those in smokers. Repeated 45-min NSE did not induce locomotor sensitization (LMS). 4-hr WBE to smoke did not enhance brain reinforcement function (i.e., decrease baseline intracranial self-stimulation (ICSS) thresholds) or reverse withdrawal from a chronic nicotine infusion (measured as increases in ICSS thresholds). In contrast, doses of s.c. nicotine producing peak nicotine serum and brain levels within the range of those achieved by smoke inhalation effectively induced LMS and reversed nicotine withdrawal.
Conclusions: Cigarette smoke did not produce robust behavioral effects in rats despite producing behaviorally relevant serum and brain nicotine levels. This model may be useful for understanding how the effects of inhaled nicotine in cigarette smoke may differ from those of pure nicotine administered by other routes.
Financial Support: Supported by National Institute on Drug Abuse Grants DA10714, T32 DA 07097, and F32 DA021935, the University of Minnesota Cancer Center Prevention & Etiology Program, the University of Minnesota Transdisciplinary Tobacco Use Research Center Pilot Grant, and the Minneapolis Medical Research Foundation Translational Addiction Research Program. The authors report no financial conflicts of interest.

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CHANGING UNIVERSITY STUDENTS' STIGMATIZING ATTITUDES TOWARD SUBSTANCE ABUSE USING A RESEARCH-BASED NEUROSCIENCE OF ADDICTION CURRICULUM INFUSION: RESULTS FROM THE NIDA ENTERS COLLEGE PROJECT.

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Aims: 1) To examine the impact of a 3-hour research-based science of addiction curriculum infusion package (CIP) on university students' stigmatizing attitudes about substance use disorders (SUDs); and 2) to examine possible discipline-specific differences in attitudes.
Methods: The study was conducted over a two-year period using introductory courses in each of three pre-professional disciplines (criminal justice, nursing, and social work). One section in each discipline was designated as the implementation (curriculum infusion) group (N = 205) and one section as the non-implementation (control) group (N = 324). Pre/post-test attitude measures based on curriculum objectives were developed using open-ended questions and 5-point Likert scale response options.
Results: A total of 366 students completed pre/post-test measures (implementation group: n = 103; control group: n = 263). Results suggest a significant decrease in stigmatizing attitudes following the curriculum infusion between the implementation vs. non-implementation groups and the implementation group pretest vs. post-test measures. In addition, significant differences in SUD attitudes were found between the three disciplines (qualitative and quantitative item level analyses will be presented).
Conclusions: Results lend support to the effectiveness of infusing a brief research-based addiction CIP into existing undergraduate courses on significantly reducing stigmatizing attitudes related to addiction and individuals with SUDs, thereby holding potentially long-term implications for preparing helping professionals to work with individuals with SUD.
Financial Support: Funded by the National Institute on Drug Abuse (NIDA) Science Education Drug and Alcohol Partnership Awards (SEDAPA) # 1 R25 DA 020472-01A1

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VARENICLINE'S IMPACT ON BOLD FMRI ACTIVATION DURING CUE-INDUCED CRAVING AND CRAVING RESISTANCE IN NICOTINE-DEPENDENT ADULTS: PRELIMINARY FINDINGS.

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Aims: Varenicline has been shown to reduce the rewarding effects of cigarette smoking and craving. The aim of this study is to investigate the neural substrates of varenicline effects during fMRI cue-induced craving and efforts to resist craving at baseline and after 5 weeks of treatment.
Methods: Participants were healthy right-handed treatment seeking nicotine dependent smokers without major psychopathology and clinically significant medical problems in this ongoing project. During fMRI scans with visual smoking and neutral cues, participants were instructed to allow themselves to crave for the first scan and to actively resist craving in the second scan. The craving and craving-resistance scans were acquired after two hours of abstinence (baseline) and after 5 weeks with standard varenicline therapy. Preliminary data was analyzed with FSL 4.1.4, using cluster thresholding (Z>2.3 and corrected cluster threshold of p=0.05), a primary contrast of the smoking minus neutral cues, and paired analysis between baseline and week 5.
Results: All subjects (n=8, 1 male) were abstinent for at least 7 days at the time of second session. For the craving scans, no brain activation was greater at baseline compared to week 5. However for the craving scans, week 5 demonstrated increased activation compared to baseline (anterior cingulate and dorsal medial prefrontal cortex). For the resist scans, brain activation was greater at baseline compared to week 5 (prefrontal cortex, anterior cingulate, orbital frontal cortex, and right inferior pole). In the resist scans, no areas of increased activation were seen comparing week 5 to baseline.
Conclusions: This preliminary data suggests that although subjective reports of craving diminish with abstinence on varenicline, in cortical areas involved in control responsiveness to cues may continue. Varenicline may work in part to increase cognitive efficiency in resisting cue-induced craving.
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GENDER DIFFERENCES IN PRESENTING CHARACTERISTICS AND SEVERITY OF SUBSTANCE USE AMONG INDIVIDUALS WITH PRESCRIPTION OPIOID DEPENDENCE.

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Aims: Prescription drug use disorders, in particular opioid abuse and dependence, are on the rise. Important gender differences in substance use severity have been observed with other substances of abuse. However, little is known about gender difference with regard to prescription opioids. This study preliminarily examines presenting characteristics and psychiatric co-morbidity of men and women (N=25) with prescription opioid dependence enrolled in a larger, ongoing study of prescription opioids and stress reactivity.
Methods: Participants completed the Addiction Severity Index (ASI), which assesses functioning in seven areas: medical, employment, legal, family/social, alcohol, drug, and psychiatric. The Time-Line Follow-Back assessed substance use during the month preceding study entry.
Results: In comparison to men, women demonstrated a significantly higher medical composite score (p=.002) and evidenced a trend toward a higher psychiatric composite score (p=.096). In comparison to women, men scored significantly higher on the alcohol use composite score (p=.006). Women reported higher percent days using opioids (60% vs. 47%) whereas men reported higher average number of prescription opioids used per day (4.7 vs. 3.9 pills). In addition, men reported higher percent days using alcohol (38% vs. 2%) and average number of drinks per day (5 vs. 2 drinks). Current psychiatric comoribidty was common and did not differ significantly by gender: major depression (16%), PTSD (8%), bipolar (4%), panic disorder (12%), agoraphobia (16%), social phobia (8%), specific phobia (4%), pain disorder (4%) and ADHD (12%).
Conclusions: Although preliminary, the findings help increase understanding of presenting characteristics of individuals with prescription opioid dependence and gender-specific differences. Data collection is ongoing and data from the full sample would be reported.
Financial Support: Funding acknowledgement: NIDA grant K23 DA021228 (SEB)

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CANNABINOIDS INHIBIT THE MIXED LYMPHOCYTE REACTION IN VITRO.

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Aims: There is a robust literature showing that cannabinoids modulate immune responses. Two cannabinoid receptors have been identified, CB1 and CB2. CB2 is primarily expressed on cells of the immune system. Our laboratory has shown that the cannabinoids delta9-tetrahydrocannabinol (THC) and anandamide are immunosuppressive in the primary and secondary plaque-forming cell assays, using mouse spleen cells, via CB2. Kaminsky's laboratory reported that THC given to mice in vivo suppresses the Mixed Lymphocyte Reaction (MLR) ex vivo (J. Leuk. Bio. 2008. 84:1574). The MLR is an assay considered to be an in vitro correlate of transplant rejection. Cannabinoids might, therefore, be a candidate class of compounds to lessen graft rejection in transplant patients.The present study sought to extend the study cited above, where cannabinoids were given in vivo, to investigate whether cannbinoids can inhibit the MLR when added to spleen cells in vitro.
Methods: In the MLR, spleen cells from two different mouse strains are incubated together. The cells of one strain are treated with mitomycin-C to block proliferation. The T-cells of the other strain respond to the foreign cells by proliferating. Inhibition of proliferation is a measure of immunosuppression. To test the hypothesis, THC, WIN 55,212-2, and two cannabinoids that are selective agonists of the CB2 receptor were added to MLR cultures.
Results: All cannabinoids tested inhibited the MLR in a dose-dependent fashion. Pre-treatment with cannabinoid receptor selective antagonists, SR141716A and SR144528, indicated that THC and the CB2 agonists were suppressive via the CB2 receptor. The CB2 antagonist partially reversed the suppression induced by WIN 55,212-2, while the CB1 antagonist had no effect.
Conclusions: These results show that cannabinoids can inhibit the MLR through the CB2 receptor, and support the possibility that they may be useful adjunct therapies to block graft rejection.
Financial Support: These studies were supported by NIH Training Grant 2T32A1007101-30 and NIH grants DA13429 and DA06650.

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PREDICTORS OF HEPATITIS C SEROCONVERSION AMONG RURAL APPALACHIAN PRESCRIPTION DRUG USERS.

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Aims: Injection of prescription opioids intended for oral use is an emerging public health problem, especially in rural areas. Hepatitis C (HCV) is easily transmissible via injection drug use (IDU); however, little is known about HCV infection in rural areas. The aim of this study is to examine risk factors for HCV seroconversion among rural prescription opioid users.
Methods: Participants (N=308) are enrolled in an ongoing longitudinal study of HIV risk among rural Appalachian drug users. Measures include sociodemographics, drug use, social networks, HIV risk behaviors, psychiatric disorders and serologic testing for HCV, HIV, herpes simplex-2 virus (HSV-2). Poisson regression was used to model HCV seroconversion from baseline to 6-month follow-up (95% follow-up rate).
Results: The majority of rural Appalachian participants are male (60%), white (93.2%) and the median age is 31 years. Most indicate a lifetime history of IDU (79.9%) and the prevalence of HCV is 47.7%, HSV-2 is 10.1% and there are no cases of HIV. Participants report using benzodiazepines (86%), hydrocodone (83.4%) and OxyContin (71.1%) most commonly in the prior 30 days. Use of heroin (5.8%) and cocaine (26.6%) is less prevalent. There were nine incident cases of HCV at follow-up, which corresponds to an incidence rate of 10.3%. Predictors of HCV seroconversion include methamphetamine injection in the prior 6 months, a greater number of sex partners in the prior 6 months and having a tattoo. When entered into a multivariable poisson regression model, only the number of sex partners was predictive of HCV serocoversion. For each additional sex partner, the risk of seroconverting was 7% (incidence rate ratio [IRR]: 1.07, 95% CI: 1.00, 1.14), adjusting for age, race and gender.
Conclusions: The prevalence of HCV is high in this population; however the results suggest that sex-risk factors may be more important than injection-risk factors for HCV seroconversion among rural Appalachian prescription drug users.
Financial Support: Research suported by NIH/NIDA R01DA024598 (JRH)

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THE RELATIONSHIP BETWEEN GENDER AND PSYCHOTIC SYMPTOMS IN COCAINE- AND METHAMPHETAMINE-DEPENDENT VOLUNTEERS.

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Aims: The primary aim of this project was to investigate gender differences in the reporting of psychotic symptoms in cocaine- vs. methamphetamine (METH)-dependent individuals.
Methods: Participants included 42 (27 m; 15 f) cocaine-dependent individuals and 43 (25 m; 18 f) METH-dependent individuals. The psychotic symptom assessment scale characterized various types of psychotic symptoms during drug use ("while high") or during periods of non-use ("while sober").
Results: There were no significant differences between male and female cocaine users with regard to ethnicity, years of use, route of administration, and amount used in the past week, though they differed with regard to age (p=0.03). Considering the "while sober" condition, more females than males reported experiencing auditory (13% vs. 0%, p=0.05) and tactile hallucinations (20% vs. 0%, p=0.016), though males were more likely to report delusions of grandeur (48% vs. 6%, p=0.006). During the "while high" condition, more cocaine-dependent females than males reported delusions of grandeur (13% vs. 0%, p=0.05), tactile hallucinations (33% vs. 0%, p=0.001), and olfactory hallucinations (13% vs. 0%, p=0.05).
There were no significant differences between male and female METH users with regard to age, ethnicity, years of use, route of administration, or amount used in the past week. Considering the "while sober" condition, more females than males reported symptoms of body dysmorphism (72% vs. 32%, p=0.009), olfactory hallucinations (39% vs. 8%, p=0.01) and disorganized thought (22% vs. 0%, p=0.01). During the "while high" condition, more females than males reported delusions of grandeur (33% vs. 16%, p=0.03), delusions of paranoia (50% vs. 16%, p=0.017), and tactile hallucinations (61% vs. 32%, p=0.05).
Conclusions: The current findings reveal gender differences for various psychotic symptoms, and that cocaine- and METH-dependent females are more likely than males to report experiencing these symptoms.
Financial Support: DA014593, DA017182, DA17705, DA17754

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METHADONE DURING PREGNANCY: SLEEP AND NEUROCOGNITIVE PERFORMANCE IN THE NEONATE.

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Aims: Although methadone is the standard of care during pregnancy, little is known about infant outcome following prenatal methadone exposure. This study examined sleep and actigraphy during withdrawal and neurocognitive performance in the first month of life.
Methods: Rural, disadvantaged mothers (N=55) were recruited from the same narcotic treatment program. Structured clinical interview of the mother using the Beck Depression Inventory-II and the Symptom Checklist 90-R, Hollingshead 4-Factor Index and comorbid alcohol, tobacco, and other drug use was verified by bi-weekly urinalysis screens and neonatal meconium. At birth, withdrawal was monitored using continuous actigraphy and Finnegan scores every three hours. Videography recorded behavioral state. In the first month, stable infant auditory recognition memory was assessed using the EEG event-related potential (ERP) oddball paradigm.
Results: Hollingshead score was associated with history of alcohol abuse (T-ACE, p <.05; MAST score, p<.05) and psychiatric status (SCL-90 Anxiety, p< .05), and correlated positively with neonatal head circumference (p=.01). Withdrawal severity comparison of actigraphy and Finnegan scores showed optimal sensitivity of 62% and specificity of 68%. Sleep fragmentation during withdrawal was associated with poorer neurocognitive performance (reduced amplitude of the infant P2, p<.002; increased nontarget latencies (parietal (Pz), p<.002; and central (Cz) sites, p<.01). Infants of mothers who entered treatment >12 weeks gestation showed reduced ERP amplitude to the rare tone (p<.03) and longer latency to the frequent tone (p<.002).
Conclusions: Adverse maternal SES was associated with comorbid alcohol exposure and reduced head circumference. Both late treatment entry and sleep fragmentation during withdrawal were associated with poorer neurocognitive performance.
Financial Support: Supported by NIDA/NIH DA024806

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ADOPTION OF HIV COUNSELING AND TESTING FOLLOWING COMPLETION OF RANDOMIZED CLINICAL TRIAL.

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Aims: Substance abuse continues to be a major factor in the transmission of HIV/AIDS, via injection and sexual risk behavior. Encouraging persons at risk for HIV to be tested is one of the main HIV prevention strategies in the US. Previous studies have shown that many substance abuse treatment programs do not offer on-site HIV testing.
Methods: LRADAC, a community-based treatment program, was one of twelve sites that participated in a randomized clinical trial sponsored by the NIDA Clinical Trials Network (CTN 0032). The purpose of CTN 0032 was to evaluate different strategies to increase the acceptance of HIV testing and reduce HIV risk behaviors among patients in substance abuse treatment. Following completion of the trial, LRADAC piloted HIV testing and counseling in the detox unit, with implementation in outpatient clinics to follow in January 2010. Demographic characteristics of clients offered and accepting testing were tracked through both phases of adoption.
Results: To date, 60% of the 120 clients offered testing in the detox program pilot accepted the counseling and test. Demographic characteristics of clients who accepted counseling and testing did not differ from the detox population. The reason most often cited for declining the offer of counseling and testing was having recently been tested. Demographic characteristics of clients accepting testing in the outpatient program will be tracked, compared to overall clinic demographic characteristics and characteristics of clients accepting testing in detox.
Conclusions: Although many community programs, especially those with a psychosocial rehab model, have been slow to integrate HIV testing into routine clinic services, clients in one program that participated in a NIDA randomized clinical trial were receptive to counseling and testing following completion of the randomized clinical trial.
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Southern Consortium Node of the Clinical Trials Network
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Florida Node of the Clinical Trials Network

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"NEUROCHEMICAL FINGERPRINTING" AS A RAPID TECHNIQUE TO DISCRIMINATE BETWEEN DRUGS WITH DIFFERENT PRESYNAPTIC DOPAMINERGIC MECHANISMS.

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Aims: Indirect dopamine mimetic drugs can increase synaptic dopamine concentrations via various distinct mechanisms. They include reuptake inhibition, firing independent release, firing dependent exocytosis and MAO inhibition as respectively exemplified by GBR 12909 (GBR), d-amphetamine (d AMP), MK-801 and tranylcypromine (TCP). We have identified unique patterns of dopamine and its metabolites ("neurochemical fingerprints") in mouse brain that discriminate between drugs acting by these specific mechanisms.
Methods: Adult, male C57/BL6 mice (n = 8) were intraperitoneally injected with GBR 12909 (10 mg/kg), d-amphetamine (10 mg/kg), MK 801 (0.3 mg/kg), tranylcypromine (5 mg/kg) or saline and brains were taken at 60 min. Striatum (STR) is a typical dopaminergic terminal field, but frontal cortex (FC) is very different because of its low density of innervation and because a substantial proportion of dopamine uptake and metabolism occurs within noradrenergic neurones. Dopamine (DA), DOPAC and HVA were determined by HPLC with amperometric electrochemical detection (ECD) (Cheetham et al, 1996) and 3 MT by HPLC with coulometric ECD (Heal et al, 1990). All changes shown by the arrows were significant ($p < 0.05$).
Results: Neurochemical fingerprints [DA; 3-MT; DOPAC; HVA; respectively]: STR (GBR = ± ± ↓ ±; d-AMP = ± ↑↓ ±; MK-801 = ± ± ± ↑; TCP = ± ↑ ↓ ↓). FC (GBR = ± ND ↓ ±; d-AMP = ↓ ND ↓ ↑; MK-801 = ± ND ↑ ±; TCP = ↑ ND ↓ ↓).
Where ± unchanged, ↑ increase, ↓ decrease, ND not detectable.
Conclusions: These results demonstrate that each of these drugs, which act via different presynaptic mechanisms, has a unique pattern of effects on DA and its metabolites. Moreover, the "neurochemical fingerprints" are not identical in STR and FC, reflecting the known differences in presynaptic regulation of dopamine release and metabolism in these two areas. This technique, therefore, provides a rapid and elegant method to identify the presynaptic mechanisms of novel compounds that alter presynaptic dopaminergic function.
Financial Support: Supported by RenaSci

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NICOTINE WITHDRAWAL IN PREGNANT CIGARETTE SMOKERS.

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Aims: A prior report by our group was the first prospective characterization of nicotine withdrawal in pregnant smokers. Our results indicated that pregnant smokers report high levels of withdrawal prior to a quit attempt. Pregnant smokers who then quit reported significantly more total withdrawal and impatience, anger, and difficulty concentrating compared to pregnant smokers who continued to smoke. It remains unclear how much 1) pregnancy and 2) smoking abstinence contribute to these observations of increased symptoms. Here, we present preliminary results from an ongoing study comparing withdrawal in pregnant smokers, pregnant non-smokers, and non-pregnant female smokers.
Methods: Participants were 36 pregnant smokers, 19 pregnant non-smokers, and 17 non-pregnant female smokers. All participants completed the Minnesota Nicotine Withdrawal Scale at baseline and at regular abstinence monitoring visits for two weeks. All participants also earned voucher incentives contingent on biochemically-verified smoking abstinence at each abstinence monitoring visit.
Results: Preliminary results indicate that pregnant smokers report significantly more total withdrawal and increased levels of anxiety/nervousness, impatience, and restlessness at baseline compared to both pregnant non-smokers and non-pregnant female smokers. Among those who were smoking-abstinent during the two weeks of abstinence monitoring, total withdrawal as well as anger/irritability/frustration, anxiety/nervousness, and impatience were significantly elevated among pregnant and non-pregnant smokers compared to pregnant non-smokers.
Conclusions: Preliminary results suggest that pregnant smokers have increased withdrawal prior to a cessation attempt, which may be a result of decreases in smoking rate upon learning of the pregnancy. Despite this increased baseline level, withdrawal after an quit attempt appears comparable to that experienced by non-pregnant smokers who smoke at a similar rate. These results have implications for the development of more efficacious treatments for pregnant smokers, including potential use of pharmacotherapies.
Financial Support: NIDA R01DA14028 & R01DA002491

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NEUROCOGNITIVE DYSFUNCTION IS ASSOCIATED WITH TREATMENT DROP-OUT IN METHAMPHETAMINE DEPENDENCE.

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Aims: Objective: To evaluate associations between cognitive function and treatment outcomes for methamphetamine (MA) dependence.
Methods: Methods: The MicroCog computerized neurocognitive battery was administered at baseline to 71 MA dependent participants in a clinical trial of modafinil versus placebo, with a platform of cognitive behavioral therapy and contingency management. Mean age- and education-adjusted MicroCog scores for MA dependent participants were compared to reference norms for MicroCog in healthy adults. Associations between baseline MicroCog scores and treatment outcomes (retention and MA use) during the 12-week medication treatment period were then assessed.
Results: Results: Relative to test reference norms (mean 100, standard deviation 15), mean scores for MA dependent participants were significantly lower for General Cognitive Function (64.9 +/- 18.4), General Cognitive Proficiency (89.8 +/- 13.5), Information Processing Accuracy (85.4 +/-16.9), Attention/Mental Control (93.0 +/- 15.4), Reasoning/Calculation (87.9 +/- 16.4), and Memory (93.5 +/- 15.0) but not Information Processing Speed, Spatial Processing, or Reaction Time. Participants completing the 12-week treatment period had significantly higher mean scores relative to non-completers for General Cognitive Proficiency (94.0 versus 87.1), Information Processing Accuracy (89.9 versus 82.6), and Reasoning/Calculation (92.1 versus 85.3), but there were no differences in mean scores for participants who did and did not achieve two consecutive weeks of MA abstinence.
Conclusions: Conclusions: Relative to test norms for healthy adults, MA dependent individuals seeking treatment have deficits in cognitive domains that support learning and memory. These deficits are associated with early treatment drop-out, suggesting that treatments that ameliorate cognitive dysfunction in MA users may improve treatment outcomes for MA dependence.
Financial Support: Funding for this study was provided by NIDA Grants 1 P50 DA 18185 (Shoptaw) and 1 K23 DA 023558 (Heinzerling).

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BUPROPION TRANSPORT BY PLACENTAL P-GLYCOPROTEIN AND BREAST CANCER RESISTANCE PROTEIN.

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Aims: Tobacco smoking during pregnancy is a preventable risk factor associated with complications in pregnancy. Bupropion is an antidepressant which was used successfully for smoking cessation in non pregnant patients. Currently, we are investigating its potential use in the pregnant patient seeking smoking cessation. Previously, we demonstrated that bupropion is transferred and metabolized by human placenta. P-glycoprotein (P-gp) and Breast Cancer Resistance Protein (BCRP) are efflux transporters with overlapping substrate specificity expressed in placental apical membrane, and influence placental disposition of their substrates. The goal of this investigation was to determine the contributions of P-gp and BCRP to placental bio-disposition of bupropion.
Methods: Bupropion stimulation of ATP hydrolysis was determined in commercially available membranes overexpressing P-gp or BCRP. Bupropion transport kinetics were determined in placental brush border membrane vesicle (BBMVs). P-gp and BCRP protein expression were determined using Western Blot analysis.
Results: Bupropion stimulated ATP hydrolysis and was transported by BCRP (Kt 3 μM, Vmax 30pmol/mg protein/min) and P-gp (Kt 0.5 μM, Vmax 6 pmol/mg protein*min). Thus, bupropion has higher affinity for transport by P-gp (as evidenced by lower Kt), while BCRP exhibits greater total transport activity (Vmax). A positive correlation was determined between P-gp and BCRP protein expression in BBMVs ($n = 200$, $p < 0.05$).
Conclusions: These data indicate that P-gp may be the first line of defense in transporting bupropion from the fetal-to-maternal direction, with BCRP serving as a second line when bupropion concentrations are elevated in the placental tissue. In conclusion, P-gp and BCRP, co-expressed in human placental brush border membrane, work in parallel to efflux bupropion in the fetal-to-maternal direction.
Financial Support: Supported by NIDA grant R01DA024094 to TN

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PRESCRIPTION OPIOIDS: MANAGING THE RISKS WHILE MAINTAINING APPROPRIATE PATIENT ACCESS.

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Aims: The 2007 FDA Authorization Amendment (FDAAA) codified a new approach to risk management termed Risk Evaluation and Mitigation Strategies (REMS). In February, 2009, FDA announced that REMS would be required for 16 categories of extended release and long acting opioids. This presentation addresses challenges in risk management that are particularly relevant to opioid analgesics.

Conclusions: For most drugs, the primary risks are to the patient, and education-based risk management tools may provide adequate control. For opioid analgesics, use by non patients is a major risk and is less effectively addressed by education. Furthermore strategies to reduce ease of diversion and abuse might prevent appropriate patient access. The first step in risk management is "evaluation" to determine the nature and extent o f the risks and benefits to thereby guide risk mitigation development and implementation. Our analysis of the 2007 National Survey on Drug Use and Health indicated that among respondents who reported nonmedical use of a prescription opioid within the past 30 days (N=1,113), 77% obtained the drug from a friend or relative, 13.4% reported stealing the drug from a friend or relative, 20% received a prescription from a single physician, and 5% reported receiving prescriptions from more than one physician (potential "doctor shopping"). About 13% purchased the drug from an illicit dealer. Other evidence indicates that many persons using without a prescription used for analgesic benefit and not to get high, confirming that there are multiple routes of abuse, diversion, and motivation for use. This presentation will discuss the use of surveillance data in a premarket risk evaluation to provide the foundation for potential risk mitigation strategies. It will also describe how surveillance data can then be used to evaluate the potential benefits and unintended consequences of the REMS, thus providing a foundation for interventions and for modification of the REMS to improve its effectiveness without posing undue barriers to patient access.

Financial Support: Pinney Associates, Inc.

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COMPARISON OF COGNITIVE PERFORMANCE IN METHADONE MAINTENANCE PATIENTS WITH AND WITHOUT CURRENT COCAINE DEPENDENCE.

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Aims: There is evidence for psychomotor and cognitive performance impairment in methadone maintenance patients (MMP), as well as in individuals with current cocaine dependence. This study examined the relationship of cocaine dependence to cognitive performance in MMP.

Methods: Baseline performance on a standard battery of tasks designed to measure psychomotor performance, attention, episodic and working memory, and executive function was compared between MMP with current cocaine dependence (MMP/CD+; N=53) and MMP without current cocaine dependence (MMP/CD-; N=24) participating in separate studies in our clinic. Median methadone dose was 100mg/day for both groups, and performance testing began 120 min after methadone dosing.

Results: There were no significant differences between the groups on gender, race, years of education, employment status, and estimated IQ; mean age was significantly higher in the MMP/CD- (47) relative to the MMP/CD+ (42.2). Performance was significantly worse ($p \leq 0.05$; independent groups t-tests) in the MMP/CD+ group relative to the MMP/CD- on measures of psychomotor speed (simple reaction time and trail-making test A), episodic memory (recognition memory), and working memory accuracy (one-back). The only measure on which performance was worse in the MMP/CD- group relative to MMP/CD+ was working memory speed (Sternberg task). There were no differences between the groups on measures of balance, psychomotor coordination, focused attention or executive function.

Conclusions: Although conclusions based on between-study comparisons must be limited, results suggest that cocaine dependence is associated with increased psychomotor and cognitive impairment in methadone maintenance patients. These findings may have important implications for daily functioning and treatment success in methadone patients with current cocaine dependence.

Financial Support: Research supported by DA021808, DA017688, and DA007209.

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RACIAL/ETHNIC DIFFERENCES IN MORBIDITY AND HEALTH STATUS AMONG ADULT METHAMPHETAMINE USERS.

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Aims: As methamphetamine (MA) use continues to affect diverse geographic regions across the U. S., ethnic minority communities are increasingly at risk for adverse health consequences associated with MA abuse and dependence. This study examines disease rates and ethnic differences in health status among individuals who routinely used MA. As health disparities affect ethnic minorities in the general U.S. population, it is hypothesized that such disparities exist among MA users.

Methods: Data are from an intensive natural history interview of a random sample of individuals admitted to treatment in 1995-1997 for MA abuse in Los Angeles county (n=276), and a cohort of MA users from the same communities who had not previously participated in formal substance abuse treatment (n=299). All participants (N=575) were interviewed in 2001-2003. Cross tabulations and comparisons of means examined health variables by race/ethnicity.

Results: The sample was 65% male, 41% White, 28% Latino/Mexican American, 8% Latino/Central or South American, and 18% African American; the mean age was 34.0 years (SD=8.8). Mean age of first MA use was 20.0 (SD=6.8) and first regular MA use was 21.9 (SD=7.3). Health conditions frequently reported were sexually transmitted diseases (STDs, 33%), severe headaches/migraines (30%), back/neck injuries (28%), severe dental problems/rotting teeth (26%) and gunshot/knife wounds (24%). Statistically significant racial/ethnic differences were observed for conditions including hepatitis and STDs disproportionately affecting African Americans, and dental and hearing problems disproportionately affecting Latinos from Central/South America.

Conclusions: Younger MA users (age 18-44) had particularly high rates of dental problems, severe headaches, asthma, hepatitis and hearing problems compared to national rates. African Americans and subgroups of Latinos who use MA may be at higher risk for specific health problems. Multivariate analyses further examine associations of race/ethnicity and health status together with other relevant factors including severity and duration of MA use.

Financial Support: NIDA grants #R01DA11020, R01DA025113

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CUE- AND COCAINE-INDUCED REINSTATEMENT OF EXTINGUISHED COCAINE-SEEKING IN METHYLPHENIDATE PRETREATED RATS.

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Aims: Recent studies have demonstrated that early methylphenidate (MPH) exposure in rodents alters the reinforcing effects of cocaine (COC) in adulthood. Interestingly, investigators have found conflicting results when reward was assessed using self-administration (SA) or condition place preference paradigms. These results suggest that early MPH treatment may differentially alter later responsiveness to COC and COC-paired environmental cues. Thus, the goal of this study was to examine the effects of early MPH exposure on reinstatement of extinguished COC-seeking behavior after cue and drug priming.

Methods: We treated rats with MPH (0, 2, or 5 mg/kg) from postnatal (PD) 11 to PD 20 and then trained rats to self-administer COC beginning on PD 60. Rats were trained to press a lever on an FR1 schedule for intravenous cocaine infusions (0.75 mg/kg per infusion) that were paired with a light/tone cue. Rats were then moved to an FR10 schedule and, after acquisition criterion was reached, rats underwent extinction training to devalue the motivational significance of the SA environment. COC-seeking behavior was then assessed in rats that received response-contingent presentation of the cues that had been paired with COC infusions during training. Afterward, rats were again put on extinction training until criterion was reached. Rats were then tested for COC-induced reinstatement where COC-seeking behavior was assessed after an injection of COC (5 or 15 mg/kg). During the COC priming session, lever presses were not reinforced with COC or tone/light stimuli.

Results: MPH pretreatment did not alter the acquisition of COC SA or cue-induced reinstatement. However, MPH-pretreated male rats given the 15 mg/kg COC prime had a greater number of active lever presses than saline-pretreated rats.

Conclusions: The present data suggest that early exposure to MPH may enhance the vulnerability of young adults to the unconditioned effects of COC but not to COC-paired environmental cues.

Financial Support: Supported by NIH grant GM073842

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IMPACT OF A NON-INVASIVE METHOD OF LIVER STIFFNESS MEASUREMENT (FIBROSCAN®) IN THE CARE OF PATIENTS SUFFERING FROM HCV IN AN ADDICTION CENTER.

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Aims: HCV in drug users is a major issue in terms of public health. In France, HCV prevalence in DU is 60% and 10% of them are co-infected HCV/HIV.Less than 15% of HCV + persons had an antiretroviral treatment. Objective: Improve the early screening for liver stiffness and access to antiretroviral treatments and improve the global care of patients in addiction center.

Methods: An early screening of liver stiffness was proposed to opiate users in Bizia Addiction Clinic from January to December 2008 thanks to the facility in the clinic of a non-invasive liver stiffness measurement device: Fibroscan®. This is a 5-minute non-invasive and painless examination. The results are immediately provided as a quantitative value (kPa).

Results: In 2008, there were 220 opiate users in the center.68% (N=136) were HCV+:37% (N=50) were cured, 56% (N=77) had a positive RNA and 27% (N=21) were co-infected VHC/VIH.16% (N=30) were HIV+.The liver stiffness was assessed for 78% (N=105) of HCV +. Among HCV+/RNA+ patients, 30% had a severe fibrosis score and 23% had cirrhosis. Among co-infected patients, 35% had cirrhosis. In 2008, 61% (N=47) of patients HCV+/RNA+ had a follow up with an liver specialist and 14 had been treated (1 co-infected).

Conclusions: The Fibroscan® seems to be a major motivational tool. It gives patients awareness of the HCV evolution. Availability of the device in the addiction center provided the mobilization of the medical staff and reinforced links with liver specialists so as to treat more patients.

Financial Support: Charles O'Brien

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NATURAL HISTORY OF CHANGES IN CIGARETTE SMOKING UPON LEARNING OF PREGNANCY.

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Aims: Cigarette smoking is the leading preventable cause of poor pregnancy outcomes in the United States. Among women who report smoking at the time they learned of their pregnancy, some quit with little or no intervention before their 1st prenatal care (PNC) visit and those still smoking at their 1st PNC visit report they have reduced their smoking an average of 50% from their pre-pregnancy rate. To our knowledge, there are no reports characterizing the trajectory of these changes.

Methods: Participants were 107 pregnant women who reported smoking at the time they learned of their pregnancy, and were recruited to participate in ongoing clinical trials examining the efficacy of voucher-based incentives to promote smoking cessation and prevent relapse in pregnant smokers. Participants self-reported their pre-pregnancy smoking rate at trial intake and completed a timeline follow-back interview to assess the number of cigarettes they smoked each individual day, from the day they learned of their pregnancy until their 1st PNC visit.

Results: On average, participants were 5 weeks estimated gestational age (EGA) when they learned of their pregnancy and 11 weeks EGA at their 1st PNC visit. In the intervening period, 27% of participants reported quitting (≥ 7 days continuous abstinence), 36% reported making a significant reduction (≥ 7 days of smoking at ≤ 50% of pre-pregnancy rate) and 37% reported no significant changes in their smoking. Fifty-five percent of quitters and 72% of reducers reported initiating abstinence or significant reduction in smoking within 1-2 days of learning of pregnancy. The majority of women who made changes in their smoking (72% of quitters and 89% of reducers) maintained those changes until their 1st PNC visit.

Conclusions: These data indicate that women who quit or significantly reduce their smoking on their own do so very soon after learning of pregnancy. Pairing interventions with a sentinel health event, such as learning of pregnancy, may increase intervention efficacy.

Financial Support: Supported by NIDA R01DA14028, NIDA R01DA002491, & T32DA007242

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EFFICACY OF GABAPENTIN IN SUBJECTS WITH CONCURRENT ALCOHOL AND CANNABIS DEPENDENCE.

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Aims: The most frequently co-occurring (and most understudied) illicit substance use disorder in individuals with alcohol dependence is cannabis dependence. Currently, there are no approved medications for the treatment of cannabis dependence. The aim of this study was to evaluate the potential of gabapentin to reduce use of these substances and symptoms of abstinence in non treatment-seeking paid volunteers with concurrent alcohol and cannabis dependence.

Methods: In this double-blind, placebo controlled human laboratory model of risk factors for relapse, 21 non treatment-seeking alcohol and cannabis dependent volunteers were randomly assigned to receive 1200 mg/d gabapentin (n = 12) or placebo (n = 9) for 1 week. Subjects were assessed on pre and post-treatment measures of alcohol and cannabis use, mood, and sleep. At the completion of the double-blind medication phase alcohol craving was measured during a cue-reactivity session where subjects were exposed to standardized pleasant, neutral, and unpleasant visual stimuli followed by alcohol beverage or bottled water in vivo cues.

Results: Gabapentin was associated with significantly greater reductions than placebo on several measures of subjective affectively-primed craving for alcohol and significantly decreased the number of joints smoked per week ($p < .05$). Importantly, gabapentin was also associated with significant improvements on several measures of sleep quality. There was 100% completion rate, 92% medication compliance and minimal side effects

Conclusions: Abstinence symptoms from both cannabis and alcohol include disturbances in mood and sleep that may relate to relapse. Results suggest that gabapentin may be effective for treating abstinence symptoms in comorbid alcohol and cannabis dependent individuals, as well as reducing cannabis use, thereby providing support for further investigation of the efficacy of gabapentin in cannabis dependence per se, and in comorbid alcohol and cannabis dependent individuals.

Financial Support: This research is supported by NIAAA RO1AA012602

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CAN FIBROSCAN® PREDICT ESOPHAGEAL VARICES AMONG CIRRHOTIC ALCOHOL ABUSERS?

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Aims: Aim: Studying the agreement between the results of Fibroscan ® and evidence of esophageal varices.

Methods: Methods: It has already been showed that a Fibroscan® result (elastomeric level in kilopascal KPa). of 14 or more correlates to cirrhosis in 97% cases. Moreover in cirrhosis, whatever etiology, Fibroscan® has been proved to predict the presence of esophageal varices. To study the agreement between Fibroscan ® and esophageal varices in cirrhosis caused by alcohol, each patient admitted to our addiction medicine healthcare unit with a diagnosis of cirrhosis caused by alcohol were tested in the first week with both gastric endoscopy and Fibroscan®. Severity of esophageal varices was then evaluated (grade 1, 2&3) and compared to Fibroscan results

Results: Results: In 50 cirrhotic patients, 14 had no EV, 14 had EV grade 1, 13 had EV grade2, 6 had EV grade2/3 and 3 had EV grade3. Fibroscan® results were ranged from 10.6 to 75 KPa. Under a threshold of 25.8 KPa in our study, it was predictable that no esophageal varices were present, with a predictive value >90% and a sensibility >95%.

Conclusions: Conclusions: A better selection for gastric endoscopy in patients suffering from cirrhosis due to alcohol would improve cost/effectiveness ratio. Fibroscan® diagnosing in one test, both cirrhosis and esophageal varices, suggests a substantial benefit in this specific and difficult kind of healthcare.

Financial Support: none

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DRUG USE ATTITUDES AND BELIEFS AND TREATMENT OUTCOME.

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Aims: This study examined whether attitudes and beliefs among opioid-dependent patients in treatment affect treatment outcomes and recovery, and whether patients' beliefs and attitudes are influenced by treatment.
Methods: Data on attitudes and beliefs were collected from 64 individuals who completed the behavioral and pharmacotherapy treatment phase (week 18) of an ongoing clinical trial of buprenorphine for opioid dependence. Preliminary analyses examined measures of attitudes and beliefs about addiction and recovery and the correlation of treatment outcomes with changes in beliefs and attitudes over the course of treatment.
Results: Changes in attitudes and beliefs were found from baseline to the end of treatment. For example, the percentage of participants who endorsed a belief that they are chemically dependent decreased from intake to week 18 (96.3% and 82.1%, respectively; $p = 0.03$), and the number of participants who endorsed the belief that they could control their alcohol/drug use increased from intake to week 18 (14.6% and 33.3%, respectively; $p = 0.05$). Participation in treatment seemed to influence attitude about the goal of treatment: at intake, 54.9% endorsed total abstinence, but at endpoint (week 18), 47.4% endorsed abstinence. Males and females had significantly different treatment goals at intake ($p = 0.008$).
Conclusions: These preliminary findings demonstrated that attitudes and beliefs about addiction and recovery change over the treatment period, indicating a potential importance in examining beliefs and attitudes over the course of treatment as well as at the beginning and end of treatment. Outcomes may be improved by treatment that reflects a better understanding of the influence of attitudes and beliefs regarding addiction and recovery.
Financial Support: NIDA 5R01 DA020210

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METHADONE DOSE AND NAS.

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Aims: Methadone maintenance is the standard of care for treatment of opioid dependence during pregnancy. Despite the benefits of maternal methadone maintenance, neonatal abstinence syndrome (NAS) has been reported in 30-80% of opioid exposed infants. Although most studies find no relationship between maternal dose and NAS, several have reported that higher maternal methadone doses at delivery predict NAS. This study aims to clarify the relationship between maternal methadone dose and NAS by exploring factors that may moderate the relationship between maternal dose and NAS.
Methods: Records from 309 methadone-maintained mothers and their neonates born between January 2005 and August 2009 were examined. Logistic regression and ordinary least squares regression were conducted to examine the relationship of maternal methadone dose at 28 weeks EGA, delivery, and postpartum to treatment for NAS, length of treatment and peak dose of neonatal opium solution (NOS) required. Additional analyses were conducted with percent increase in maternal dose in the third trimester, percent decrease in dose from delivery to 4 weeks postpartum, and length of maternal methadone treatment.
Results: Maternal methadone dose at delivery and postpartum were significantly correlated with neonate NAS treatment ($p=.017$; $p=.005$), length of NAS treatment ($p=.004$; $p=.013$), and peak NOS dose ($p=.003$; $p=.024$). Length of time in methadone treatment, 28 week EGA dose, and percent increase of dose in third trimester were not significant. Percent of postpartum dose decrease was significantly positively associated with receipt of NAS treatment ($p=.044$), but not length of treatment or peak NOS dose. This association remained when delivery dose was controlled for, but became non-significant when postpartum dose was controlled.
Conclusions: Results suggest that maternal methadone dose at delivery does impact the emergence and severity of NAS. Additionally, extending attention to changes in maternal methadone metabolism in the postpartum period may offer insight into individual differences in development of NAS.
Financial Support: None

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RETROSPECTIVE EVALUATION OF ASAM CRITERIA IN ADOLESCENTS RECEIVING WEEKLY OUTPATIENT TREATMENT FOR CO-OCCURRING PSYCHIATRIC AND SUBSTANCE USE DISORDERS.

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Aims: To conduct a retrospective evaluation of ASAM criteria in adolescents with co-occurring psychiatric and substance use disorders(SUD) participating in a medication trial + weekly outpatient cognitive behavioral therapy(CBT). Although the ASAM criteria are widely used to determine level of care, research on the validity of ASAM criteria in adolescents is quite limited.
Methods: ASAM criteria were determined by retrospective chart review of 32 adolescents with DSM-IV ADHD and SUD participating in a 16 week randomized clinical trial of psychostimulant medication + weekly CBT.
Results: 18% of the adolescent sample met ASAM criteria for Level 1 (OP treatment); 41%, Level 2 (IOP treatment); and 41%, Level 3 (residential treatment). All participants,(100%)meeting ASAM Level 1 completed 16 weeks of treatment and were 80.3% compliant with CBT session attendance. Of participants meeting ASAM Level 2, 77% completed 16 weeks of treatment and were 72.5% CBT attendance compliant. Of participants meeting ASAM Level 3, 72.5% completed 16 weeks of treatment and were 70.7% CBT attendance compliant. Mean pre-post reduction in past 28 day drug use was (- 1.0 day; - 3.7 days; 0.7 days, respectively).
Conclusions: Treatment compliance and completion was higher than expected given the severity of substance abuse and psychopathology in this sample. Treatment outcomes were also comparable across all three groups despite the fact that 82% would have been assigned to more intensive treatment based on retrospectively determined ASAM criteria. Small subgroup sample sizes prevent meaningful statistical analyses (between group comparisons). However, these preliminary data support the need for additional research in larger samples addressing the validity of ASAM criteria in adolescents and/or the potential to utilize less intensive treatment with integrated mental health and substance treatment approaches in comorbid adolescents.
Financial Support: None

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ATTITUDES AND BEHAVIORS TOWARD SMOKING CESSATION INTERVENTIONS BY THE DENTAL TEAM.

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Aims: Tobacco use has harmful effects on all systems of the body, including the oral cavity. While the effectiveness of brief tobacco cessation intervention has been proven to be effective including in the dental setting, adherence to clinical recommendations as standard of care are not universally practiced by dental professionals.
The goal of this study was to evaluate changes in the attitudes, knowledge and behaviors of the "5A's" of smoking cessation among dentists, dental students, assistants and hygienists following a contributing educational effort by the School of Dental Medicine.
Methods: The University's Dental Alumni Association hosts an annual meeting that is well attended by practitioners in the Western New York Region. This meeting served as the recruiting venue for survey administration. Surveys consisted of 20 self-report items indicating providers' knowledge about smoking cessation interventions as well as the frequency of performing the "5A's". Surveys were completed in 2007 and 2008 with an intensive school-wide smoking cessation educational initiation undertaken in 2007.
Results: In the 2007 survey, 80 providers completed the questionnaire and in the 2008 survey, 390 practitioners completed the survey. Following the education efforts, practitioners' knowledge about smoking cessation, as well as frequency of performing counseling increased. For instance, in 2007, 37% were familiar with the ADA procedure code for tobacco counseling whereas more than half (51%) were familiar with this code in the 2008. Further, there was a 9% increase in the frequency of assessing a patient's interest in making a quit attempt and 5% increase in providing practical support.
Conclusions: Dental team providers can be a valuable resource in smoking cessation programs. School wide programs of educational materials can provide dental professionals with important tools to help patients stop smoking.
Financial Support: The State University of New York at Buffalo and by Health Research, Inc.

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REVISION OF THE REYNOLDS HORTON THEORY OF EXECUTIVE FUNCTIONING: IMPLICATIONS FOR ADDICTIONS TREATMENT.

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Aims: Recently the Reynolds Horton Theory of executive functions postulated that the crucial elements in executive functioning are monitoring and updating short-term memory, inhabitation of pre-potent responses and task-shifting. Past theories related to executive functioning, have focused on frontal lobe functioning to an excessive degree.
Conclusions: The new revision of the Reynolds Horton Theory of executive functioning, proposes a more appropriate neural net work model of executive functioning. Using the work of A. R. Luria, the Russian neuropsychologist, multiple interacting neuroanatomical areas are postulated to sub serve executive functioning skills. Crucial to understanding executive functioning is the association of executive functioning skills with particular brain areas and the important role played by multiple association areas in planning, monitoring and evaluating human behavior, including addictive behaviors. Suggestions for re-conceptualizing drug abuse treatment will be offered.
Financial Support: None

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METHAMPHETAMINE AND OTHER DRUG USE IN NATIVE AMERICAN COMMUNITIES.

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Aims: Methamphetamine use has been endemic in the Western United States for over two decades, and higher rates of meth use have been reported in the Western US. New Mexico represents a severe case, ranking in the top 10 states for meth use in recent years. While the actual scope of meth use remains unknown for most tribal communities, surveys suggest elevated rates of substance use among American Indians and Alaska Natives (AIAN) compared with other racial/ethnic groups. The present study was designed to examine the treatment needs and impacts of meth and other drugs on AIAN individuals, families, and communities, using a community-based participatory research approach.
Methods: Data were collected from three AIAN sites in New Mexico. All Addiction Severity Index (ASI) data were collected by chart review (N=212). Amphetamine use as reported in the ASI was used as a proxy for meth use. Multivariate analysis of variance was used to test for differences across gender and sites in ASI composite scores.
Results: Descriptive statistics revealed that 24.9% of participants reported some lifetime amphetamine use, with 3.8% reporting amphetamine use in the previous 30 days. One participant reported amphetamine as their primary problem substance, while alcohol was reported as the major problem substance by 95.0% of respondents. MANOVA revealed a Gender×Site interaction for ASI drug and psychiatric composites, with Sites 1 and 3 reporting more severe psychiatric problems for females and Site 1 reporting more severe drug problems for females.
Conclusions: Despite a high self-reported rate of lifetime amphetamine use, most participants viewed alcohol, not amphetamine, as the primary problem substance in their lives. Analyses also revealed different effects of gender across sites, highlighting the challenges at AIAN sites within the same region. Participants at all sites reported significant employment problems. In general, our results suggest that meth treatment at AIAN sites must be customized to meet the unique needs of these communities.
Financial Support: NIDA CTN

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THE DIRECT IN VIVO SCREENING OF MIXTURE-BASED COMBINATORIAL LIBRARIES FOR THE IDENTIFICATION OF NOVEL ANALGESICS.

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Aims: Typical compound screening to identify potential drug candidates often tend not to have desired drug like properties and thus have a high inherent rate of attrition in the later stages of drug development. One approach to circumvent this high attrition rate would be to use phenotypic in vivo models directly in the discovery phase to identify enhanced hits with desired biological profiles.
Our working hypothesis is that the use of mixture-based combinatorial libraries directly for in vivo testing offers a unique opportunity to carry out successful preliminary studies in which 10s to 100s of thousands of compounds are screened directly in translational in vivo assays.
Methods: Two studies will be presented involving the mouse tail flick test (8 animals per time point; times tested were 30 minutes, 1.0 hours, 2.0 hours, 3.5 hours, 5.0 hours, 8.0 hours and 24.0 hours; differences in mixture results were carried out by summing the area under the curve) of a tetra-peptide library which contains Dmt-DALDA (the library in total is made up of 17,850,625 peptides with each mixture composed of 274,625 peptides—these were successfully tested at 5 and 25 mgs/kg) and a classic small molecule library (made up of a total of 738,192 compounds; the single position defined mixtures were made up of 17-28,000 compounds each). These libraries were tested by IP administration at 5-25mgs/kg).
Results: In both instances, highly active individual compounds were identified that had enhanced in vivo properties (longer lasting activity, little of no respiratory depression, little or no hyperactivity) as well as desirable conditioned place preference activity and toxicity.
Conclusions: It has become clear that the direct screening of mixture-based libraries can yield highly active individual compounds having enhanced in vivo activity.
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ACT HEALTHY: EFFECTIVENESS OF A BEHAVIORAL ACTIVATION AND HIV MEDICATION ADHERENCE TREATMENT FOR AFRICAN-AMERICAN HIV POSITIVE SUBSTANCE USERS.

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Aims: Depression affects 35-50% of HIV positive individuals and is associated with higher rates of substance use and poor HIV medication adherence, yet few interventions targeting depression have been developed for low income HIV positive substance users. The 12-week ACT HEALTHY intervention integrates a behavioral activation treatment for depression (LET'S ACT; Daughters et al., 2008) with a CBT HIV medication treatment (Life Steps; Safren, Otto, & Worth, 1999). Initial pilot work established feasibility and initial effectiveness of ACT HEALTHY (Daughters et al., in press), yet further work including an increase in sample size and a contact control condition is needed.
Methods: 20 African American HIV infected substance users were randomly assigned to receive ACT HEALTHY or Nondirective Therapy plus Life Steps (NDT-LS) upon entry into residential substance abuse treatment. All participants regardless of condition receive 4 weeks (8 sessions) of individual treatment while in the residential treatment, followed by 8 weeks (8 sessions) of outpatient treatment for a total of 16 treatment sessions over 12 weeks. Baseline assessments and post treatment 1-month follow-up data were collected on rates of HIV medication adherence, depressive symptoms, behavioral activation, and relapse to substance use.
Results: Compared to NDT-LS, repeated measures and chi-square analyses indicate that the ACT HEALTHY participants reported significantly greater improvements in depressive symptoms and behavioral activation and were less likely to relapse to substance use.
Conclusions: This is the first study to compare ACT HEALTHY to a contact matched control condition, and findings suggest that ACT HEALTHY is significantly more effective in improving depression and substance use outcomes. Future directions including long term follow-ups and an examination of the mechanisms underlying treatment gains will be discussed.
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HISPANIC PARENTING WOMEN IN WOMEN-ONLY VS. MIXED-GENDER DRUG TREATMENT.

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Aims: Abuse of alcohol and illicit drugs causes serious health problems for mothers and their children. In recent years, increased numbers of women-only (WO) programs, in contrast to traditional mixed-gender (MG) programs, have offered special services to address the unique problems and service needs among substance-abusing mothers. However, Hispanic women appear to be underrepresented in WO programs; Hispanic women represented 22.2% in a large statewide treatment sample of 4,448 parenting women, but accounted for only 16.8% of women treated in WO programs. We examine Hispanic parenting women (with children under 18), and compare those treated in WO (n=126) versus MG (n=853) programs on problems and needs at treatment intake.
Methods: Subjects were recruited at admission to 44 treatment programs in 13 California counties. The Addiction Severity Index was administered.
Results: Mean age was 31 (33 in WO, 31 in MG), 57.6% did not complete high school, most were never married (48%) or divorced (34%), only 22% were employed (15% in WO, 23% in MG), and 38% received public assistance (48% in WO, 37% in MG). On average, women had 2.7 children under age 18, while 39% reported that children lived with others by court order and 17% had parental rights terminated. About 47% reported methamphetamine as their primary drug problem, and heroin was the primary drug reported by 33% of women in WO vs. 14% in MG. Most women (76%) reported a history of arrest (84% in WO, 75% in MG). Hispanic parenting women in WO also demonstrated high levels of lifetime psychiatric problems (33% vs. 23% taking psychiatric medications, 75% vs. 56% serious depression, 72% vs. 48% serious anxiety, 29% vs. 23% attempted suicide).
Conclusions: Hispanic parenting women, particularly those treated in WO programs, face many problems in key life areas. Barriers contributing to underrepresentation of Hispanic women in WO programs should be addressed given that WO programs potentially address the service needs of these troubled women.
Financial Support: Supported by NIDA R01DA021183, P30DA016383, & K05DA017648 (PI: Hser).

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THE STATUS OF DRUG USE AMONG CLUB DRUG USERS IN TAIWAN.

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Aims: This study was to investigate the status of drug/substances use among club drug users in Taiwan.
Methods: Data were collected from 159 adult club drug users who reported using MDMA 5+ times lifetime with a least once in the past 12 months. A Chinese version of Substance Abuse Module for Club Drugs (CD-SAM) and Washington University Risk Behavior Assessment (WU-RBA) was used to assess lifetime and recent drug use, co-administration of other drugs with Ecstasy, self-reported effects of Ecstasy, the history of substance/drug use, and risky, unsafe behaviors. Data were analyzed using SAS 9.1 for windows.
Results: The top 5 most frequent drug/substance with co-administration of Ecstasy were ketamine (76.7%), alcohol (66.7%), marijuana (49.1%), nitrous oxide (14.5%) and viagra (14.5%) respectively among 159 club drug users (77% males; M/F ratio 3.3). The places for club drug use are head-shaked parties (82.4%), bar and residences respectively. Out of curiosity (82.4%) was the major cause of using club drugs, to relieve stress was next and to numb your mind was the third.
Conclusions: The status of polydrug use among drug abusers is serious in Taiwan, especially the club drug users, by comparison to other countries. The club drug users even developed a specific administration of drugs; they took MDMA first, then ketamine, and then marijuana. Because most of the club drug users were young, polydrug used and curious about drugs, it is imperative to prevent club drug use by educating the youth. The results of this study reveal important information for further research and policymaking.
Financial Support: This study was supported by grants from National Institute of Drug Abuse, U.S.A. and National Bureau of Controlled Drugs, DOH, Taiwan.

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THE SAFETY OF PRAZOSIN IN DRUG-ABUSING POPULATIONS.

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Aims: Prazosin (MINIPRESS®), an α1 adrenergic antagonist, is being tested for the treatment of PTSD symptoms and alcohol abuse in military and veteran populations. These investigations typically exclude patients using illicit drugs, yet widespread adoption of prazosin as a treatment agent will result in its prescribing to drug abusers. We have attempted to identify the safety of prazosin in the drug abusing population.
Methods: We searched the literature, the DIOGENES® Adverse Drug Events Database (DADED), and the Veterans Integrated Service Network 20 (VISN20) electronic medical records (EMR) system.
Results: Literature reports suggested that prazosin-related side effects were rare and mainly appeared in patients who were experiencing renal failure, diabetes mellitus and/or other severe diseases. There were no reports of drug-drug interactions involving illicit drugs.
Prazosin was named as the primary or secondary suspect in 543 adverse drug event (ADE) cases in DADED dating back to 1976. The majority of ADEs involved known cardiac-related and neurological side effects of prazosin listed in the FDA label for Minipress®. There were no mentions of illicit drugs in DADED. To better estimate the risk of administering prazosin to illicit drug users, we examined all 53 cases that involved co-administration with prescription psychotropic drugs and found little evidence that they increased the risk of prazosin side effects.
A search of the VISN20 EMR database found 708 people who were prescribed prazosin in combination with either methadone or buprenorphine during FY 2007-8. 590 of these had a recent clinical diagnosis of PTSD and were on both prazosin and one of the other medications for an average of 234 days. The number of their ER visits and inpatient admissions during periods when they were on both medications was lower than periods when they were not taking both medications simultaneously.
Conclusions: The evidence suggests that the risk of experiencing harmful side effects when administering prazosin to patients using drugs of abuse is low.
Financial Support: NIDA & Veterans Administration

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GESTATIONAL AND POSTNATAL TOLUENE EXPOSURE IMPAIRS LEARNING AND MEMORY IN JUVENILE RATS.

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Aims: Memory impairment occurs after chronic solvent exposure and in the offspring of mothers exposed to inhalants during pregnancy. The aim of this work was to study the effects of acute and chronic toluene exposure during gestational and postnatal periods on learning and memory in juvenile rats.
Methods: To evaluate acute effects, five-week old Wistar rats were exposed to 6000 ppm toluene (T) or air (A) for 30 min in a static exposure chamber and tested immediately afterwards in the novel object recognition (OR) test or the step-through inhibitory avoidance (IA) task. For prenatal treatment, pregnant Wistar rats were exposed to 6000 ppm T or A, 30 min twice a day in the static exposure chamber from gestational day (GD) 8 to 22. After birth, pups were evaluated in a developmental battery test from postnatal day (PN) 4 to 21. A non-handled group was used as a control to compare development in treated groups. For postnatal treatment, male animals were divided at PN22 in two groups to be re-exposed either to 6000 ppm T or A (30 min, twice daily) until PN35, when rats were tested immediately after exposure in the OR test or IA task.
Results: Acute toluene exposure impairs both short and long term memory in the OR and IA tasks, respectively. Gestational exposure to toluene and postnatal exposure to air (T/A) impairs OR, but does not modify IA performance when compared with air-treated rats (A/A). Postnatal exposure to toluene (A/T and T/T groups) impairs animal performance in both tasks independently of gestational treatment. Pups exposed in uterus to 6000 ppm toluene had not significant differences in development compared to air-exposed pups. Nevertheless, both groups showed a decrease in body weight gaining and an increase in the righting reflex compared to pups non-exposed to air or toluene during gestation.
Conclusions: The results show that toluene differentially impairs short-term and long-term memory in acutely- and chronically-treated juvenile rats.
Financial Support: Supported by CONACyT fellowship 200327 (AHR)and grant 50636-M (CLR).

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CHARACTERISTICS OF INCARCERATION AMONG BLACK SOUTH AFRICAN DRUG USERS.

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Aims: Despite high rates of HIV, HBV, and drug use in South Africa, few studies have examined relationships between disease status, drug use, and incarceration. The present study sought to examine characteristics of lifetime histories of incarceration among a sample of adult black drug users recruited from the Pretoria region of South Africa.
Methods: This cross-sectional study included 378 black South African drug users from the Pretoria Region aged 18-40 years of age. Descriptive statistics were used to describe the sample. Chi-Square tests were used to examine the association between incarceration status and demographic characteristics, substance use (positive urinalysis for cocaine, opiates, and cannabinoids), and infectious diseases(seropositivity for HIV and Hepatitis B Virus (HBV).
Results: Of the 378 black South African drugs users, 194 were female and 184 were male. Bivariable chi-square analyses indicated significant associations between incarceration during the respondent's lifetime and positive urinalyses for cocaine ($\chi 2(df)=1.7$ (1), $p=.01$) and opiate use ($\chi 2(df)=7.0(1)$, $p<.01$) for males, and cocaine use ($\chi 2(df)=14.8(1)$, $p<.01$), opiate use ($\chi 2(df)=17.3(1)$, $p<.01$), and cannabinoid use ($\chi 2(df)=5.8(1)$, $p=.02$) for females.
Conclusions: HIV seropositivity was not associated with having a history of incarceration for either gender. Incarceration was associated with HBV seropositivity for females but not for males. The study findings underscore the public health significance of addressing drug use and infectious disease among incarcerated populations in South Africa.
Financial Support: This research was supported by grants 2T32DA007292 and R01DA014498 from the National Institute on Drug Abuse (PI: William Latimer, Ph.D., M.P.H).

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COMPUTER-BASED IDENTIFICATION OF SUBSTANCE USE IN PRIMARY CARE PATIENTS.

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Aims: Most people with substance use disorders go undetected and untreated. Proactive screening, brief intervention, and referral for treatment approaches (SBIRT) have tremendous potential for identifying and influencing undetected substance abuse, but efforts to use practitioner-delivered SBIRT approaches in clinical practice have not been successful. Computer-delivered SBIRT approaches are promising alternatives that have shown positive effects on substance use outcomes in specific populations. This research was designed to develop and test a computer-delivered general health screening survey, substance use assessment, and single-session, motivational interviewing-based intervention to be used in a RCT to compare the effects of computer- and therapist-delivered interventions on substance use in general medical patients.
Methods: An SBIRT program was developed and piloted in 115 patients attending an urban, academic medical center primary care clinic. Participants completed screening and assessment using an interactive program on a laptop computer in the clinic waiting area. Participant demographic, medical, psychological, and behavioral variables were examined.
Results: Participants were middle-aged (46.4/13.3), African-American (53%) and Caucasian (37%), women (61%) and men (39%) who reported regular smoking (58%). 13% of participants were using illicit drugs (including prescription drug misuse) alone, 14% were abusing alcohol alone, and 14% were abusing both. The majority of participants reporting illicit drug use were using marijuana. Substance abusers were more likely to smoke, engage in risky sexual behaviors and report intimate relationship violence.
Conclusions: Clearly, a computerized SBIRT program can be used to identify and assess general medical patients at risk for heavy/problem substance use and potentially provide a unique opportunity to affect substance use behavior. Further, the general health questionnaire can be used as a true control group in the planned RCT, allowing the evaluation of substance abuse assessment itself as an intervention in primary care patients.
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RELATIONAL AND TECHNICAL PROCESSES OF MI, COGNITIVE, AND CLIENT-CENTERED THERAPIES.

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Aims: The aim of this study was to compare the relational and technical processes of three psychotherapies used in addiction treatment, Motivational Interviewing (MI), Cognitive Therapy (CT), and Client-Centered therapy (CCT) by "master" therapists using a set of reliable and validated coding measures. Explaining the robust effects of MI on drinking despite its relative brevity could advance treatment refinement for addiction.
Methods: Sample and Procedures. We coded a demonstration video of a single session for each treatment. Six coders were trained to good inter-rater reliability and all rated each full-length video.
Measures. Therapy processes including MI Fidelity, therapist beahviors, client behaviors, characteristic psychotherapy elements, traps, strategies, and interpersonal dimensions and transactions were rated using the,MITI-3, MISC-2, Psychotherapy Q Set MISTS, Checklist of Psychotherapy Transactions, Yale Adherence and Competence Scales and Strategies Checklist.
Results: As predicted, global and behavior counts measures showed that MI fell between client centered and cognitive therapy on MI Spirit, Direction, Empathy, and Client Self-exploration, and on specific ratios of therapist behaviors such as reflection to question. The 3 treatments differed in the patterns of PQS rankings. The interpersonal characteristics of therapists using these three techniques differed on the Interpersonal Circumplex, with CCT the warmest and submissive, MI warm and neutral in dominance/submission, and CT warm and dominant.
Conclusions: These findings provide support for the idea that MI is distinct from CT and CCT and for the hypothesis that MI is more directive than CCT and more empathic than CT. The integration of relational and technical processes in MI may represent a unique combination responsible for its robust findings in the treatment of addiction. Attention to interpersonal constructs can deepen an understanding of relational processes in treatment.
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HE SAID, SHE SAID: GENDER DIFFERENCES IN LIFETIME NMUPD DEPENDENCE RATES IN TWO EPIDEMIOLOGICAL SAMPLES.

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Aims: Though gender differences in the use of illicit substances have been examined extensively, there is a paucity of research looking at differences in the nonmedical use of prescription drugs (NMUPD). NMUPD is a growing concern, as rates have increased. Though gender differences for specific drugs have been observed, research to date is mixed depending on the sample. The present study examines gender differences in lifetime NMUPD dependence rates using two national epidemiological samples.
Methods: Data were derived from epidemiological samples, the Natl. Longitudinal Alcohol Epidemiological Survey (NLAES; 1991-1992) and the Natl. Epidemiological Survey on Alcohol & Related Conditions (NESARC; 2001-2002). The NLAES was a face-to-face survey of adult respondents (N=42,862). The NESARC was a representative sample of adults (N=43,093) interviewed face-to-face. Dependence was defined using items matched to DSM-IV criteria. Chi-square analyses were conducted to examine the relationship between gender & prescription drug dependence for opioids, tranquilizers, stimulants & sedatives.
Results: Findings from the NLAES analyses demonstrated higher rates of lifetime dependence for men. A significant proportion of men reported greater stimulant dependence (.8 vs .6%). Men were 2x as likely to report opiate dependence (.4 vs .2%)& sedative dependence (.5 vs .2%). Also, men were 2x as likely to report tranquilizer dependence (.4 vs .2%). The NESARC demonstrated similar findings. Men were 2x as likely to report tranquilizer dependence (.2 vs .1%). However, women were slightly more likely to report amphetamine dependence (.5 vs .4%). All findings were at $p<.01$. NMUPD dependence rates were higher in NESARC sample, indicating that an increase in NMUPD rates.
Conclusions: In general, men were 2x as likely as women to report NMUPD dependence across all prescription drugs. Rates of NMUPD increased during the decade between surveys, indicating a rise in NMUPD. These findings suggest the need for an increasing awareness of NMUPD and effective screening measures to identify such dependence problems in the general population.
Financial Support: NIAAA

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HOW DO PREDICTION ERRORS IN CONDITIONED DRUG-REWARD INFLUENCE COCAINE PLACE PREFERENCE?

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Aims: Prediction errors in Pavlovian conditioning have a major role in learning and memory processes. Results from studies on natural reward suggest that positive prediction errors (outcome better than predicted) increase associative strength whereas negative prediction errors (outcome less than predicted) decrease associative strength. The present study investigated how prediction errors in drug-reward influence the acquisition and extinction of cocaine conditioned place preference (CPP).
Methods: Adult B6129S male mice were conditioned by cocaine for four days in one of the following schedules: a) ascending daily dose (3,6,12 and 24mg/kg), b) fixed daily dose (20mg/kg) and c) descending daily dose (24,12, 6 and 3mg/kg). Subsequently, acquisition and extinction of place preference were investigated.
Results: The magnitude of place preference was similar in all three groups, suggesting that the schedule of cocaine administration had only a minor effect on the acquisition of CPP. Extinction studies, however, revealed major differences between the groups. The ascending-dose group showed persistent place preference over a period of two weeks (resistance to extinction training). The fixed-dose group extinguished place preference within 5-6 days, while the descending-dose group extinguished place preference within 2-3 days.
Conclusions: This is the first study that demonstrates the influence of prediction errors in Pavlovian conditioning by drug reward. When the outcome was better than expected (ascending dose; positive prediction error) the associative strength between the context and the drug was maximized (resistance to extinction). When the outcome was similar to the expected (fixed dose; no error prediction) the associative strength was reduced. When the outcome was less than expected (descending dose; negative prediction error) the associative strength was minimal. These results are in accordance with the theory of prediction errors' influence on incentive learning, and suggest that these paradigms can better model the consequences of human drug use.
Financial Support: Supported by DA026878

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SEROTONIN DEPLETION BLOCKS THE EFFECTS OF A KAPPA-OPIOID AGONIST ON COCAINE SELF-ADMINISTRATION.

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Aims: Pretreatment with the kappa-opioid receptor agonist U-69593 decreases locomotor activity and reduces activity in response to a cocaine challenge three days later. This effect is attenuated significantly if serotonin is depleted by administration of parachloroamphetamine (PCA) prior to treatment with the kappa opioid agonist, suggesting that serotonin plays an important role in mediating the effects of kappa-opioid receptor agonists on the behavioral response to cocaine. This study was done to determine if serotonin also plays a role in mediating the effects of U-69593 on cocaine reinforcement.
Methods: Chronic indwelling catheters were implanted and three days later, 7.5 mg/kg PCA or saline was administered s.c. Starting ten days later, rats were injected daily for five days with 0.32 mg/kg U-69593 or vehicle (20% DMSO/80% sterile water) s.c. and two days later self-administration was begun. Training sessions were 2 h/day until the rats reached a criterion of three days of injections (0.25 mg/kg/inj) with less than 20% variability. Once criterion was reached, dose-effect curves were done with multiple doses tested in a descending series on a single day. Each dose was available for 45 min and there were 45 min intervals between doses during which rats were removed from the box.
Results: Treatment with PCA followed by vehicle had no effect on cocaine self-administration compared to saline/vehicle. A saline injection followed by U-69593 decreased cocaine self-administration by shifting the dose-effect curve downwards. This effect was blocked by prior administration of PCA. Thus, serotonin depletion prevented U-69593 from decreasing the reinforcing effects of cocaine.
Conclusions: These findings show that serotonin plays an important role in mediating the interaction between the kappa-opioid system and cocaine reinforcement. A better understanding of this interaction may lead to additional treatments that will produce long-lasting diminishment of the effects of cocaine without the side effects of the currently available kappa-opioid receptor agonists.
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PRELIMINARY ANALYSIS OF TASC OFFENDERS WITH CO-OCCURRING SUBSTANCE USE AND MENTAL HEALTH DISORDERS.

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Aims: Current evidence suggests that persons with co-occurring disorders (COD) are at risk for poorer treatment outcomes in terms of substance use and recidivism. Studies have examined this phenomenon in incarcerated individuals, but few have examined the factors that may prevent successful treatment of COD individuals under community supervision. The purpose of this preliminary study is to compare demographic and social histories for offenders under TASC supervision with COD compared to substance use only (SUD) or neither diagnosis.
Methods: Between 2002 and 2007, a total of 1,845 offenders were identified as having COD at the time of their intake interview. These offenders were compared to 1,876 SUD offenders and 1,874 controls. Key demographic and social risk behaviors of these offenders were compared using a series of Chi-Square and ANOVA analyses.
Results: COD offenders differed from SUD and controls on a variety of factors, with COD offenders being more likely to be White (69%; 38%; 30%; p< .001), female (42%; 20%; 26%, p< .001) divorced (37%; 22%; 20%, p< .001), and have some post-secondary education (36%; 22%; 30%, p< .001). COD offenders were less likely to be charged with drug sales/trafficking (1.8%; 2.3%; 2.8%, p= .006) and robbery (2.4%; 4.1%; 3.6%, p= .016) than both SUD and controls. COD offenders were more likely to identify crack cocaine (9.6%; 7.0%, p= .002) or opiates (22%; 10%; p< .001) as their drug of choice in comparison to SUD only. Finally, COD offenders more frequently reported a history of overdose (2.7%; 1.3%; 1.4%, p< .001), suicidal ideation (40%; 9%; 5%, p< .001) and/or attempt (31%; 5.4%; 3%, p< .001), and intravenous drug use (20%; 10%; 2%, p< .001) than both comparison groups.
Conclusions: While these preliminary findings indicated a number of barriers to treatment for COD offenders, future analyses will be needed to assess overall treatment success, as measured by substance abstinence and program discharge status, among this special population.
Financial Support: None

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IS NICOTINE SUSCEPTIBLE TO THE BLOCKING EFFECT?

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Aims: Redish (2004) hypothesized that the ability of drugs of abuse to pharmacologically stimulate dopaminergic transmission would render them permenantly associable, including in conditions where they are already fully predictable, meaning that they would be insensitive to the blocking effect. We attempted to test Redish's hypothesis by examining the conditioned reinforcing properties of nicotine- or food-associated cues. The present experiment used nicotine (NIC) as the drug reward because it stimulates phasic dopamine activity.
Methods: A total of 77 rats (25 food, 52 Nicotine) were assigned to either a food reward or NIC reward condition. Animals were first exposed to environmental cues (overhead light or pulsing tone) that were paired or unpaired with either food delivery or intra-venous NIC. Training for the primary CS continued for 10 days after which a second cue, always paired with the reward stimulus, was added. This procedure resulted in conditions where the secondary cue carried new predictive value or was "blocked" because the reward was already fully predicted by the primary cue. Following 4 days of training in phase two, animals were subjected to two lever-pressing CR tests that assessed reinforcement for the secondary and primary CS's respectively.
Results: A CR ratio variable was created for both the primary and secondary cues. When compared against a hypothetical null learning condition ($\mu = 1.00$, SD = 0) analysis of this variable revealed that the primary cue, when presented in a paired fashion, supported conditioned reinforcement for food ($\mu = 5.47$, SD = 2.86, $p < .0001$) or NIC ($\mu = 3.85$, SD = 4.21, $p = .001$). When examining responding for the secondary cue, ANOVA analysis revealed no blocking effect for NIC but a trend for blocking in the food animals ($t(23) = 1.63$, $p = .11$) that must be substantiated by further experimentation.
Conclusions: These on-going studies provide preliminary support for Redish's hypothesis.
Financial Support: This work was supported by NIH grant #1F31DA025448-01A1 and Phillip Morris.

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THE EFFECT OF METHAMPHETAMINE ADDICTION ON EXECUTIVE FUNCTION AND COGNITION IN THE HUMAN BRAIN USING FUNCTIONAL MAGNETIC RESONANCE IMAGING AND THE STROOP TASK.

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Aims: MA abuse has become a global epidemic in recent years with a corresponding increase in violent crime and hospitalisations. Clinically, a greater distractibility is observed in MA users. Studies using the Stroop task have reported attentional deficits in this group which may be attributed to an inability to suppress unrelated information and decreased cognitive inhibition. This study was to determine the effect of current MA use on neurocognition using fMRI.
Methods: 14 MA-dependent and 18 healthy control participants aged 18-46 years were scanned using fMRI (Siemens Magnetom Avanto 1.5T). Echo-planar images were collected while participants performed an overt Stroop paradigm. SPM8 was used to pre-process and analyse images and SPSS16 was used to analyse reaction time (RT) and accuracy, in order to determine the significance of differences between MA-dependent and control participants.
Results: Both groups exhibited longer RTs for incongruent relative to congruent and neutral stimuli. MA-dependent participants showed longer RTs than controls during congruent and neutral conditions ($p<0.05$). There were no significant differences in accuracy. The areas of activation corresponding to incongruent-congruent stimuli comparison differed between the two groups. The control participants exhibited activation in the cingulate gyrus at Brodmann (BA) area 32 on both the right and left sides, as well as the right medial frontal gyrus at BA 8. In comparison, MA-dependent participants only displayed activation in the right cingulate gyrus, but at BA 24 and 32 ($p<0.01$).
Conclusions: Behaviourally, both groups showed the typical Stroop interference effect. However, significant differences in regional activation suggest that MA-dependent participants utilise compensatory mechanisms during the Stroop task.
Financial Support: Trecia Wouldes

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BRAIN REACTIVITY TO SMOKING CUES IS GREATER IN SMOKERS WITH AN ATTENTIONAL BIAS FOR SMOKING WORDS.

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Aims: Tobacco smokers with an attentional bias for smoking words are more likely to relapse (Waters et al., 2003). Identifying differences between smokers with or without such bias may facilitate development of relapse prevention treatments.
Methods: We used an emotional Stroop task (ES) to identify smokers having a smoking word attentional bias, defined as having longer reaction times (RT) for naming font color of smoking-related versus neutral words. Smokers then underwent functional MRI (fMRI) involving presentation of smoking-related and neutral images. Functional MRI data were analyzed with BrainVoyagerQX and a whole brain random effects analysis was run comparing subjects with and without a smoking word attentional bias on their brain reactivity to smoking verses neutral images.
Results: Of 28 women smokers, 16 had a smoking cue attentional bias and 12 did not. Smokers with an attentional bias had longer RT for color naming of smoking words ($t=7.7$, $p<0.001$). There were no group differences on the Fagerstrom test for nicotine dependence, Hamilton depression scores, age, smoking pack-years, or expired carbon monoxide levels. The smoking word attentional bias group had greater activation (smoking>neutral images) in the insula, dorsal medial frontal cortex (dmFC), parahippocampal cortex, hippocampus, and cerebellar vermis ($t=2.8$, $p=0.005$).
Conclusions: The insula and dmFC have been associated with interoceptive activity while the parahippocampal cortex, hippocampus, and cerebellar vermis may be involved with recall of emotional episodes. Our findings suggest that smokers with an attentional bias to smoking words may, upon exposure to smoking cues, be more likely to recall smoking-related emotional memories and attend to the resultant interoceptive states. Such memories and states may interfere with ES performance, possibly other cognitive processes, and increase relapse vulnerability.
Financial Support: Supported by DA19378, DA017324, DA014013, DA015116, DA022276 & DA15036.

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FETAL NEUROBEHAVIORAL EFFECTS OF MATERNAL METHADONE VS. BUPRENORPHINE ADMINISTRATION.

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Aims: Methadone, a pure μ-opioid agonist, is currently used as the standard of care for opioid dependence during pregnancy in the U.S. Buprenorphine, a μ-opioid partial agonist, appears safe and effective for this population. Neither medication is approved by the FDA for use during pregnancy, and little is known about the effects of these medications on the fetus. The purpose of this study is to evaluate the differential effects of methadone and buprenorphine on fetal neurobehaviors across gestation.
Methods: This study was conducted as part of a double-blind study comparing methadone and buprenorphine for the treatment of opiate dependence during pregnancy. 19 opiate dependent pregnant women underwent 60 minutes of maternal-fetal psychophysiological and neurobehavioral monitoring at 24 (n= 9), 28 (n = 13), 32 (n = 8) and 36 (n = 10) weeks gestation at the time of peak (for all) and additionally at trough (at 36 weeks) maternal medication levels.
Results: Preliminary results of an interim analysis using non-parametric analytic techniques show significant or trend-level differences between groups in several fetal neurobehavioral measures at various gestational ages. For example, fetuses exposed to methadone had significantly lower heart rate variability ($p<.05$), less motor activity ($p<.05$) and fewer coupled movements (an indicator of fetal nervous system integrity; $p<.10$) than buprenorphine exposed fetuses at 24 weeks gestation. A clinician highly experienced in evaluation of fetal monitor tracings, blinded to maternal medication category, ranked the tracings in terms of fetal well-being. Buprenorphine exposed fetuses were ranked higher than methadone exposed fetuses at 24 and 28 weeks gestation ($p<.05$).
Conclusions: It appears that there are significant differences in fetal neurobehaviors in response to exposure to maternal methadone vs. buprenorphine administration. These results may have implications for the optimal treatment of the opioid dependent pregnant woman.
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EFFECTS OF NALTREXONE ON AMPHETAMINE-INDUCED CHANGES IN THE BRAIN DOPAMINE SYSTEM.

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Aims: We have previously shown that the opioid antagonist, naltrexone attenuates several of the amphetamine-induced effects, in humans as well as in rodents.The present study utilised a translational approach to compare the change in amphetamine-induced DA levels by naltrexone in human and animal experimental models.
Methods: The effect of naltrexone on amphetamine-induced DA release was investigated in both a) the human striatum using the technique of PET and [11C] raclopride binding b) the rat striatum using the technique of microdialysis.
Results: In humans, amphetamine (0.3mg/kg intravenously) caused a decreased binding of [11C] raclopride in the ventral striatum accompanied with an increase in the positive ratings of subjective drug effects. Administration of naltrexone (50mg), 1h prior to amphetamine, significantly attenuated the subjective effects (liking, euphoria and wanting) induced by amphetamine without altering the specific binding of raclopride. In rats amphetamine caused a dose dependent increase in DA release as measured by microdialysis Administration of naltrexone (3mg/kg) 30 minutes before the amphetamine injection (0.5 and 2.0mg/kg i.p.) did not modulate the amphetamine-induced DA release.
Conclusions: In conclusion, naltrexone significantly blunted the subjective effects of an intravenous dose of amphetamine in humans. There was no change in dopaminergic activity by naltrexone as measured by reduction raclopride displacement, a finding supported by microdialysis in the rat.Collectively, this suggests a DA-independent mechanism might be involved in the psychotropic subjective effects of amphetamine. The neurobiological interaction between NTX and amphetamine needs to be addressed also in the diseased brain to further elucidate the therapeutic mechanism of naltrexone.
Financial Support: Swedish Science Council (grant 14645-01A), Swedish National Drug Policy Coordinator and the Stockholm county council

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EFFECTS OF DOPAMINE D1 AND NMDA RECEPTORS ON ACUTE COCAINE-INDUCED FOS PROTEIN EXPRESSION AND MKP-1 PHOSPHORYLATION IN THE STRIATUM OF FISCHER RATS.

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Aims: The aim of our study was to systematically investigate the role of dopamine D1 and NMDA receptors on IEG protein expression and phosphorylation in the CPu and NAc, areas known to regulate cocaine treatment response, after acute cocaine administration.
Methods: For p-ERK, 60-day-old male Fischer rats received an injection of saline (1 ml/kg) or cocaine (30 mg/kg) and sacrificed 5, 15, 30, or 60 min later. For IEG, animals were sacrificed 45, 90, 180 or 360 min later.
D1 receptor antagonist (SCH 23390; 0.25 mg/kg) or NMDA antagonist (MK-801; 0.25 mg/kg) was administrated 30 min before cocaine or saline injection and rats were sacrificed 60 min after the last injection.
The CPu and NAc were dissected and subjected to Western blotting analysis
Results: In this study, we show that a single cocaine administration (30 mg/kg) time-dependently increases ERK phosphorylation, c-Fos and FosB protein expression, and MKP-1 phosphorylation (p-MKP-1), in the caudate-putamen (CPu) and nucleus accumbens (NAc) of Fischer rats. In the CPu, one hour after cocaine injection, the increases in c-Fos and FosB proteins are totally abolished by pre-administration of dopamine D1 receptor antagonist, SCH23390. In the NAc, SCH23390 also inhibits cocaine-induced c-Fos protein expression. The pre-treatment of NMDA receptors antagonist, MK801, partially reduces cocaine-activated c-Fos protein expression in the CPu. Furthermore, the augment of p-MKP-1 after acute cocaine administration is dependent on both dopamine D1 and NMDA receptors activation in both brain regions examined.
Conclusions: Through the activation of dopamine D1 and NMDA receptors, acute cocaine may modulate ERK signaling, subsequently influencing IEG expression/phosphorylation.
The increase of p-MKP-1 protein levels which may inhibit p-ERK resulting a transient ERK activation in response to acute cocaine.
Financial Support: This work was supported by DA12136, 506-GM60654, RR-03037 and PSC-CUNY

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ONLINE SELF-HELP FOR METHAMPHETAMINES USERS: DEVELOPMENT AND EVALUATION OF AN AUSTRALIAN WEBSITE.

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Aims: The Internet provides an excellent opportunity to offer evidence-based, self-help information to meth users who are otherwise unreachable by health care providers, yet such sites are few. The aim of the current program was to fill a gap in online resources for methamphetamine users.
Methods: With funding from the Australian Government ATS Grants Program, Turning Point created a novel website, meth.org.au, which was launched in March 2009. The site has a number of interactive elements including:
a) an on-line self assessment tool: the ASSIST, developed by the World Health Organisation;
b) self-help information derived from evidence based materials;
c) an optional SMS and email sign-up to receive weekly tips automatically;
d) resources and support information for alcohol and drug workers, carers and family members.
An evaluation of the site useage has been undertaken.
Results: In this presentation, we will describe the development of the website, provide results from a program evaluation, and discuss the role of the World Wide Web for the future of methamphetamine treatment. there have been nearly 6000 unique visitors and more than 35000 page views in the first 6 months with and average of 175 per week. Each visitor views an average of 6 pages and has spent an average of 30 minutes at the site. Close to 1000 users have accessed self help worksheets and downloaded self help information.
Conclusions: Self help via the Internet is a feasible and attractive option for methamphetamien and other stimulant users. Future work sould be focused on developing and trialing online brief interventions.
Financial Support: This project was funded through the Australian Government Department of Health and Ageing ATS Grants Program.

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DRINKING AND DRUG USE FROM A PROSPECTIVE PERSPECTIVE.

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Aims: To investigate the relationships between putative triggers, including alcohol consumption, and drug use and craving.
Methods: The day-to-day experience of addiction and recovery was examined using ecological momentary assessment (EMA) as a real-time data collection method in a prospective, longitudinal, cohort study of heroin and cocaine users; individuals who met DSM criteria for alcohol abuse or dependence were excluded. 114 methadone-maintained participants carried handheld data collection devices (PDAs: personal digital assistants) during all waking hours for up to 25 weeks. Participants responded to 2-5 random prompts per day by reporting their locations, moods, and activities, including whether they were drinking alcohol. Participants also initiated an entry when they used or craved heroin or cocaine; drinking was assessed at these "event-contingent" entries as well.
Results: Participants reported drinking alcohol in 1.6% of random-prompt entries. Frequency of drinking was over two times higher in event-contingent entries when craving for cocaine and/or heroin was reported, and almost 8 times higher in event-contingent entries when actual use of cocaine or heroin was reported.
Conclusions: The association between alcohol and drug use previously established in retrospective studies was confirmed here in this prospective EMA study. Even among participants with low baseline rates of alcohol consumption, alcohol was associated with drug craving and actual use.
Financial Support: Supported by the Intramural Research Program (IRP) of the National Institute on Drug Abuse (NIDA), National Institutes of Health.

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GENDER EFFECTS IN THE STEP'N OUT STUDY OF SUBSTANCE-USE TREATMENT MANDATED PAROLEES.

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Aims: The transition of drug-involved offenders from incarceration to the community is a critical issue for public health and public safety. Drug-involved women face especially daunting challenges at reentry. Despite calls for research to inform gender-specific correctional programming, well-controlled studies comparing differential treatment responses of males and females at community re-entry are rare. The current study examines gender by treatment interactions in the Step'n Out Study, a multisite randomized trial comparing a model of enhanced correctional supervision (CBM) to standard parole.
Methods: Parolees (N = 391) with pre-incarceration substance use disorders who were at moderate-to-high risk of recidivism were randomized to CBM or to standard parole. Logistic regression analyses used treatment condition, sex, and the treatment*sex interaction to predict yes/no use of drugs (verified by urine screens), alcohol, and prison recidivism during months 4-9 after baseline.
Results: CBM had differential gender effects on alcohol use, with a dramatically and significantly larger effect for women than for men. In addition, CBM halved the risk of recidivism for women, but had no effect on recidivism for men. Neither gender, treatment condition, nor their interaction was a significant indicator of drug use at 4-9 months post-release.
Conclusions: Findings lend support to the idea that optimal transitional treatments may differ for men and women. Correctional supervision involving clear expectations, positive reinforcement, recognition of successes, emphasis on consistency and fairness, and focus on overall life functioning may result in less recycling through the system for the more than 1,000,000 U.S. women currently under correctional supervision.
Financial Support: This study was supported by grants U01DA016191 and K23DA021159

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SEXUAL DISCOUNTING: HIV/AIDS RISK BEHAVIOR AND THE DELAY DISCOUNTING OF SEXUAL REWARDS IN COCAINE DEPENDENCE.

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Aims: Cocaine dependent individuals show high rates of sexual risk behavior and HIV infection. Little is known about the mechanisms responsible for this increased sexual risk behavior. An ongoing study is examining whether the discounting of delayed sexual rewards may explain the high rates of sexual risk behavior in cocaine dependence.
Methods: Individuals meeting DSM-IV criteria for cocaine dependence are shown 60 photos of individuals (30 female, 30 male) and asked to select the most attractive individual with whom he/she would be willing to have casual sex. With the photo in sight, the participant rates his/her likelihood of using a condom with this person for sex now if a condom were immediately available, using a visual analog scale (VAS) ranging from definitely not using, to definitely using a condom. Then, several related questions are asked in which condom availability is delayed, so that VAS ratings range from definitely having sex now without a condom, to definitely waiting a specified delay for sex with a condom. Seven delays are examined ranging from 1 hour to 3 months.
Results: Of the 9 participants completed in this ongoing study, 3 were ≥95% likely (i.e., VAS≤5mm) to have unprotected sex even when a condom was available at no delay. Of the remaining 6 participants, 5 were ≥95% likely to use an immediately available condom, and 1 participant was 16% likely to use an immediately available condom. For all 6 of these participants, delaying the option for sex with a condom decreased the reported likelihood of using a condom. For 2 participants, an immediate switch to unsafe sex (i.e., ≥95% likely to have unprotected sex) occurred at the shortest delay of 1 hour. In the remaining 4 participants, the decreasing likelihood of condom use with delay was consistent with a hyperbolic function commonly observed in delay discounting studies.
Conclusions: These data provide preliminary evidence that delay discounting for sexual rewards may help in understanding the high rates of sexual risk behavior and HIV infection in cocaine dependence.
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TOBACCO USE AND SPIRITUALITY AMONG FRESHMAN STUDENTS IN A HISTORICALLY BLACK UNIVERSITY.

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Aims: The aim of this study was to determine the association between spirituality/religiosity and tobacco use controlling for SES and stress. It was hypothesized that there is a negative association between spirituality/religiosity and tobacco use controlling for SES and stress.
Methods: In this study, the College Health and Wellness Project used data from freshmen students attending a Historically Black University. The study setting is the college dormitory (dormitory residence is a requirement of first year students). Students were recruited during the first week at the beginning of spring semester 2009 while in attendance of mandatory dorm meetings. Participation was voluntary, confidential, and anonymous and this study was approved by the IRB of Morgan State University. Overall 73% of freshmen residents attended the meetings, of whom 93% took the survey, resulting in 759 participants with a complete baseline survey (81% were 21 years old; 89% African American). A paper-and-pencil survey derived from standardized instruments was used to assess tobacco involvement (NSDUH), spirituality (Brief Multidimensional Measure of Religiousness/Spirituality: Harris et al, 2007; alpha=0.92), and stress (PSS: Cohen, 1994; alpha=0.71), among other constructs.
Results: One in five students had smoked cigarettes in their lifetime (20.4%). Among them, one in five of them smoked in the past month (20.8%). Half of the students who smoked tried to quit smoking last year (50%). Those with the lowest quartile of spirituality had almost twice the odds of smoking, relative to those with the highest spirituality quartile, controlling for SES and stress (OR= 1.8, 95%CI= 1.01-3.30).
Conclusions: These results underscore the importance of spirituality/religiosity among African American students at Historically Black Colleges and Universities.
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PROJECTED LIFETIME RISK OF CO-OCCURRING SUBSTANCE USE AND MENTAL DISORDERS AMONG ADULTS IN THE US.

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Aims: To facilitate the planning of treatment and prevention services for the substance abuse and mental health systems of care epidemiologic studies focus on identifying the lifetime prevalence, age-at-onset distributions, and projected lifetime risk of substance use and mental disorders. Projected lifetime risk uses survival analysis techniques to identify periods of greatest risk for the occurrence of disorders and assess the full societal burden across the life course. Although the majority of projected new onset psychiatric disorders are thought to occur among those with at least one prior disorder, the projected lifetime risk of co-occurring disorders have not been examined. Focusing on three classes of disorders (substance use, mood and anxiety) we examined: the projected lifetime risks and age-at-onset distributions for profiles of pure and co-occurring disorder classes; the sequences of disorder classes within profiles and the age-of-onset distributions for secondary disorders; and the degree to which individual disorders contribute differentially to the projected lifetime risk of disorder classes.
Methods: Data come from the National Epidemiologic Study of Alcohol and Related Conditions (N=43,093). Weighted analyses were conducted using SUDAAN.
Results: SUD-Mood was the most prevalent co-occurring disorder class profile (5.3%) and the one with the highest projected lifetime risk by the age of 75 (9.2%). The SUD only disorder class profile showed the expected rapid onset of disorders beginning in adolescents carrying through age 30, with attenuated onset thereafter. However, the SUD-Mood and SUD-Mood-Anxiety profiles show steady increases in the cumulative probability of lifetime co-occurring diagnosis through approximately age 50 which was largely due to onset of Mood disorders, and particularly major depression, secondary to SUD.
Conclusions: These results highlight the substantial impact of continuing onset of secondary disorders across the life course and the potential role of secondary interventions in reducing the lifetime societal burden of these disorders.
Financial Support: DA020901

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CHARACTERIZING THE SUBJECTIVE, REINFORCING AND ANALGESIC EFFECTS OF OXYCODONE IN BUPRENORPHINE/NALOXONE-MAINTAINED CHRONIC PAIN PATIENTS.

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Aims: While significant misuse of opioid drugs among chronic pain patients occurs, the risk factors and motivation for abuse may differ from that of other opioid abusers. This study sought to examine the abuse liability of oxycodone among chronic pain patients who misuse their prescription opioids, by assessing its subjective and reinforcing effects.
Methods: Eighteen opioid-dependent patients with chronic pain were admitted to an inpatient unit of the New York State Psychiatric Institute where they resided for this 7-week study. Participants were given several doses of oral oxycodone (0, 10, 20, 40, 60 mg/70 kg) while maintained on various doses of sublingual buprenorphine/naloxone (2/0.5, 8/2, 16/4 mg). All of the medications were administered under randomized, double-blind conditions using a cross-over design.
Results: Oxycodone produced a blunted, but overall positive subjective effects profile that was similar to recreational opioid users without pain. However, unlike recreational opioid users and more similar to non-drug abusing individuals, oxycodone failed to serve as a reinforcer. Under maintenance conditions, buprenorphine/naloxone produced pain relief and, at larger doses, antagonized the effects of the acutely administered oxycodone.
Conclusions: These data suggest that sublingual buprenorphine/naloxone may be an ideal medication for producing pain relief and reducing prescription opioid abuse. This medication profile may be particularly useful for treating chronic pain patients who abuse opioid drugs.
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DELAY DISCOUNTING PREDICTS VOUCHER REDEMPTION AMONG PARTICIPANTS IN A CONTINGENCY MANAGEMENT PROGRAM.

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Aims: Delay discounting rates describe the subjective change in value of a delayed reward. Researchers have found that discounting rates predict differences between substance users and non-users (Bickel & Marsch, 2001) and the likelihood of becoming abstinent (Yoon et al., 2007; Krishnan-Sarin et al., 2007). For treatment-seeking addicts in programs offering voucher contingencies, the principles behind delay discounting are similar to behaviors related to voucher redemption. This study examines relationships of voucher redemption behaviors with delay discounting among 159 opioid dependent participants offered 12 weeks of buprenorphine treatment combined with cash voucher contingency management (Higgins et al. 1991; 2003).
Methods: Participants submitted urine specimens 3 times a week which were screened for drug use. Successive negative urine specimens were reinforced with increasing amounts of money. After each negative urine specimen, the participant could redeem their earnings or allow it to accumulate in an account.
Results: Baseline discounting predicted whether a participant would be among those making more than the median number of redemptions; specifically, an increase of 1 unit in discounting corresponded to a 27.6% increase [95% CI: (3.5%, 57.4%)] in the odds of being a frequent redeemer.
Conclusions: Delay discounting rates predicts voucher redemption behaviors in a contingency management treatment program and these findings are consistent with other measures of temporal estimation and saving behavior.
Financial Support: This work was funded by NIDA Grant R01 DA 12997; Wilbur Mills Chair Endowment; and in part by the Arkansas Biosciences Institute/Tobacco Settlement Proceeds Act of 2000.

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DRUG USERS IN HCV LIMBO: GOT WHAT? NOW WHAT? PERCEPTIONS OF DRUG USERS IN AND OUT-OF-DRUG TREATMENT REGARDING HCV SCREENING AND CARE.

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Aims: Drug users (DUs) have high HCV prevalence and are central to the HCV epidemic in the U.S. Despite the availability of effective HCV treatment, few DUs have been tested, evaluated or treated for HCV. Factors contributing to poor engagement in care are incompletely understood.
Methods: Sixteen mixed-gender focus groups of either African-American or Hispanic DUs (N = 130) investigated perceived barriers to HCV testing and treatment. Themes were identified through content analysis of focus group discussions.
Results: Many DUs reported little or no knowledge about HCV testing, transmission and treatment, and were unaware of places to obtain an HCV test. While some DUs had been tested in institutional settings many did not understand their diagnosis or what to do about it. Many DUs perceived treatment as unavailable or unimportant because they lacked symptoms. Race/ethnicity was not perceived as a barrier to HCV testing or treatment among racial/ethnic minority DUs. DUs of all race/ethnicities reported that a lack of information about HCV and access to HCV services was due to economic factors and their DU status. DUs in MMTPs reported that on-site HCV services would be valuable and indicated interest in utilizing them.
Conclusions: DUs in and out of drug treatment have poor knowledge of HCV testing, transmission, and of the potential value of treatment. DUs perceive barriers to HCV testing and when tested, often do not understand the results or the next steps in care. Enhanced post test counseling may be beneficial.
Financial Support: National Center on Minority Health and Health Disparities, California HIV/AIDS Research Program (ID06-SF-198), and NIDA Grants (R01DA20781, R01DA02084, P30DA 011041, P50DA09253 & U10DA15815)

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CARDIOVASCULAR EFFECTS OF THE NICOTINE RECEPTOR PARTIAL AGONISTS CYTISINE AND VARENICLINE.

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Aims: The cardiovascular changes produced by nicotinic receptor partial agonists in conscious rats are relatively unknown. Therefore, this study investigated the effects of the nicotinic partial agonists cytisine and varenicline on blood pressure and heart rate in freely-moving rats and the receptor subtypes that contribute to these cardiovascular changes.
Methods: Cardiovascular changes were evaluated in conscious, freely-moving rats using a telemetry devices following administration of cytisine, varenicline, or nicotine.
Results: High doses of nicotine, varenicline, and cytisine produced a rapid, pronounced decrease in heart rate followed by increases in heart rate and blood pressure. These effects were dose-dependent and the magnitude of response was described by the following rank order: nicotine > varenicline > cytisine. The selective $\alpha4\beta2$ antagonist dihydro-beta-erythroidine (DHβE) did not alter significantly the cardiovascular effects of nicotine, varenicline, or cytisine. The non-selective, non-competitive antagonist mecamylamine produced differential effects on the nicotinic agonists. Pretreatment with 1 mg/kg mecamylamine prior to a high dose of nicotine produced a robust decrease in blood pressure, but this was not observed with cytisine. The $\alpha7$ nicotinic antagonist attenuated the agonist-induced decrease in heart rate without altering other agonist actions.
Conclusions: These data demonstrate that cytisine and varenicline produce partial agonist activity at nicotinic receptors as compared with nicotine, and efficacy rank order is consistent with other in vitro and in vivo paradigms.
Financial Support: These studies were supported by USPHS Grant T32 DA007268 and the University of Michigan Tobacco Research Network.

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FINDINGS FROM A CLINICAL TRIAL OF BUPROPION FOR SMOKERS IN ALCOHOL RECOVERY.

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Aims: The aim of this study was to investigate the incremental efficacy of adding bupropion to transdermal nicotine plus counseling for smokers with a recent history of alcohol dependence.
Methods: 124 subjects were randomly assigned to either 300-mg bupropion or placebo for 8 weeks, including a 1 week prequit period. In order to be eligible, prospective subjects had to smoke at least 10 cigarettes per day and have between 2 and 12 months of alcohol abstinence at the time of enrollment. All subjects received the nicotine patch for 7 weeks and 7 weekly counseling sessions, including 1 prequit counseling session. Self-reported smoking abstinence was biochemically confirmed via carbon monoxide level at end-of-treatment (7 weeks following a subject's scheduled quit day) and cotinine level at subsequent follow-up assessments 11 weeks and 26 weeks after the end of treatment. Sociodemographic characteristics of subjects are: 82% male, 69% white; mean age was 42.4 (SD=9.6). Subjects smoked 20.8 (SD=11.2) cigarettes per day, were moderately nicotine dependent, 89% had a past year history of severe alcohol dependence; the mean number of months of alcohol/other drug abstinence at time of enrollment was 4.2 (SD=3.0).
Results: Overall quit rates at weeks 7, 11 and 26 week follow ups were 20.2%, 11.3%, and 8.9%. To examine the effect of treatment within the context of other covariates, we ran repeated measures analyses using Generalized Estimating Equations with 7-day point prevalence abstinence at each follow up as the dependent variable. Differences between groups were not statistically significant (odds ratio = 0.97, CI = 0.90 – 1.05). There was also no evidence that active medication preferentially benefitted more dependent smokers or smokers with more depressive baseline symptoms. Number of months of alcohol and other drug abstinence did not predict outcome.
Conclusions: Findings do not support the addition of bupropion to the nicotine patch to enhance smoking outcomes in this population.
Financial Support: Supported by NIDA Grant # 5R01DA017370

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THE ABILITY OF INITIAL URINE DRUG SCREEN RESULTS TO IDENTIFY GOOD PROGNOSIS PATIENTS AMONG INDIVIDUALS ADDICTED TO BOTH COCAINE AND ALCOHOL.

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Aims: Cocaine dependent patients who enter treatment with a benzoylecgonine (BE) negative urine drug screen (UDS -) have been shown to have a better prognosis than patients who enter treatment with a BE positive urine drug screen (UDS +). UDS - patients are more likely to complete treatment and more likely to achieve a period of cocaine abstinence, compared to UDS + patients. UDS - patients may therefore be more suitable for treatment with relapse prevention medications. Until now UDS - patients have only been identified in trials in which cocaine abstinence was not required prior to entry. Whether or not patients compelled to have a BE negative drug screen will have the same baseline characteristics and the same good prognosis as patients who become UDS - without being compelled to do so is not known.
Methods: Baseline characteristics of cocaine dependent patients from two recent cocaine pharmacotherapy trials were compared. In one trial, a negative urine drug screen was required prior to entry and patients were given up to 3 weeks to accomplish this (N=170). In the other trial, patients were not required to be cocaine abstinent and 92 completed a two-week baseline UDS -, and 82 entered treatment UDS positive. Baseline characteristics and response to treatment of the three groups were compared.
Results: Preliminary results suggest that patients required to submit a BE negative urine drug screen in order to enter treatment have similar baseline characteristics and the good prognosis of UDS - patients who are not compelled to submit a negative drug screen prior to starting treatment. Both groups of UDS - patients had lower cocaine dependence severity, lower cocaine withdrawal scores and submitted more BE negative urines during their treatment compared to UDS + patients.
Conclusions: Preliminary analyses indicate that entering treatment UDS - may be less influenced by motivational factors and more reflective of cocaine dependence severity.
Financial Support: NIAAA R01 AA014657 and NIDA P50 DA012756

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VIVIDNESS OF MENTAL IMAGERY (TRAIT ABSORPTION) AND IMPULSIVITY (TRAIT CONSTRAINT) PREDICT SELF-REPORTED CONSUMPTION OF CANNABIS IN HEALTHY VOLUNTEERS.

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Aims: Aim: This study investigated the correlation between trait Absorption and Constraint ratings on drug usage in a healthy sample of males and females 18-35 years old. Background: Absorption is "a full commitment of available perceptual, motoric, imaginative and ideational resources to … [an] attentional object"; and involves a heightened sense of the reality of the attended object, imperviousness to distraction, and an altered sense of reality (Tellegen and & Atkinson, 1974). Although personality traits such as impulsivity, extraversion, social inhibition, inquisitiveness, and nonconformity have been linked to drug use, few studies have considered the relationship between absorption and drug use. Studies investigating this trait find that it modulates the experience of drugs acutely, for instance, individuals with high absorption report greater positive subjective effects and greater drug desire after consumption of low and moderate doses of d-amphetamine (White et al, 2006).
Methods: Method: The present study investigated whether trait absorption is related to drug consumption in the real world, as assessed by interviewer query of drug use patterns in a sample of 69 healthy volunteers aged 18-35. Personality was assessed using the brief form of the Multidimensional Personality Questionnaire (MPQ-BF) (Patrick et al, 2002).
Results: Results: In a sample of 69 participants, Trait Absorption was positively related to self-reports of lifetime amounts of cannabis used (0 = never, 1 = 1-50 times, 2 = 51+ times; $r = +.23$, $p < .05$), and Trait Constraint was negatively related to self-reports of lifetime amounts of cannabis used (0 = never, 1 = 1-50 times, 2 = 51+ times; $r = -.35$, $p \leq .005$).
Conclusions: Conclusion: These data indicate that traits of absorption and constraint are likely related to self-reported lifetime cannabis consumption in healthy young adults.
Financial Support: Supported by National Institute on Drug Abuse (NIDA) grant DA020725.

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HUMAN MDMA USE IS ASSOCIATED WITH CHRONIC ALTERATIONS IN CEREBELLAR ACTIVATION DURING A MOTOR TASK: AN FMRI STUDY.

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Aims: MDMA (3,4-methylenedioxymethamphetamine) produces long-lasting changes in brain serotonin (5-HT) function. 5-HT innervates cerebellum and motor function is chronically altered by MDMA. We predicted that MDMA use would alter cerebellar neurophysiology during motor task performance.
Methods: We used fMRI to study cerebellar activation (as intensity and spatial extent) in 24 subjects (14 abstinent MDMA users and 10 controls) during performance of a visually-cued finger tapping task (1, 2 or 4 taps) using the right index finger. Cerebellar regions of interest were (bilateral III, IV-V, VI, VII, VIII, IX, X, Crus 1 and Crus 2).
Results: There was no difference in reaction time between groups. The MDMA group had lower signal intensity during Tap 1 bilaterally in VII (Left [L]: p=0.02; Right [R]: p=0.01), Crus 2 (L: p=0.01; R: p=0.02), R III (p=0.02), R IV-V (p=0.01), R VI (p=0.02), and L VIII (p=0.01). The MDMA users showed greater spatial extent of activation than controls in bilateral VI (L: p=0.04; R: p=0.03) for Tap 2 and L VI (p=0.02) and L Crus 1 (p=0.03) for Tap 4. After controlling for other drug use and age, lifetime MDMA use was positively correlated with activation in multiple regions. For signal intensity, MDMA use correlated positively with L VII(r=0.98, p=0.02), R VIII (r=0.96, p=0.04), R Crus 1 (r=0.98, p=0.02), R Crus 2 (r=0.96, p=0.04) for Tap 2 and R IV-V (r=0.98, p=0.02), R VII (r=0.97, p=0.04), R VIII (r=0.97, p=0.03), R Crus 1 (r=0.96, p=0.04), R Crus 2 (r=0.99, p=0.001) for Tap 4. For spatial extent, MDMA use correlated positively with R IV-V (r=0.98, p=0.03) and R VI (r=0.97, p=0.03) for Tap2.
Conclusions: In conclusion, MDMA users had lower activation intensity for lower demand and greater spatial activation for higher demand compared to controls. Overall, lifetime MDMA use correlated positively with brain activation. These results suggest that MDMA may chronically alter cerebellar neurophysiology, resulting in changes in excitatory threshold and neural efficiency.
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PREDICTORS OF OPIATE USE FOLLOWING OPIOID DETOXIFICATION.

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Aims: (1) To examine the impact of Intensive Role induction (IRI), IRI plus Case Management (CM) and Routine orientation (RC) on engagement indicators at 1-month follow-up; (2) To examine the impact of engagement strategy and indicators of engagement on opiate use at follow-up.
Methods: Applicants to a 30-day buprenorphine detoxification ($N = 239$) were randomly assigned to: RC; IRI (i.e., weekly individual sessions during detox focused on post-detox retention); or CM (i.e., case management added to IRI). Distress (Beck Hopelessness Scale), Motivation and Counselor Rapport (TCU Client Evaluation of Self and Treatment) were assessed at 1-month. Opiate use was assessed from results of urine drug screens at 3 months or by self report at 6 and 12 months. Session attendance during detox and days retained in treatment following detox were assessed.
Results: At 1-month follow-up, IRI ($\underline{M} = 6.1$, $SD = 1.3$; $p = .012$), but not CM ($\underline{M} = 5.7$, $SD = 1.2$; $p > .05$), participants rated counselor rapport as significantly higher than RC ($\underline{M} = 5.5$, $SD = 1.4$) participants. IRI participants were marginally less likely than RC participants to be opiate-positive at 3-months (OR = .47; $p = .052$). In prior research, IRI participants achieved longer post-detox retention than RC participants (Katz et al., 2009). Thus, post-detox retention (OR = .68; $p = .005$) mediated the association between engagement strategy (Step 1: OR = .47; $p = .052$; Step 2: OR = .85; $p = .71$) and opiate use at 3 months. Session attendance was marginally associated with a lower likelihood of opiate use at 6-months (OR = .76; $p = .051$). There were no significant predictors of opiate use at 12 months.
Conclusions: The finding of improved rapport, combined with earlier findings of greater post-detox retention by IRI participants, suggests that IRI is effective for laying a foundation for treatment engagement but is not, by itself, effective for producing long-term behavior change.
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LONG-TERM MEMORY OF CUE-INDUCED INCENTIVE LEARNING IS DEPENDENT ON THE NNOS GENE AND CREB.

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Aims: The formation of drug-associated contextual and cued LTM plays a major role in the development of drug addiction. We investigated the roles of the nNOS gene and the transcription factor cyclic AMP-response element binding protein (CREB) in the formation of LTM of context- and cue-dependent incentive learning in two distinct paradigms involving: drug reward (experiment 1) and footshock (experiment 2).
Methods: In experiment 1, WT and nNOS KO mice were conditioned by cocaine (20mg/kg) in a distinct context containing a visual light cue (modified conditioned place preference [CPP] paradigm). In experiment 2, mice of both genotypes were conditioned by footshocks paired with a distinct context and a light cue. Subsequently, mice were tested for preference for the cocaine-associated context and cue (exp. 1) or freezing response to the footshock-associated context and cue (exp. 2). The expression of CREB and phosphorylated CREB (pCREB) were investigated in naïve mice as determinants of LTM formation and synaptic plasticity
Results: WT mice acquired robust context- and cue-dependent LTM in both paradigms. Namely, WT mice exhibited preference for the context and cue that had been associated with cocaine administration, and freezing response to the context and cue associated with footshock administration. nNOS KO mice acquired normal context-dependent LTM in both paradigms but, in contrast, did not acquire cue-dependent LTM. Hippocampal and amygdalar CREB expression was similar in both genotypes, however pCREB was significantly higher in naïve nNOS KO than WT mice.
Conclusions: Results demonstrate first, the dissociation between context- and cue-dependent incentive learning in a novel CPP paradigm and second, the role of the nNOS gene and pCREB in cue-dependent a) cocaine-induced conditioned behavior and b) cue-dependent fear conditioning. Thus, similar mechanisms may underlie the formation of LTM of cue-dependent appetitive and aversive learning. Overexpression of pCREB in the absence of the nNOS gene may hinder cue-dependent LTM formation.
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PREDICTORS OF TREATMENT ENTRY IN A SAMPLE OF METHADONE MAINTENANCE PATIENTS.

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Aims: To examine baseline differences in ASI problem severity, motivation, and attitudes toward methadone between individuals in and out of treatment.
Methods: 350 opioid-addicted individuals entering treatment and 164 opioid-addicted individuals not entering treatment were administered the Addiction Severity Index (ASI), Texas Christian University (TCU) Motivation scales, and Attitudes Toward Methadone questionnaire at baseline. Logistic regression analyses were conducted to investigate whether scores on the seven ASI composites, three Motivation scales (Problem Recognition, Desire for Help, and External Pressures), and the Attitudes Toward Methadone scale predicted group membership.
Results: Four of the seven ASI composites were associated with group membership. Individuals who showed greater problem severity on the Employment, Drug, and Legal composites were less likely to be entering treatment (all ps < .01), while individuals showing greater problem severity on the Psychiatric composite were more likely to be entering treatment ($p < .05$). Additionally, individuals who scored higher on the Desire for Help scale were more likely to enter treatment, as were individuals who were more positive toward methadone (both ps < .001).
Conclusions: Individuals entering treatment appear to have less severe drug, legal, and employment problems and more severe psychiatric problems than individuals not entering treatment, greater interest in help-seeking, and a more positive attitude toward methadone treatment. This constellation of differences suggests that outreach efforts to attract out of treatment opioid addicts into treatment must have multiple foci.
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NEUROBEHAVIORAL EFFECTS OF INTRANASAL D-AMPHETAMINE.

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Aims: This study tested the hypotheses that the onset and magnitude of behavioral and cardiovascular effects of d-amphetamine would be enhanced following intranasal relative to oral administration and that regional changes in brain activation associated with neurobehavioral effects of intranasal d-amphetamine could be identified.
Methods: A double-blind, double-dummy, placebo-controlled, randomized design was first used to compare the effects of intranasal and oral d-amphetamine (0, 16, 24 and 32 mg), followed by a double-blind placebo-controlled, randomized study to examine the time course of neurobehavioral effects of intranasal d-amphetamine in 6 healthy volunteers. Intranasal d-amphetamine solution was administered using a mucosal atomization device. Assessments were conducted before, and at regular intervals following drug administration, and included self-reported drug-effect questionnaires, cardiovascular indices, a psychomotor performance task, and two measures of impulsivity/reward seeking. Neurobehavioral effects were determined using fMRI and self-reported drug-effect questionnaires.
Results: ANCOVA analyses indicated prototypical d-amphetamine-induced stimulant effects (e.g., increased subject ratings of Stimulated and Like Drug, elevated heart rate and blood pressure, and improved rate and accuracy on the DSST) irrespective of dose, but the onset of these effects was generally earlier following intranasal administration, with significant effects emerging at 15-30 minutes after intranasal dosing and 45-60 minutes after oral dosing. Analysis of the fMRI data is ongoing.
Conclusions: This investigation directly compares the neurobehavioral effects of a common stimulant medication administered via a traditional oral therapeutic route with intranasal administration (a route associated with nonmedical use). Additional analyses of regional brain activation associated with the behavioral effects of intranasal d-amphetamine will be presented to further elucidate processes associated with this route of administration.
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EFFECT OF COCAINE DOSE AND SEX IN SELECTING BETWEEN FOOD AND COCAINE.

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Aims: Sex differences in the profile of cocaine dependence have indicated that women relative to men transition faster from first use to entering treatment and report shorter cocaine-free periods. In addition, female rats relative to males display greater propensity to acquire cocaine self-administration and show enhanced cocaine self-administration under a progressive ratio schedule. Given that males and females exhibit differences in their response to cocaine, we reasoned that they should exhibit differences when presented with a choice between food and cocaine. To address this issue, we examined male and female rats during forced selection of either food or cocaine.
Methods: Rats were trained to respond on the "food" lever for food and were trained to respond on the "cocaine" lever for cocaine (0.4 or 1.0 mg/kg/0.1 ml infusion/4 sec) on a FR1 (20s TO) schedule - during training only 1 lever was extended with the available lever and reinforcer alternating between successive days. After training, rats completed "discreet-trial tests" during which both levers were extended and rats could choose between the two reinforcers.
Results: When presented with the choice between food and cocaine (0.4mg/kg/inf) females earned significantly more cocaine infusions than males; with males predominately selecting food over cocaine. Conversely, preliminary data indicates that males will choose a higher dose of cocaine (1.0 mg/kg/infusion) over food during discrete trials.
Conclusions: The present findings indicate that sex modulates the relative motivation for cocaine and food under forced choice conditions and that the sex difference appears to be cocaine dose dependent. Accordingly, it appears that females are more sensitive than males to cocaine reinforcement relative to food reinforcement with females, but not males, forgoing food reinforcement for even small amounts of cocaine.
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PERSISTENT NONMARIJUANA DRUG USE TRAJECTORIES AND GENERAL HEALTH STATUS AMONG ADULTS FOLLOWED OVER 18 YEARS (THE CARDIA STUDY).

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Aims: Characterizing long-term health outcomes of drug use in general population samples is difficult because use often declines with age and long-term follow-up is rare. The Coronary Artery Risk Development in Young Adults study (CARDIA) allowed us to test if the longitudinal trajectory of nonmarijuana drug use was associated with worse general self-reported health at 18-year follow-up in a 4-city sample, and to assess whether tobacco or alcohol use explained such associations.

Methods: Past month drug use was assessed at 3-5 year intervals in a biracial cohort of adults (n=4301) from 1987/88 (aged 20-32) to 2005/06 (aged 38-50). Participants were sorted into groups based on their longitudinal drug use trajectory with semiparametric group-based statistical models. We compared drug trajectories for the outcome of general self-reported health (Excellent, Very Good, Good, Fair and Poor). Converting the health outcome to a numerical value using standard techniques (Diehr et al), statistical models adjusted for demographics, alcohol, tobacco, and multiple baseline measures of health and psychosocial vulnerability.

Results: Four trajectory groups emerged: Current Non-Users (n=3691), Brief Early Occasional Users (n= 340), Persistent Occasional Users (n= 160), and Early Frequent/Late Occasional Users (n=110). At 18 years, Persistent Occasional Users most likely to report Fair or Poor Health (22.4%, versus <15% for all other groups, p<.001). Adjusting for health and psychosocial characteristics at baseline, Persistent Occasional Users remained more vulnerable to this outcome. However, the association was rendered nonsignificant after controlling for tobacco and alcohol use at last follow-up.

Conclusions: Among young to middle-aged adults in the general population, nonmarijuana drug use trajectory was not associated with worse general health status 18 years later, after controlling for tobacco and alcohol in middle age.

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BLOOD LEVELS OF FLUOXETINE IN RHESUS MONKEYS AT DOSES THAT ATTENUATE THE ABUSE-RELATED EFFECTS OF COCAINE.

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Aims: Fluoxetine, a selective serotonin reuptake inhibitor, has been investigated as a potential medication for cocaine abuse. While it shows promise in preclinical, acute dosing regimens, it has not been successful in clinical trials using chronic dosing. Fluoxetine is known to have a long half-life, and thus the blood levels may differ between acute and chronic dosing. However, the pharmcokinetics of fluoxetine in rhesus macaques are not known. The aim of this study was to describe the pharmacokinetics of both acute and chronic doses of fluoxetine that are able to suppress the abuse-related effects of cocaine.

Methods: Female rhesus macaques (n=2) were administered (i.m.) doses of fluoxetine that suppress cocaine self-administration and reinstatement, and blood levels were measured for the next 24 hours. Subsequently, the highest dose (5.6 mg/kg) was administered (s.c.) for 6 consecutive days, followed by an additional 6 days of blood monitoring.

Results: Following acute injections, peak fluoxetine levels at 1.0, 3.0 and 5.6 mg/kg were 31 ng/ml at 15 minutes, 70 ng/ml at 30 minutes, and 165 ng/ml at 60 minutes, respectively, and then declined at subsequent time points. However, as fluoxetine levels declined, the level of norfluoxetine, the active metabolite, increased. When fluoxetine and norfluoxetine levels were summed, total levels remained stable with no decline even at 24 hours post injection. During chronic dosing, combined fluoxetine/norfluoxetine levels steadily increased beyond the levels seen after a single injection and declined over the course of several days following the end of drug treatment. Blood levels comparable to human therapeutic levels were observed.

Conclusions: These data highlight two important considerations for the use of fluoxetine in preclinical drug studies: 1) dose accumulation across several days is needed in order to achieve human therapeutic levels, and 2) the significant levels of fluoxetine/norfluoxetine evident even after 24 hours could affect behavioral or neurochemical measures post-treatment.

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BRAZILIAN CRACK USERS WHO SEEK TREATMENT SHOW MORE ANTISOCIAL PERSONALITY AND LESS DRINKING THAN OTHER DRUG USERS.

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Aims: to evaluate psychiatric comorbidities and the severity of alcohol and other problems among Brazilian crack users.

Methods: A cross-sectional multi-center study was conducted in 4 Brazilian state capitals. Each center interviewed 150 adult patients from in- and outpatient clinics, yelding a total of 740 substance abusers. Quality was ensured due to extensive training, local oversight and support provided to the field interviewers. Subjects were evaluated with the sixth version of the ASI and MINI-Plus. From the original sample, 293 crack users were compared to 126 cocaine users and 324 patients that used alcohol or other drugs. All subjects used these drugs in the last 30 days.

Results: crack and cocaine users were significantly younger than others (31.1 ± 8.1, 32.9 ± 8,8 and 42.4 ± 12, respectively - p<0.001). The group of crack users presented more individuals (28 – 25%) with antisocial personality than cocaine users (3 – 9%) and other drug users (9%), even when adjusted for age and gender, with an OR of 2.73 (IC95%: 1.10-6.76). As for ASI composite scores, crack users had significantly more occupational, family and legal problems mainly due to drug traffic and robbery. However, they had less alcohol problems (51.9 ± 10.3) than cocaine users (55.7 ± 9.3) and other drug users (59.6 ± 9.2), p<0.001.

Conclusions: Our results suggest that crack users have a higher prevalence of antisocial disorder which could explain the several legal problems related to this population. The extensive brain damage caused by crack and its withdrawal symptoms may also be associated to the impulsive and aggressive behavior. This is the first study that shows this association in a Brazilian multi-center sample. Other studies in the literature also pointed that severe crack users drink less than other substance abusers but more studies required to confirm these data.

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PERCEPTIONS OF ALCOHOL STIGMA: CONSEQUENCES FOR TREATMENT UTILIZATION IN A GENERAL POPULATION SAMPLE.

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Aims: Despite advances in the efficacy of treatments for alcohol disorders, individuals in need of such treatment are unlikely to seek care. Perceived stigmatization of alcoholism has been hypothesized to reduce treatment utilization, but has not previously been tested empirically. We tested whether perceived stigmatization of alcoholism was associated with lower likelihood of alcohol service utilization.

Methods: Data were drawn from an epidemiologic survey of 34,653 adults aged 20 years and older residing in households and group quarters in the United States. DSM-IV alcohol abuse and dependence were diagnosed from in-person AUDADIS-IV interviews. Stigma was operationalized with the Perceived Devaluation Scale.

Results: Individuals with a lifetime diagnosis of an alcohol use disorder were less likely to utilize alcohol services if they perceived higher stigma for alcohol disorders (OR=0.37, 95% C.I. 0.18-0.76). These results held for self-help (e.g., 12-step) (OR=0.63, 95% C.I. 0.49-0.81) as well as professional (OR=0.68, 95% C.I. 0.53-0.88) service utilization. Individuals with closer contact with an alcohol disordered individual (formerly married or living with someone with an alcohol problem, family history of an alcohol problem) reported lower perceived stigma.

Conclusions: Perceived stigma of alcohol disorders is a barrier to receiving alcohol services among those in need. Drug disorders are also highly stigmatized and treatment services are underutilized; further research on the impacts of stigma, and effective interventions to reduce stigma, are needed.

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WHAT'S WITH THAT KID? THE RELATIONSHIP BETWEEN FAMILIAL SUBSTANCE USE AND CHILD BEHAVIOR PROBLEMS IN A GENERAL PEDIATRIC SETTING.

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Aims: The relationship between substance use and ADHD has received much attention. Research has shown that adolescents diagnosed with ADHD are more likely to experiment with drugs and alcohol at an earlier age (Wilens & Biederman,2006), and more likely to develop substance use disorders (SUDs)(Schubiner et al, 2000). Research has also found that both SUDs and ADHD run in families(Merikangas et al 1992; Biederman et al, 1992). Although the co-morbid occurrence of ADHD and SUDs has been studied,less is known about the association between parental SUDs and ADHD in offspring.The majority of research has looked at parents sampled through SUD treatment where co-morbidities are more prevalent.The present study examined the relationship between familial alcohol problems and behavior disorders (eg ADHD,ODD)in low SES children attending an urban pediatric clinic.
Methods: Study participants were 159 biological parents of children seeking pediatric care. Participants completed a brief research interview with measures of demographics, family stressors, parental and grandparent SUDs and child behavior problems (Vanderbilt Child ADHD Scale, Parent Form).Families were categorized as FHP (alcoholism in 1+ parents and/or grandparents) or FHN (no alcoholism in parents/grandparents). Target children were then compared for ADHD diagnosis (present/absent) using chi-square.
Results: Demographically,participants were primarily female (93%), African-American(90%),and never married (64%),with a mean age of 33 years(SD=6.5). Chi-square results found that FHP children were almost twice as likely to manifest behavior problems congruent with ADD diagnosis than FHN children (38% vs 20%,p<.05). Further,FHP children were more likely to exhibit behavior problems meeting diagnostic criteria for Oppositional Defiant Disorder(ODD),(23% vs 10%, p<.05).
Conclusions: Study findings provide additional evidence for the relationship between substance use and behavior problems. Further exploration of the relationship between familial history of substance misuse and child behavior is warranted.
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INCARCERATION AND SEXUALLY TRANSMITTED INFECTION/HIV IN BUSHWICK, BROOKLYN, NY: A SOCIAL NETWORK PERSPECTIVE.

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Aims: The aim of this study was to describe the association between incarceration and STI/HIV from a social network perspective.
Methods: We used data collected during a social network study conducted in Brooklyn, NY(N=343) to measure associations between incarceration and infection with herpes simplex virus-2, chlamydia, gonorrhea, syphilis, or HIV (STI/HIV) and sex with an STI/HIV-infected partner, adjusting for respondent characteristics.
Results: Substantial proportions of respondents had been incarcerated (40%) or recently had sex with a former inmate (55%). STI/HIV was associated with incarceration of <1 year (adjusted PR: 1.33, 95% CI: 1.01-1.76) and ≥1 year (adjusted PR: 1.37, 95% CI: 1.08-1.74). Sex in the past 3 months with an STI/HIV-infected partner was associated with sex in the past 3 months with 1 partner (adjusted PR: 1.42, 95% CI: 1.12-1.79) and ≥2 partners (adjusted PR: 1.85, 95% CI: 1.43-2.38) who had ever been incarcerated.
Conclusions: The results highlight the need for STI/HIV treatment and prevention for current and former prisoners and provide preliminary evidence to suggest that incarceration may influence STI/HIV, and that this may occur because incarceration increases risk of sex with infected partners.
Financial Support: Supported by NIDA 5T32 DA07233.

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DO RACE AND SEX ALTER THE ASSOCIATION BETWEEN NON-MARIJUANA DRUG USE TRAJECTORIES AND DEPRESSIVE SYMPTOMS IN A COMMUNITY-BASED ADULT COHORT? (THE CARDIA STUDY).

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Aims: Illicit drug use often co-occurs with depressive symptoms and can worsen mental health over the life course. There are race/sex differences in illicit drug use among young adults. This study assessed whether race and sex modify the association between non-marijuana drug use and depressive symptoms.
Methods: Repeated measures of drug use were collected in the Coronary Artery Risk Development in Young Adults (CARDIA) study, a cohort of 4861 healthy young adults (balanced for race, gender, and education) assessed in 1987-88 and followed for 18 years. SAS PROC TRAJ was used to iterate drug use trajectories based on repeated measures of self-reported recent (last 30 days) cocaine, opiate and amphetamine use over 18 years. We tested whether drug use trajectories were associated with depressive symptoms (≥16 on CES-D scale) at Year 18, and whether race/sex moderated the associations found, controlling for other psychosocial characteristics.
Results: Four trajectory groups emerged: Current Non-Users (n=3691), Brief Early Occasional Users (n= 340), Persistent Occasional Users (n= 160), and Early Frequent/Later Occasional Users (n=110). More African Americans (AA) had CES-D ≥ 16 than European-Americans (EAs) at 18 years' follow-up (24% of AA men, 20% of AA females, compared to 15% of EA men and 13% of EA women) (p<0.001). In unadjusted comparisons, AA female Persistent Occasional Users and Early Frequent/Later Occasional Users had the highest mean CES-D scores over all four assessments. The Early Frequent/Later Occasional Users had higher odds of CES-D ≥16, in adjusted analyses (OR=1.9, 95%CI=1.03-3.49). However, this association was not statistically modified by race or sex.
Conclusions: Early Frequent/Later Occasional non-marijuana drug use was associated with later self-reported depressive symptoms in both EA and AA, and this association did not differ by race or sex.
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REDUCING DRUG USE AND OTHER RISK BEHAVIORS IN SYRINGE EXCHANGE PARTICIPANTS.

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Aims: Participation in syringe exchange programs (SEPs) is associated with reductions in the use and sharing of non-sterile syringes and related injection equipment, and with lower incidence of HIV seroconversion. Unfortunately, this intervention is not associated with reduced drug use. The continuation of high frequency drug use in this population sustains an elevated risk of transmitting HIV and other blood-borne diseases to self and others. The enrollment of SEP participants in substance abuse treatment has the potential to lower the frequency of drug use and other high-risk behaviors in injection drug users. The present study evaluated the effects of methadone maintenance on rates of drug use, injection use behaviors, and illegal activities in SEP participants.
Methods: This study was part of a larger evaluation of strategies to increase substance abuse treatment enrollment in SEP participants (Kidorf et al., 2009). T-tests compared SEP subjects enrolling in methadone maintenance (n = 70) to those that failed to enroll in any treatment (n = 113) on days of opioid and cocaine use, days of injection drug use, and days of illegal behavior and incarceration over a 4-month period. Analyses were conducted in subjects that completed all follow-ups (75% of the sample). The average duration of treatment exposure for subjects enrolled in methadone maintenance was 67 days.
Results: Results showed that SEP subjects enrolled in treatment reported fewer days of opioid (51 vs. 92 days; p < .001) and cocaine (36 vs. 55 days; p < .01) use, less days of injection behavior (54 vs. 89 days; p < .001), and less days of illegal activity (15 vs. 25 days; p < .05), and incarceration (3 vs. 10 days; p < .01) than SEP subjects not enrolled in treatment. Additional analyses evaluate the independent and combined effects of days in treatment and use of the SEP on outcomes.
Conclusions: The preliminary findings suggest that opioid-agonist treatment significantly expands the harm reduction benefits of SEP participation.
Financial Support: This study was supported by research grant R01 DA 12347 (M. Kidorf, PI) from the National Institute on Drug Abuse.

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MODIFIED THERAPEUTIC COMMUNITY APPROACH IN PARTIAL-DAY OUTPATIENT SUBSTANCE ABUSE TREATMENT: ATTENDANCE, RETENTION, AND COMPLETION.

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Aims: Phoenix Programs, Inc. provides a continuum of substance abuse treatment services to rural populations in Missouri. This study hypothesized that integrating the Modified Therapeutic Community (MTC) approach with a rural, partial-day outpatient substance abuse treatment program would affect attendance, retention, and completion positively.
Methods: In 2009, the MTC philosophy and approach, which uses the peer community as an agent of healing, and which incorporates a variety of activities (e.g., community meetings, psychoedcuational groups, relapse prevention), was integrated with a partial-day outpatient substance abuse treatment program. Cross-sectional analysis compared two groups, one constituted in 2008 (n=22), the other constituted in 2009 (n=27). The study examined the number of days participants attended, the number of participants, and the number of individuals who completed the program.
Results: The average number of days that participants attended partial-day outpatient treatment more than doubled, from 5.79 days in 2008 to 11.86 days in 2009. Average group size increased 69%, from 6.6 participants in 2008 to 11.18 participants in 2009, and the number of completers tripled, from 6 in 2008 to 18 in 2009. Counselors reported that participants became more involved in their treatment, reported feeling more empowered, and developed strong peer support networks. A positive impact on the treatment culture of the entire agency was also noted.
Conclusions: The results indicate that integrating the MTC approach with partial-day outpatient treatment improves attendance, retention, and completion, increasing the potential for long-term individual success.
Financial Support: Support provided by the Missouri Department of Mental Health.

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EFFECTS OF REPEATED DISULFIRAM ADMINISTRATION ON THE BEHAVIORAL-STIMULANT EFFECTS OF COCAINE IN SQUIRREL MONKEYS.

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Aims: Antabuse (disulfiram, DS) has been used effectively to treat alcoholism but recent clinical studies have shown that DS also has efficacy in reducing craving for cocaine in cocaine-dependent alcoholic and nonalcoholic patients. The mechanism for this effect is thought to be via DS inhibition of dopamine-β-hydroxylase, the enzyme responsible for the conversion of dopamine to norepinephrine. In rodents, acute administration of DS results in a decrease in norepinephrine and a subsequent increase in tissue dopamine levels. However, the continued decrease in noradrenergic drive following repeated DS administration results in decreased dopamine release. Repeated administration of DS also enhances the locomotor-stimulant effects of cocaine. The effects of DS on the neurochemical and behavioral effects of cocaine have not been reported in non-human primates. The aims of this study were to determine the these effects of acute and chronic treatment with DS alone and in combination with cocaine in squirrel monkeys.
Methods: In vivo microdialysis was used to determine changes in caudate dopamine levels following systemic DS administration. Behavioral-stimulant effects of drugs were measured using a fixed interval schedule of stimulus termination. The effects of acute cocaine were determined before and after 5d of treatment with 10 mg/kg DS.
Results: While acute DS produced a slight but significant decrease in extracellular dopamine in the caudate, it did not alter baseline behavior or the behavioral-stimulant effects of cocaine. However, repeated treatment with DS significantly increased the behavioral-stimulant effect of cocaine (0.1 mg/kg).
Conclusions: These results suggest that repeated, but not acute, treatment with DS may affect the sensitivity to the behavioral properties of cocaine.
Financial Support: This work was supported by U.S. Public Health Service grants DA00517, DA12514, and RR00165.

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PSYCHIATRIC DISTRESS PREDICTS TREATMENT ENROLLMENT IN SYRINGE EXCHANGE PARTICIPANTS.

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Aims: The present study evaluated psychiatric distress as a predictor of treatment enrollment in out-of-treatment injection opioid users newly registered at the Baltimore Needle Exchange Program (BNEP).
Methods: Study participants (n = 281) completed the Addiction Severity Index (ASI) and the Symptom Checklist-90-Revised (SCL-90-R), and were randomly assigned to one of three different conditions for 4-months that evaluated referral strategies designed to promote substance abuse treatment interest and enrollment. The Global Severity Index (GSI) of the SCL-90-R was used as a measure of psychiatric distress. The 4-month follow-up period used in this analysis corresponded to the duration of the study interventions.
Results: Study participants were on average 41.0 (SE = .51) years old, were more likely male (71.2%), Non-white (75.4%) versus Caucasian (24.6%), unmarried (89.7%), and reported 11.4 (SE = .11) years of education. Overall, 40% of participants (n = 115) enrolled in substance abuse treatment during the study period. Logistic regression analysis demonstrated a main effect for GSI scores as a predictor of enrollment: participants with high GSI scores were more likely to enter treatment (51.7% enrollment) than those with low scores (32.6% enrollment) after controlling for study condition, demographic variables, syringe exchange site, and severity of drug use (Adjusted OR = 2.18, CI = 1.13 - 4.19, $p < .05$).
Conclusions: This study is the first to show that psychiatric distress is prospectively associated with treatment acquisition in this population of out-of-treatment injection substance users. The results suggest that the assessment of psychiatric distress at syringe exchange settings can support motivational strategies for encouraging syringe exchange participants to pursue substance abuse treatment.
Financial Support: This study was supported by research grant RO1 DA 12347 (M. Kidorf, PI) from the National Institute on Drug Abuse.

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LESS EFFICIENT PSYCHOMOTOR FUNCTION IN CHRONIC CANNABIS USERS.

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Aims: Cannabis is the most abused illegal substance in the United States. Alterations in brain function, cognition, and motor behavior have been reported in chronic cannabis users, but the results have been variable. The current experiment evaluated psychomotor function in relation to brain activation in chronic cannabis users and controls.
Methods: 29 cannabis users (22 males and 7 females, ages 25.37 ± 1.27 years) were compared to 16 controls (8 males and 8 females, ages 28.34 ± 1.85 years). Each subject performed the Grooved pegboard task with both hands and a finger tapping task during functional MRI scan. All scans were performed on a 3 Tesla Siemens Trio scanner (Erlangen, Germany). The imaging method involved a spectral-spatial RF pulse implemented in a spiral in-out sequence. In the checkerboard task, a round, black and white checkerboard, with a red X in middle was presented at 2 or 4 Hz. The subjects were instructed to sequentially tap the fingers of their left hand every time the checkerboard flashed.
Results: The cannabis users were slower than the control subjects on the pegboard task for both the dominant and non-dominant hand. For the 2 Hz task, the cannabis users had greater activation than controls in BA 7 (-12, -60, 44, z = 2.7) and 19 (-22, -78, 22, z = 3.96). For the 4 Hz task, the cannabis users had greater activation than the controls in BA 4 (-37, -16, 48, z = 4.43) 6 (56, 8, 46, z = 13), 10 (-28, 58, 4, z = 4.67) and 24 (6, 36, 8, z = 4.43).
Conclusions: Chronic cannabis use is associated with slower fine motor speed despite greater brain activation, which is more evident on the more demanding task. Both BA 6 and 24 are important for motor control, particularly in finger sequencing tasks. These findings suggest that chronic cannabis use may decrease the efficiency of psychomotor speed.
Financial Support: This study is supported by: NINDS and NIDA (U54 NS56883-03, 2K24 16170), NCRR (G12RR003061 & P20RR11091), and the U.S. President's Office of National Drug Control Policy.

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PRENATAL STRESS INCREASES COCAINE-SEEKING IN C57BL/6J MICE.

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Aims: Early environmental insults can impact neurodevelopment resulting in elevation of an individual's predisposition to a wide range of neuropsychiatric disorders. In particular, prenatal stress (PNS) has been shown to increase adult responsiveness to stressors and psychomotor stimulant drugs in rats. Here, we examine the impact of PNS in C57BL/6J mice on cocaine-seeking behavior as measured by conditioned place preference (CPP).
Methods: Pregnant dams were subjected to repeated restraint stress (1h, 3 x day) from E14 until birth (PNS) or left undisturbed (control) and cocaine-induced CPP was assessed in the offspring during adulthood. CPP was induced by repeated pairings of cocaine exposure (4 x 10 mg/kg, i.p.) with one of two distinctive compartments of the test apparatus and repeated pairings of vehicle (saline) exposure (4 x 10 mg/kg, i.p.) with the other compartment. Then, each mouse was allowed to move freely between the two compartments and the amount of time spent in the cocaine-paired compartment versus the saline-paired compartment indexed CPP. Next, all mice were subject to a series of extinction trials followed by a cocaine-primed test.
Results: Both control and PNS mice exhibited substantial CPP but the magnitude of the CPP was greater in the PNS mice than controls during both the drug-free and cocaine-primed CPP tests. Conversely, the PNS and control mice did not exhibit differences in locomotion following either initial or repeated cocaine exposure.
Conclusions: Thus, PNS increases cocaine-seeking behavior in mice but does not alter the response to the psychomotor stimulant properties of cocaine. Accordingly, the present finding extends prior operant studies in rats, demonstrating that PNS elevates cocaine seeking in multiple procedures in at least two species of rodents and suggests that early environmental stress is an important factor in determining vulnerability to drug addiction.
Financial Support: Supported by a NARSAD Young Investigator and INIA-Stress pilot project awards (TEK) and NIDA grant DA024038 (KKS).

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QUANTIFICATION OF RISK FOR SUBSTANCE USE DISORDER USING COMPUTERIZED ADAPTIVE TEST FORMAT: A SIMULATION STUDY.

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Aims: Employing a prospective paradigm, the phenotype, spans cognitive, emotion, and behavioral domains of psychological functioning associated with risk for substance use disorder was validated at ages 10-12, 12-14, 16, 19, and 22 in Center for Education and Drug Abuse Research. In this simulation study, a 65-item paper and pencil (P&P) version of the transmissible liability index (TLI) at age 19 was translated into a computer adaptive test (CAT) format to maximize administration efficiency, privacy of responses, reduction of administration time, and elimination of scoring time.
Methods: The P&P and the CAT protocols were derived using item response theory. A sample of 433 subjects were utilized to compare P&P and the CAT protocols.
Results: This simulation study showed that the correlation between two latent traits obtained from P&P and the CAT versions was .95 when the maximum number of items administrated was set to 20. The average number of items administrated was 17 and standard error of estimate was .36. Mean scores of TLI obtained from P&P and CAT protocols were not significantly different (t=-.01, p=.99). The CAT protocol produced significantly lower standard error of estimates than the P&P (t=47.28, p<.001). The latent trait score of P&P and CAT protocols both predicted cannabis use disorder at age 22 with odds ratios of 2.94 (95% CI: 1.87-4.62) and 2.23 (95% CI: 1.47-3.40).
Conclusions: The CAT version of the TLI is valid, reliable, and efficient. The findings support the feasibility of accurately identifying high risk youths for targeted intervention. In addition, the results potentially have heuristic value for research aimed at elucidating the etiology of SUD.
Financial Support: Funding for this research is from the NIH: NIDA (P50-05605, K02DA017822, K02DA018701)

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EFFECTS OF INTRANASAL D-AMPHETAMINE AND METHAMPHETAMINE ADMINISTRATION IN HUMANS.

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Aims: Data from previous studies investigating low, oral doses of methamphetamine and d-amphetamine in humans have indicated that the acute behavioral and physiological effects of the two stimulants are nearly identical. However, there is a dearth of data comparing the two drugs employing a route of administration and dose levels commonly associated with abuse. This ongoing outpatient, within-participant, double-blind study examines the effects of larger doses of intranasal methamphetamine and d-amphetamine on physiological and behavioral measures.
Methods: To date, ten non-treatment seeking methamphetamine users completed the study, which consists of five 2-day blocks of sessions. On the first day of each block, participants completed a sample trial, where they were given one methamphetamine or d-amphetamine dose (0, 12, 50 mg/70 kg) and a monetary reinforcer ($5 or $20). Amphetamines plasma levels, cardiovascular, subjective, and psychomotor performance effects were assessed before drug administration and repeatedly thereafter. On the second day, participants completed one choice trial, where they had the opportunity to work for the sampled reinforcers (drug and money).
Results: Both amphetamines produced dose-dependent increases on cardiovascular and 'positive' subjective-effect measures; the drugs also improved some measures of psychomotor performance. Collapsed across drug conditions, participants selected more drug doses when the non-drug alternative was $5 compared to $20 (31% versus 1%). There were no significant differences between methamphetamine and d-amphetamine on the majority of measures.
Conclusions: These preliminary data are consistent with previous findings investigating oral doses and suggest that these two amphetamines also produce similar acute effects on human behavior and physiology when administered intranasally.
Financial Support: Supported by DA019559 and DA023883-02.

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EFFECT OF D-AMPHETAMINE ON FMRI DURING CUE-REACTIVITY TASK IN COCAINE-DEPENDENT SUBJECTS COMPARED TO CONTROLS.

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Aims: This study examines the effect of 20 mg d-amphetamine or placebo on BOLD activation during cocaine Stroop task in cocaine-dependent subjects (COC) and non-drug using controls (CTL).
Methods: 9 COC and 8 CTL underwent cocaine Stroop task. Subjects were asked to respond to word color during fMRI. D-amphetamine (AMP) 20 mg p.o. and placebo (PLAC) were given during different fMRI sessions to the same subject (double-blind randomized order). BOLD activation (cocaine words condition minus neutral words condition) was compared between groups after PLAC and AMP using SPM8 (FDR corrected cluster p<0.05).
Results: ANCOVA was used with age as a covariate in both analysis of behavior and fMRI activation (mean age COC 40.8 +/-8.6, CTL 28.6 +/-9.0). Response time on cocaine Stroop task was shorter in COC than CTL with PLAC. With AMP dose, reaction time for COC moved closer to CTL response time with PLAC dose. CTL showed little change in reaction time after AMP compared to PLAC.
Activation in COC was decreased compared to CTL during PLAC dose, and showed a different pattern of activation after AMP. Regions with less activation (relative to CTL) after PLAC increased significantly after AMP and were no longer significantly different than CTL.
Conclusions: These results are preliminary, but 20 mg AMP in COC subjects appeared to improve behavioral performance and result in changes in BOLD activation. Improvement in behavioral performance and change in activation pattern after AMP in COC may represent baseline decreased dopaminergic neurotransmission, with a resultant alteration in neurotransmission after AMP. A larger sample of subjects balanced for age is necessary to confirm these findings.
Financial Support: NIDA Grants: P50 DA018197 (Kosten), K02 DA00403 and P50 DA009262 (Moeller)

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EFFECTS OF METHADONE ALONE AND IN COMBINATION WITH ALCOHOL ON COGNITIVE PERFORMANCE IN METHADONE-MAINTAINED VOLUNTEERS.

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Aims: Polydrug abuse is common in opioid abusers, and methadone maintenance patients often use other drugs while in treatment (e.g., alcohol). The combined use of methadone and alcohol might produce impairments in psychomotor and cognitive performance that could negatively impact daily functioning. However, the performance impairing effects of methadone combined with alcohol have not been systematically examined. The aim of the present study was to examine the performance effects of methadone alone and in combination with alcohol.

Methods: Eight opioid dependent volunteers (4 women) aged 31-54, maintained on a stable daily dose of methadone (80 - 100 mg) for at least two weeks, completed six testing sessions in which methadone alone (100% and 150% of daily dose) and each dose of methadone conjointly with each of two doses of alcohol (0.25, 0.50 g/kg) were administered in a double-blind, double dummy, crossover design. Psychomotor and cognitive performance tasks were completed before (baseline) and repeatedly after drug administration.

Results: Preliminary analyses (paired-samples t-tests) comparing baseline to post-drug values during the period of peak effects revealed that although all drug conditions impaired certain aspects of performance (i.e., visual acuity/flicker fusion threshold, divided attention, recognition memory, and working memory), these impairments were generally largest in magnitude and significant (ps < .05) in high dose alcohol conditions. In contrast, other outcomes showed no reliable changes from baseline (e.g., psychomotor and simple reaction time tasks).

Conclusions: The concurrent administration of alcohol with methadone was more detrimental to performance than methadone alone, in particular a dose of alcohol equivalent to approximately 2-3 standard drinks. These decrements have the potential to negatively impact a methadone-maintained patient's daily functioning.

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NOVELTY DETECTION AND RECOGNITION MEMORY AMONG INDIVIDUALS VARYING IN REWARD SEEKING AND IMPULSIVITY.

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Aims: Previous literature has demonstrated that the personality dimensions of reward seeking and impulsivity are associated with the initiation, escalation and development of problems associated with drug use. In this ongoing study, human subjects were recruited based on these personality dimensions, and performance on an old/new recognition memory task was assessed using electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) technology.

Methods: 80 subjects (40 female, 18-30yrs old) were categorized with respect to gender-adjusted scores on the Zuckerman-Kuhlman Personality Questionnaire into one of four groups: low impulsive and reward-seeking, high impulsive and reward-seeking, and high in either impulsivity or reward-seeking while low in the other dimension. During a familiarization session, each subject studied a randomized set of 100 computer-displayed line drawings. Retention of these stimuli was assessed during a practice test during which each subject had to demonstrate > 90% recognition accuracy. During the task, subjects were presented with previously studied (old) and unstudied (new) stimuli, and asked to discriminate between the two by pressing one of two buttons quickly upon stimulus presentation.

Results: Preliminary analyses from the first 64 participants indicated significant interactions between reward seeking and impulsivity on both reaction time and accuracy, with differences in both reaction time and accuracy between low and high impulsive subjects varying as a function of reward-seeking status. Ongoing analysis of the EEG and fMRI imaging data will elucidate the neural substrates of these dimensions.

Conclusions: Presentation of novel stimulus materials engenders differential performance and possibly differential brain responses among individuals varying in reward sensitivity and impulsivity. Future research will determine how novelty detection and recognition memory can be used to enhance treatment and prevention interventions among populations at risk for drug use and abuse.

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COUNSELOR ATTITUDES TOWARD BUPRENORPHINE IN THE CLINICAL TRIALS NETWORK.

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Aims: Research on counselors' perceptions of buprenorphine's effectiveness and acceptability largely occurred in its initial phase of availability. We hypothesized that there are measurable gaps in these attitudes, but that training is positively associated with perceived effectiveness and acceptability.

Methods: Counselors in the CTN were mailed surveys (n = 797; 60% response rate) in 2005-2006. Measures included: perceived effectiveness and acceptability of buprenorphine, buprenorphine-specific training, program-level adoption, and professional/demographic characteristics. Multinomial logistic regression was used to analyze the data.

Results: About 39.2% of counselors perceived buprenorphine to be effective, 38.1% specified they did not know if it was effective, 12.1% indicated it was neither effective nor ineffective, and 10.6% stated it was ineffective. About 51.7% reported that buprenorphine was acceptable, 30.2% chose the "don't know" option, 8.6% indicated it was neither acceptable nor unacceptable, and 9.5% labeled it as unacceptable. Greater training were negatively associated with the odds of reporting that 1) buprenorphine was ineffective, 2) buprenorphine was unacceptable, and 3) choosing the "don't know" option for effectiveness and acceptability. Perceived utility of scientifically supported treatments and program-level adoption of buprenorphine were associated with both perceived effectiveness and acceptability. Other significant covariates of perceived effectiveness included certification/licensure and race/ethnicity, while personal recovery status and 12-step orientation were associated with acceptability.

Conclusions: Substantial proportions of counselors reported that they did not know if buprenorphine was effective or acceptable, suggesting that additional dissemination efforts and training are needed. Such efforts may improve counselor attitudes, given that these data indicated that greater buprenorphine-specific training was positively associated with both perceived effectiveness and acceptability.

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PREFRONTAL-SUBCORTICAL PATHWAYS MEDIATING SUCCESSFUL REGULATION OF CRAVING IN CIGARETTE SMOKERS.

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Aims: To identify brain systems that underlie and mediate effective regulation of craving in cigarette smokers.

Methods: Twenty-one cigarette smokers were scanned while viewing images of cigarettes and food. While viewing these images, participants were instructed to think about either the (a) immediate sensory experience ("craving trials"), or (b) long-term negative physical health implications associated with consuming each item ("regulation trials") - a strategy taught in cognitive-behavioral treatment for substance use disorders. After each trial, participants indicated their level of craving for each item.

Results: We previously reported that participants reported significantly less craving for both cigarettes and food on "regulate craving" trials. This effective down-regulation of craving was associated with activity in regions previously implicated in cognitive control and with regulating negative emotion including dorsomedial, dorsolateral, and ventrolateral prefrontal cortex (PFC). This was accompanied by decreased activity in regions previously associated with craving, including the ventral striatum (VS), subgenual cingulate, amygdala, and ventral tegmental area. Here we report that decreases in craving correlated with decreases in VS activity and increases in dlPFC activity. Importantly, VS activity fully mediated the relationship between dlPFC and reported craving.

Conclusions: These results suggest that effective regulation of craving depends upon the recruitment of systems implicated in cognitive control, and upon modulation of activity in systems implicated in reward, including VS. Further, this study provides a methodological tool and conceptual foundation for studying this ability across substance abusing populations and for developing more effective treatments for substance use disorders.

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MORPHINE-INDUCED MOTOR STIMULATION AND MOTOR INCOORDINATION: AGE-RELATED DIFFERENCES IN MICE.

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Aims: Given evidence for age-related differences in effects of drugs of abuse, surprisingly few preclinical studies have explored effects of opioids in adolescents (versus adults). The present study compared the motor stimulating and ataxic effects of morphine in adolescent and adult mice.
Methods: Adolescent (post-natal day 29), late adolescent (post-natal day 44), and adult (post-natal day 64) male C57BL/6J mice were used. Locomotion was measured during two 2 h periods, one 24 h before and one immediately after i.p. administration of drug or vehicle. Ataxia was measured in the horizontal wire test, before and after drug administration.
Results: Morphine (3.2 – 56 mg/kg) increased locomotion along an inverted U-shaped dose-response curve in adolescent, late adolescent, and adult mice. In all age groups, the minimum effective dose to enhance locomotion was 10 mg/kg, and maximal stimulation was observed at 17.8 mg/kg. However, maximal stimulation was significantly higher in adolescents than in adults. In contrast, adolescents showed significantly less ataxia than adults when given morphine (5.6 – 100 mg/kg). Morphine-induced motor stimulation and ataxia did not differ significantly between late adolescents and adults.
Conclusions: The finding that adolescent mice show larger locomotor-stimulating effects of morphine than adults is consistent with previous findings in rats. This might indicate that adolescent animals are more sensitive to motor stimulating effects of morphine. Alternatively, larger locomotor effects of morphine in adolescent animals could be due to less interference by its ataxic effects. Thus, it is possible that morphine-induced motor stimulation appears larger in adolescents than in adults not because adolescents are more sensitive to the motor stimulating effects of morphine, but because they are less sensitive to its ataxic effects.
Financial Support: Supported by DA23261(WK)and DA17918(CPF)

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POSITIVE REINFORCEMENT IMPROVES ATTENDANCE AND ACHIEVEMENT ON SELF-PACED TYPING TRAINING PROGRAMS IN A THERAPEUTIC WORKPLACE FOR ALCOHOL DEPENDENCE.

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Aims: The Therapeutic Workplace is an effective drug abuse treatment that integrates abstinence reinforcement into a work setting, using wages that drug abusers earn for work to reinforce abstinence. It was hypothesized that offering vouchers for attending job-skills training at the TW would improve attendance and performance in the training programs.
Methods: In the current study, individuals who were homeless, unemployed and dependent upon alcohol were assigned to a Work Only (n = 42), Abstinence and Work (n = 43) or No Voucher (n = 39) group. All participants were invited to work in the Therapeutic Workplace 4 hours per weekday for 26 weeks. Participants in the Work Only and Abstinence and Work groups could earn up to $5 per hour in base pay and additional earnings for performance on computerized, self-paced typing training programs. Work Only and No Voucher participants could work independent of daily and random breath results, while Abstinence and Work participants could work only when their breath samples demonstrated alcohol abstinence.
Results: The differential reinforcement contingencies in place impacted attendance and typing training performance, with the No Voucher group making significantly less progress than the Abstinence and Work and Work Only groups.
Conclusions: This demonstrates that performance-based contingencies can improve attendance and training program progress. Training program results in relation to the attendance and performance-based contingencies and alcohol use will be discussed.
Financial Support: This research was supported by NIH grants R01 AA012154 and T32 DA007209.

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PARENTAL APPROVAL AND ADOLESCENT SMOKING: GENDER AND RACE/ETHNICITY DIFFERENCES.

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Aims: National surveys indicate racial/ethnic disparities in adolescent smoking behavior. This study assessed if parental approval of adolescent smoking affects whether an adolescent ever smoked, and if this differs by ethnicity/race and gender.
Methods: Regression analysis was used to examine data from a cross-sectional high risk behavior survey conducted in high schools in Connecticut. A total of 1,695 high school students (45% boys, 55% girls) completed questions on gender, race/ethnicity, and parental approval/disapproval on smoking frequency.
Results: The ethnic/racial breakdown of the sample was: 75% White, 15% Hispanic, 7% African American and 3% Asian. Girls (54%) reported experimenting (smoking once or twice or occasionally) slightly more than boys (48%). African American adolescents smoked significantly less frequently than other ethnic/racial groups, β = -.11, $t(1,695) = -3.40$, $p < .01$. Adolescents smoked more frequently if they perceived their parents to approve of smoking, β= .42, $t(1,695) = 10.73$, $p < .01$. The parents' approval/disapproval of smoking was less influential on the smoking behaviors of African American (β = .13, $t(1,695) = -3.37$, $p < .01$) and Hispanic adolescents (β = .08, $t(1,695) = -3.45$, $p < .01$) than on the smoking behaviors of non-Hispanic and non-African American adolescents. We also observed a significant three-way interaction among Hispanic race/ethnicity, gender, and parental approval of adolescent smoking, β = .12, $t(1,695) = 2.88$, $p < .01$. Further examination of the data revealed that Hispanic girls smoked more often when they perceived their parents to approve of their smoking compared to non-Hispanic girls; similar findings were not observed in Hispanic boys.
Conclusions: The results indicate that the influence of parents' approval of smoking differentially affects boys and girls from different race/ethnic groups. This may have important implications in the development of culturally sensitive tobacco prevention/cessation programs.
Financial Support: P50 AA15632, P50 DA09421 and T32 DA07238.

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CHILDREN OF WOMEN ON OPIOID MAINTENANCE THERAPY: A FOLLOW-UP STUDY 4 YEARS LATER.

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Aims: Although several studies have investigated the effects of prenatal methadone and buprenorphine exposure on infant's development, little is still known about the long-term effects of prenatal methadone and buprenorphine exposure on children's cognitive development. The aim of this study was to evaluate the cognitive function of young children (aged 4) prenatally exposed to methadone or buprenorphine.
Methods: In this ongoing study, 76 children (26 methadone-exposed, 12 buprenorphine-exposed, and 38 controls) followed-up since birth were evaluated at 4 years of age. Children's cognitive performance was measured with a battery of cognitive tasks as well as four different questionnaires that were filled out by the children's mothers.
Results: Preliminary results revealed that exposed children scored lower than non-exposed children on inhibition (NEPSY, $F=9.25$, $p=0.010$, $\eta^2=.44$) and working memory (WPPSI-r, $F=13.56$, $p=0.003$, $\eta^2=.53$) tasks. No significant differences were found on other measures of cognitive development.
Conclusions: The findings suggest that prenatal methadone and buprenorphine exposure affect some, but not all, areas of cognitive functioning in 4-year-olds. Possible mechanisms behind the effects of prenatal exposure on cognition, including alterations in brain architecture and functioning, will be discussed. The finding that prenatal exposure may affect cognition in 4-year-olds emphasizes the need to follow up children prenatally exposed to methadone and buprenorphine not only at birth and during infancy, but also throughout childhood.
Financial Support: The study was supported by the Norwegian Research Council.

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CHANGES IN RISK-TAKING BEHAVIOR AS A FUNCTION OF MOTIVATIONAL SALIENCY AND VALUE.

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Aims: Risk taking behaviors involve the simultaneous pursuit of two goals: maximization of reward and minimization of loss (approach-avoid conflict). We propose that the likelihood of engaging in highly risky behaviors may be a joint function of the saliency and value (commitment) corresponding to each of these two goals (motivations). The present research aimed to test empirically the above notions in two studies using a computerized laboratory measure (The Balloon Analogue Risk Task or BART.

Methods: In study 1, we manipulated the saliency of the potential for loss in two experimental conditions. In low saliency condition participants the monetary earnings (potential for gain) were visible on the screen during BART. In the high saliency condition the possibility of losing money was visible on the screen during the task. Study 2 manipulated goal value (importance) through an evaluative priming procedure in two experimental conditions: decreased value of risk taking and increased value of avoiding risk.

Results: In study 1, participants' risk taking behavior was significantly reduced when the possibility for loss was salient. The results of study 2 showed that risk taking behavior decreased significantly, even when the potential for earnings was subsequently highly visible when the value of avoiding risk was subtly enhanced compared to when the value of risk taking was decreased.

Conclusions: The results of these two studies indicate that risk taking behavior is likely to take place due to the fact that risk taking benefits may be highly salient compared to the potential for risk taking negative consequences. In support of this notion our research showed that risk taking behavior decreases significantly when the saliency of such negative consequences increases. Additionally, increasing the value (importance) of avoiding risk (but not decreasing the value of risk taking) results in less risk taking behavior even in the presence of highly visible positive consequences.

Financial Support: Center for Addictions, Personality and Emotion Research
Department of Psychology
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PREDICTORS OF STUDY RETENTION IN DRUG ABUSE TREATMENT TRIALS.

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Aims: Participant retention is critically important for clinical research studies in the area of addictions. We sought to examine predictors of retention in a series of treatment outcome studies.

Methods: Data from fifteen trials conducted in the NIDA Clinical Trials Network (CTN) were included in the analysis. We combined studies, defining retention through the final follow-up visit. We fit multivariate logistic regression models to assess predictors of study retention, focusing on age, gender, and ethnicity (three categories: Non-Hispanic White (NHW), African American (AA), Hispanic/other).

Results: 5191 individuals were included in the analysis. Overall retention was 70.5%, and varied across protocols, ranging from 51.0% to 83.0%. No clear pattern was evident; however, retention seemed higher in adult pharmacologic trials, and lower in sexual risk reduction trials. Subjects were aged 15 to 76 (mean 36.2), and 55% were male. Logistic regression modeling showed that younger participants were more likely to drop out ($p<0.0001$); in addition, in comparison to AA participants, we found that NHW were more likely ($p=0.01$) and Hispanic/other were less likely ($p=0.02$) to drop out. Overall, there was no significant difference between males and females ($p=0.13$); however, a significant interaction was observed between gender and ethnicity: in comparison to NHW males, we observed better retention in AA females ($p=0.07$) and Hispanic/other males ($p=0.048$), whereas we observed worse retention in Hispanic/other females ($p=0.004$).

Conclusions: These results show substantial differences in retention between studies and between gender/ethnic groups. In ongoing analyses we will explore other participant and protocol characteristics that may help to explain observed differences in study retention. Our results suggest that strategies focused on improving study retention in younger subjects, and in Hispanic females, may be particularly important for increasing participant retention and improving the validity of clinical trial data.

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NEUROPSYCHOLOGICAL PREDICTORS OF SUBSTANCE USE AND ADHERENCE IN HIV+, METHAMPHETAMINE-USING MEN WHO HAVE SEX WITH MEN.

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Aims: The management of HIV requires HIV+ individuals to maintain near-perfect medication adherence. Both HIV and substance use have been associated with neuropsychological dysfunction that hinders adherence. The present study seeks to identify cognitive factors that predict substance use, medication non-adherence and the co-occurrence of the two.

Methods: Men who have sex with men (n=44) were recruited from a behavioral intervention for methamphetamine use and HIV medication non-adherence. Neuropsychological predictors included the IGT and variant, the D-KEFS trails, the Grooved Pegboard (GP), the WCS, the Counting Span, and a Go-Nogo. A Time Line Follow Back procedure was used to collect the frequency of missed med days, substance use events and days on which the two co-occurred. Linear regression was used to determine significant neuropsychological predictors.

Results: The # of drug use events was predicted by motor slowing (GP time with both hands) ($p=.02$), accounting for 11.8% of the variance. The # of missed med days was predicted by motor slowing (GP time with the nondominant hand) ($p=.05$), and hypersensitivity to punishment (IGT variant score) ($p=.02$), accounting for 19.8% of the variance. The # of co-occurrence days was predicted by the # of errors on the D-KEFS trails ($p=.01$), accounting for 14.5% of the variance. Thus motor function predicted both substance use and missed med days, but not the co-occurrence of the two.

Conclusions: Deficits in different aspects of neuropsychological function are associated with substance use, non-adherence and their intersection. It was expected that motor function would predict non-adherence and substance use, as both methamphetamine and HIV cause damage to the dopaminergic neurons of the basal ganglia. However, the lack of a relationship between motor function and the co-occurrence of substance use and non-adherence suggests these participants may have a distinct pattern of neuropsychological deficits.

Financial Support: NIDA R01 DA023395 and F31 DA026320.

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COORDINATION BETWEEN SINGLE STATE AUTHORITIES AND DEPARTMENTS OF CORRECTIONS IN THE TREATMENT OF OFFENDERS WITHIN THE COMMUNITY.

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Aims: Little is known about the funding and organization of community-based substance abuse treatment for offenders. Previously we surveyed all 50 states on the presence of state-level Department of Corrections (DOC) purchasing and regulating substance abuse treatment in the community. Our investigation revealed that in 35 states DOC is purchasing treatment - often from the same providers as the Single State Authority (SSA) (Kubiak et al, in press). Moreover, the data suggested different arrangements in purchasing and collaboration with SSA. We hypothesized that organizational factors would influence the coordination between DOC and SSA in the funding /organization of community-base substance abuse treatment for offenders.

Methods: Case study analysis, including interviews in seven states with three key informants from each state-level DOC and SSA, and review of written documents. Analytic induction used to assess the phenomenon within and between states.

Results: Organizational configurations (e.g. centralized vs. decentralized) within both DOC and SSA - as well as organizational culture, communication styles and lack of informal networks across systems - contribute to difficulties creating a coordinated and seamless approach to treatment for offenders re-entering the community.

Conclusions: Unfortunately, those individuals involved with criminal justice face an array of access and payment arrangements, depending on the state and/or county in which they reside. Improving care and reducing the heavy societal cost of recidivism, requires coordination across organizational units within and between departments, as well as across levels of government.

Financial Support: Robert Wood Johnson Substance Abuse Policy Research Program

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DETERMINING THE ACUTE EFFECTS OF BENZYLPIPERAZINE COMBINED WITH TRIFLUROMETHYLPHENYLPIPERAZINE ON COGNITION AND EXECUTIVE FUNCTIONING USING FUNCTIONAL MAGNETIC RESONANCE IMAGING.

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Aims: Party pills containing BZP/TFMPP have been marketed as safe and legal alternatives to illicit recreational drugs. BZP is a stimulant with similar effects to dexamphetamine (DEX),while TFMPP is reported to have effects similar to low potency MDMA. There is a paucity of information known about the effects of BZP/TFMPP in humans. This study is a randomized double blinded cross-over trial to determine the effects of BZP/TFMPP on cognition and executive function in comparison to DEX and placebo using fMRI

Methods: 11 healthy participants aged 18-40, were recruited from the Auckland area. Subjects were imaged by fMRI, at the Centre for Advanced MRI,at the University of Auckland. Imaging was performed whilst participants undertook the Stroop paradigm 90minutes after an oral dose BZP/TFMPP(100mg/30mg),DEX(20mg)or Placebo. Participants were tested with each condition on a separate occasion. Echo-planar images were collected on a MRI scanner (Siemens Magnetom Avanto 1.5 T, Germany).Data was preprocessed, analyzed with SPM8 and then used to identify regional activation

Results: BZP/TFMPP and DEX caused changes in activation in the Dorsolateral Prefrontal Cortex (DLPFC) compared to Placebo in the Stroop (Incongruent-Congruent) condition (p=0.001). BZP/TFMPP also caused a change in activation in the Anterior Cingulate Cortex. Reaction Time (RT) was increased to a great extent by BZP/TFMPP when compared to DEX and Placebo. DEX showed increased RT when compared to placebo

Conclusions: This study is the first to investigate the effect of BZP/TFMPP using fMRI. Our results propose that using BZP/TFMPP at these doses induces characteristics typical of other psychostimulants such as DEX in their effect on the DLPFC and RT, suggesting there is additional cognitive resources required to perform this paradigm relative to placebo

Financial Support: School of Pharmacy,The University of Auckland

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THE EFFECTS OF OSTRACISM ON BEHAVIOR AND BRAIN ACTIVITY IN CHRONIC COCAINE USERS.

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Aims: Social factors can be important contributors to increased risk of substance abuse. Ostracism can lead to maladaptive behavior such as alienation, depression and substance abuse. Interpersonal conflicts have been reported to lead to relapse to cocaine use after treatment. The aim of this study was to compare the response to social rejection in cocaine users and controls using a task that has been shown to be sensitive to the sense of belonging, locus of control and group cohesiveness.

Methods: The perception of ostracism was measured using the Cyberball Social Exclusion Task with fMRI. In this task, the subject and two fictitious partners passed a digital ball to each other on the computer screen. Conditions assessing ostracism included "inclusion"-receiving the ball on 33% or more throws; "exclusion"-receiving the ball on 20% or less throws. After the task, participants were assessed on feelings of belonging, meaningful existence, control, and self-esteem.

Results: Cocaine users (n=16) and controls (n=12) were from the Winston Salem, NC area. Behavioral analysis revealed that ostracism affected users and controls differently, as demonstrated by significant group interactions on measures of belongingness (F=9.77, p=0.0043), locus on control (F=9.51, p=0.0049) and meaningful existence (F=4.31, p=0.0479). There was no effect on measures of self esteem. fMRI analysis also demonstrated that the effects of ostracism differed between groups. There were no differences between groups during inclusion. However, during exclusion, relative to controls, cocaine users had elevated activity in brain areas involved in limbic processing including the anterior insula bilaterally and the ventromedial prefrontal cortex ($p<0.05$, corrected clusters), suggesting greater response to rejection.

Conclusions: Taken together these data suggest that ostracism affects both behavior and brain activity in cocaine users differently than controls. These brain areas affected by ostracism are also ones involved in drug seeking, suggesting a link between social stress and drug addiction.

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IV GESTATIONAL NICOTINE EXPOSURE INCREASES BRAIN-DERIVED NEUROTROPHIC FACTOR IN ADOLESCENT RATS.

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Aims: This study determined the effects of intravenous (IV) gestational nicotine exposure on methamphetamine (METH)-induced locomotor sensitization and brain-derived neurotrophic factor (BDNF) levels in the nucleus accumbens, striatum, prefrontal cortex and hippocampus of rat offspring. Gestational nicotine exposure, via osmotic mini-pump, has been shown to produce increased sensitization of the behavioral response to cocaine challenge (Franke et al. 2007). No studies have reported the effects of gestational nicotine on neurotrophic factor content.

Methods: Female dams were injected with IV nicotine (0.05 mg/kg/inj; 3X/day) or saline on gestational days (GD) 8–21. Offspring were culled to 10 rats/litter and were weaned on postnatal day (PD) 21. On PD28 all rats were injected with saline and baseline activity was measured for 60 min. Rats received daily METH injections (0.3 mg/kg; s.c.) or saline injections for 7 consecutive days (P29-35) and locomotor activity was measured after the 1st and 7th injections. Brains were harvested 24 hours after the last injection (P36) and the nucleus accumbens, striatum, prefrontal cortex and hippocampus was dissected, flash frozen, and stored at -80° C. BDNF was measured by Elisa. Behavioral and BDNF data were analyzed using ANOVA.

Results: Gestational nicotine did not alter pup weights compared to controls. Repeated METH increased activity [$F(2, 124) = 76.2$, $p<.001$] and produced behavioral sensitization [day X treatment: $F(2, 124) = 44.2$, $p<.001$]; this was not altered by the factors of sex or gestation. Prenatal nicotine significantly increased BDNF in accumbens [gestation: $F(1, 37) = 5.1$, $p<.03$], striatum [gestation: $F(1, 38) = 6.2$, $p<.02$], prefrontal cortex [gestation: $F(1, 38) = 5.4$, $p<.03$] and hippocampus [gestation: $F(1, 37) = 5.0$, $p<.03$].

Conclusions: This study demonstrates that IV prenatal nicotine increased BDNF in brain areas important for reinforcement and cognitive function. Repeated METH did not alter BDNF. Implications towards brain plasticity will be discussed.

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CONTINGENCY MANAGEMENT FACILITATES HIV POST-EXPOSURE PROPHYLAXIS IN METHAMPHETAMINE-USING MSM.

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Aims: To demonstrate safety, feasability, and acceptability of a drug reduction intervention to facilitate adherence to post-exposure prophylaxis (PEP) following potential sexual exposure to HIV

Methods: A prospective safety and feasibility study using Contingency Management (CM) with PEP to prevent HIV seroconversion

Results: Between 3/09 and 11/09, 27 participants enrolled. Mean age was 34 (SD 7.6), race was mostly Caucasian(63%) or Latino (26%), the majority identified as gay (85%), had earned a high school diploma (63%) or a bachelor's degree (26%), and earned < $15,000/year (63%). Participants reported elevated historical rates of chlamydia (n=9, 33%), gonorrhea (n=8, 30%), and syphilis (n=5, 19%). At baseline, participants had high rates of chronic hepatitis B (n=2, 7 %), syphilis (n=1, 4%), rectal/pharyngeal gonorrhea (n=3, 11%) and urethral Chlamydia (n=1, 4%). 20 of 27 participants (74%) initiated PEP. Median time from high-risk exposure to PEP initiation was 38 hours (range 14-68). Of the PEP-initiators, 18(90%) initiated PEP after a sexual exposure and two (10%) after injection drug exposure. The mean medication adherence rate estimated by self-report and pill count was 76%. The adherence rate includes 4 participants who discontinued PEP due to intolerable side effects, incarceration (2), and methamphetamine use. No incident HIV seroconversions were observed.

Conclusions: When integrated with CM, PEP use among meth-using MSM appears to be safe and feasible for HIV prevention. PEP adherence does not appear to differ from other populations. Based on these preliminary pilot data, a randomized trial of CM and a control behavioral intervention when delivering PEP in stimulant-using MSM is planned.

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NICOTINE IS THE THING: REDUCING HARM FROM TOBACCO THROUGH PROPER LABELING.

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Aims: Tobacco products are nicotine delivery systems, varying in bioavailability, dosing efficiency, and the nature and amount of contaminants delivered. Tobacco product labeling poses a challenge due to compensatory smoking of smoked products and variable portion size of smokeless products. This research seeks a means of labeling resistant to manipulation or artifactual variation, and to establish standards for clear, effective labeling of tobacco product contaminants to guide consumer choices.
Methods: Data from the scientific literature, trial documents and public health projects listing smoked and smokeless tobacco contaminants were collected and standardized into common units. The data was analyzed with respect to unit of use, grams tobacco, and various potential internal markers of consumption.
Results: Analysis of common tobacco carcinogens and toxins (e.g "tar", aromatic hydrocarbons, tobacco-specific nitrosamines [TSNAs], carbon monoxide, etc.) shows that conventional classifications with respect to yield understate toxicity of such products, while presentation per milligram nicotine delivered does not. Due to compensatory smoking, tar and TSNA content per milligram of nicotine delivered may actually be higher in "low-yield" cigarettes, consistent with current epidemiological studies showing no reduction in risk for such products. Analysis reveals a wide divergence of nicotine and carcinogenic TSNA content across smokeless products. There is about a 1000-fold difference in TSNA content between the most toxic (fermented dry snuffs) and the least toxic (low-TSNA) smokeless products not revealed in current labeling.
Conclusions: It is not enough to give the toxin content of a tobacco product per unit weight, due to differences in nicotine delivery. Expressing toxic contaminants as a weight percentage relative to nicotine, the desired drug, will prevent a repeat of the "low-tar, low-nicotine" problem of artificially understated exposures using artificially low portion sizes.
Financial Support: This work was funded by Rock Creek Pharmaceuticals, Inc., Gloucester, MA.

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PRESCRIPTION STIMULANT MISUSE AMONG ADOLESCENTS AND YOUNG ADULTS.

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Aims: Children and adolescents prescribed stimulants, such as Ritalin or Adderall, for ADHD may be at increased risk for misuse of stimulants. The aims of this qualitative study were to describe: patterns of initiation into prescription drug misuse; and relationships between prescribed use and misuse of stimulants, including abuse of street stimulants, e.g. methamphetamine.
Methods: Eligible subjects were between 16 and 25 years old and misused one or more prescription drugs at least three times in the past three months. Subjects (n=150) were recruited using targeted sampling in public locations in Los Angeles and New York between 2008 and 2009. Interview questions focused on histories of prescribed drug use, patterns of prescription drug initiation, and recent patterns of misuse. Sampling was stratified by recent patterns of risk behaviors – polydrug use, homelessness, and injection drug use – to create three subgroups for analytical purposes.
Results: The sample was largely white, male, straight-identified, and early 20s. Nearly 75% reported lifetime misuse of a prescription stimulant while 25% misused a prescription stimulant with the past 30 days. Context for diagnosis of ADHD and prescribed use of stimulants differed by subgroup. Stimulant misuse often began with the discovery that pills prescribed for ADHD had euphoric and/or performance enhancing properties. Misuse of prescription stimulants manifested in a variety of ways: taking the drug other than as prescribed; to enhance performance; to regulate mood; and as a substitute for methamphetamine. Early initiation of stimulant misuse was associated with becoming an injection drug user and/or homeless. Current stimulant misuse was more common among polydrug users for performance enhancement.
Conclusions: Greater research and clinical attention should focus on the potential for stimulant misuse and long-term negative health trajectories associated with misuse of prescribed stimulants.
Financial Support: This research was supported by a grant from NIDA (R01 DA021299).

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MALTREATMENT AND EARLY SUBSTANCE USE.

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Aims: Most studies of the child abuse-substance use association used adult samples and retrospective reports. We hypothesized that adolescents who self-report a history of child maltreatment (CM) would be more likely to use tobacco, alcohol, and marijuana at age 14 and to report an earlier age at onset of use than those not exposed to CM.
Methods: The sample is from a longitudinal study of prenatal tobacco exposure among offspring of teenaged mothers. At 14 years, use of tobacco, alcohol, and marijuana was assessed; CM was measured by the Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998). We used suggested cut-points for moderate-to-severe abuse to dichotomize the 5 CTQ subscales (no/yes); the sum of these represented CM exposure severity (range 0 - 4+). The CM-substance use association was tested with logistic regression; correlates of onset age were examined using Cox Proportional Hazards. Covariates included maternal age, race, sex, custody status, household income, and maternal substance use.
Results: The mothers had 12.8 years of education; 44% were married or living with a man, 68% were employed or attending school. Mean household income was $2152. 250 adolescents completed the assessments. Their average age was 14.4 years (13.8-16.1); 60% were age 14; 50% were male; 73% were African-American; 27% were Caucasian; 14.6% did not live with their mothers. A total of 5% reported tobacco use, 15% drank alcohol, and 15% used marijuana; 16.4% were classified as positive for CM. Youth with a history of maltreatment were more likely to use alcohol (OR 1.56; 95% CI=1.08-2.26) and marijuana (OR 1.50; 95% CI=1.03-2.18), but not tobacco. They began to use alcohol ($p < .025$) and marijuana ($p < .025$) at a significantly younger age than did youth without a history of maltreatment.
Conclusions: A history of CM is a significant risk factor for early marijuana and alcohol use among community-dwelling, low SES 14-year olds; early use is a noted risk factor for later problem use. Interventions for young mothers regarding child-rearing practices could prevent maltreatment and thus help reduce early substance use in the teenage years.
Financial Support: NIDA

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SUB-REGION SPECIFIC CONTRIBUTION OF THE VENTRAL HIPPOCAMPUS TO DRUG CONTEXT-INDUCED REINSTATEMENT OF COCAINE-SEEKING BEHAVIOR.

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Aims: The ventral hippocampus (VH) plays a critical role in both cue-induced and cocaine-primed reinstatement of cocaine seeking (Rogers and See, 2007). Because the VH has extensive reciprocal connections with elements of the brain relapse circuitry thought to mediate context-induced reinstatement, the VH may also critically contribute to cocaine seeking elicited by a drug-paired context. Hence, the current study was designed to evaluate whether the VH makes a subregion-specific contribution to drug context-induced cocaine seeking. Specifically, we predicted that functional inactivation of the CA3/CA1 subregion– but not the dentate gyrus (DG) – would impair cocaine seeking elicited by a drug-paired context.
Methods: Rats were trained to lever press for intravenous cocaine infusions (0.15 mg/infusion, i.v.) in a distinct environmental context (cocaine-paired context) followed by extinction training in a distinctly different context (extinction context). Rats were then re-exposed to either the cocaine-paired context or the extinction context to assess cocaine-seeking behavior (i.e. non-reinforced lever responding). Rats received bilateral microinfusions of baclofen+muscimol (1.0/.01mM) or vehicle into the CA3/CA1, DG, or an anatomical control region, the posterior dorsal hippocampus (pDH), immediately prior to each test session.
Results: Exposure to the cocaine-paired context, but not the extinction context, reinstated extinguished cocaine-seeking behavior following vehicle infusions. While functional inactivation of the DG and pDH failed to alter this behavior, functional inactivation of CA3/CA1 significantly attenuated context-induced cocaine seeking.
Conclusions: The VH likely contributes to context-induced cocaine seeking in a subregion-specific manner, with the functional integrity of CA3/CA1 necessary for the incentive motivational effects of a cocaine-paired environmental context on addictive behavior.
Financial Support: NIDA R01DA0176373, NIDA R01DA0176373-S1, T32 DA07244

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PREDICTORS AND OUTCOMES OF TREATMENT READMISSION: THE CASE FOR CONCURRENT RECOVERY MONITORING.

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Aims: A subgroup of substance dependent persons require multiple treatment episodes prior to, if ever attaining stable abstinence. Research on treatment readmission is limited: it has focused on fixed client domains as potential predictors, limiting its clinical usefulness. Capitalizing on a prospective cohort of outpatient clients, we explore prevalence, predictors and outcomes of readmission, and reasons for seeking additional help.
Methods: Consecutive admissions at 2 NYC publicly funded outpatient programs were reassessed 4 times over the 12 months following their leaving the index episode (N = 219; 89.9% retention).
Results: Participants were from under-served groups, 55% males, with a long history of polydrug dependence; 85% had prior treatment exposure, 60% left the index episode before completion. In the post treatment year, 30.6% sought treatment again. At intake, clients who were and were not readmitted (AT and N-AT respectively) did not significantly differ demographically, in service needs, expectation of help, or recovery resources (e.g., social support, 12 step participation); ATs cited a greater number of problem substances and more prior treatment exposure, had higher scores on powerlessness over substances and lower abstinence self-efficacy. ATs and N-ATs did not differ in treatment duration but significantly fewer ATs completed treatment (22.4% vs. 50.7%); ATs had significantly worse substance use outcomes at the end of the study. In multiple regressions including fixed client characteristics and in-treatment clinical measures, the only predictor of readmission was dependence severity DURING the index episode.
Conclusions: A subgroup of clients is at high risk for cycling through the revolving doors of the treatment system without reaching abstinence. This emphasizes the need to implement in-treatment clinical monitoring such as Concurrent Recovery Monitoring (CRM; McLellan et al, 2005) that are more consistent with the chronic nature of addiction. Implementing CRM may help adjust level and intensity of services as clinically indicated and contribute to better outcomes for this vulnerable subgroup.
Financial Support: NIDA Grant R01DA015133

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GENDER DIFFERENCES IN MOTIVES TO USE AND SOURCES OF PRESCRIPTION OPIOIDS.

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Aims: Research on alcohol and drug use reveals important gender differences in motives to use and sources of substances. To date, little research has investigated gender differences in the motivation to use and sources of prescription opioids. The current study sought to address this gap in the literature by using data from a larger, ongoing study examining the relationship between prescription opioid dependence and stress.
Methods: Participants (10 men, 15 women) currently dependent on prescription opioids completed the Inventory of Drug Taking Situations (Turner et al., 1996), Pain Medication Questionnaire (Adams et al., 2004), and modified items from McCabe et al.'s (2004) study to determine motives to use and sources of opioids.
Results: Overall, men and women reported similar motives to use, the most common including pain (84%), to get a high (76%), decrease anxiety (56%), help sleep (41.7%), and experimentation/curiosity (32%). Results suggest, however, that women were motivated to use prescription opioids more often than men because of physical discomfort (p= .018) or negative situations (p=.095), and less motivated to use to get a high (p=.051). Overall, men and women reported similar sources, the most common including friends (84%), the ER (69.6%), acquaintances (44%), drug dealers (44%), and boyfriends/girlfriends (32%). However, women were more likely to have family members obtain prescriptions from their doctors (p=.06), obtain prescription opioids from a parent (p=.061), and reported more difficulty obtaining prescription opioids from their doctors (p= .04).
Conclusions: The findings highlight potential gender-sensitive motives to use and sources of prescription opioids. Although preliminary, the findings may help inform the design of screening, prevention and treatment interventions for individuals with prescription opioid dependence. Data collection is ongoing and the final sample would be reported.
Financial Support: Acknowledgements: NIDA grant K23 DA021228 (SEB).

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INSULA INACTIVATION AS A NOVEL THERAPEUTIC STRATEGY FOR NICOTINE ADDICTION.

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Aims: Nicotine is the principal component of tobacco smoke that leads to addiction and recent evidence suggest that damage to the insular cortex (insula) disrupt tobacco addiction in human smokers. Our aim was to investigate the effect of an inactivation of this structure in an animal model of nicotine addiction.
Methods: We have investigated the effect of reversible inactivation of the granular insula through local bilateral infusions of the GABA agonists (0.3 nmol baclofen + 0.03 nmol muscimol) on nicotine self-administration under fixed and progressive ratio and on reinstatement of nicotine seeking induced by nicotine priming or nicotine-associated cues in rats. We have also evaluated the effect of insula inactivation on food self-administration and relapse as a control. Only rats with correct bilateral placement of the cannulaes in the granular insula have been included for data analysis.
Results: Infusion of the balofen-muscimol mixture into the insula significantly reduced nicotine self-administration compared to vehicle administration in the insula ($P<0.05$) under both fixed and progressive ratio schedules of reinforcement. In contrast, insular cortex inactivation did not modify responding for food (NS). Significant reinstatement of nicotine seeking was obtained by cues presentation and nicotine priming (0.15 mg/kg). Both reinstatements ($P<0.05$) were attenuated by insular cortex inactivation, whereas reinstatement for food seeking was not affected (NS).
Conclusions: Our study indicated that the integrity of the granular insula is necessary to the rats to exhibit motivation to take nicotine and to relapse to nicotine seeking, but not for their motivation to consume food pellets or to relapse for food seeking. Indeed, methods those are able to modulate the activity of the insula, such as repetitive transcranial magnetic stimulation or deep brain stimulation, may represent a new therapeutic way to treat tobacco addiction and relapse in humans.
Financial Support: GRAND Award 2008. Global Research Award on Nicotine Dependence program funded by Pfizer

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GENDER DISPARITY IN THE ASSOCIATION BETWEEN STRESS AND ADDICTIVE BEHAVIORS.

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Aims: Substance use and gambling are correlated addictive behaviors, but is there a gender disparity between stress and gambling as there is between stress and substance use?
Methods: The study used the 11th grade data of an urban cohort (n=678; 86% African American, 53% males, mean age=17.0). The Life Events Questionnaire Adolescent Version, South Oaks Gambling Screen-Revised for Adolescents, and Substance Use, Abuse, & Dependence-Youth Self-Report assessed past year stressful life events, gambling behavior, and substance use, respectively. Upon gender stratification, logistic models accounting for design clustering, race, and subsidized lunch status, analyzed the associations between stress and behaviors.
Results: Stressful events were common (88% in both males and females); a larger proportion of males than females engaged in an addictive behavior (68% and 61% respectively; 58% males and 37% females gambled). Stress linked more strongly with substance use than gambling with gender disparities found by the number and type of life event. As compared to same sex peers with no past year event, males with 3 or more events were more likely to use alcohol (OR=5.4, p<.001), tobacco (OR=4.2, p<.01), and drugs (OR=4.5, p<.001) and gamble (borderline significance OR=2.0, p=.06), and females with 3 or more events were more likely to use alcohol (OR=3.7, p<.001), tobacco (OR=2.9, p<.01), and drug (borderline significance OR=2.3, p=.06). The odds of substance abuse/dependence increased among males and females (all three substances p<.05) with each additional event experienced, but the odds of problem gambling increased only for males.
Conclusions: Our findings suggest potential gender disparities in the linkage between stressful life events and the type of addictive behavior. This area warrants more research as a majority of the sample have experienced at least one stressful life event and engaged in at least one activity in the past year.
Financial Support: This study is supported by NICHD grant HD060072 (P.I.: Dr. Martins).

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NON-PRESCRIBED USE OF VICODIN® AND OXYCONTIN® AMONG US YOUTH.

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Aims: We sought to characterize non-prescribed use (NPU) patterns of selected opioids among U.S. youth from 2002-08 by assessing prevalence and identifying risk factors.
Methods: The public use data set from the Monitoring the Future on Vicodin and OxyContin NPU in the past 12 months was analyzed. Samples sizes ranged from 12,519 in 2002 to 15,959 in 2008 for 8th, 10th, and 12th grades combined. We postulated that NPU of these opioids would be higher for older youth, driven primarily by substance abuse and polydrug history.
Results: The fraction endorsing NPU of either of these opioids increased over time (6.6% to 7.7%, p<.001). Within that group, the fraction reporting NPU of both opioids also increased (31% to 37%, p<.064), reaching statistical significance for 12th graders and the West. Teens living on farms had higher rates of NPU of both medications. While NPU of either opioid was higher in whites than blacks (6.9% vs 2.4%), the reverse was true for the NPU of both category (34% vs 56%). The reporting of NPU of both is bimodal (23% report 1-2 times/yr NPU of each; 25% report >10 times/yr NPU of each). The fraction of higher NPU of both, however, has been declining since 2006. Males and 8th graders showed disproportionately higher NPU amounts of both. Risk factor analyses (2006-08 only) showed that the number of other concurrent licit or illicit drugs abused, first use of marijuana, residence locale, friends dropping out of school, and concurrent use of psychotherapeutic drug under medical supervision discriminate between NPU of none vs either opioid (91%), and between NPU of one vs both (76%).
Conclusions: Risk management of NPU of opioids by teens must be seen in the context of reducing polydrug abuse. Primary prevention efforts should include a focus on the identified high-risk groups.
Financial Support: None

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MARIJUANA SELF-ADMINISTRATION UNDER A MODIFIED PROGRESSIVE-RATIO PROCEDURE: EFFECTS OF MARIJUANA USE HISTORY.

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Aims: Previous research indicates that heavy marijuana users are less sensitive to the subjective and performance effects of THC. However, it is unclear if marijuana use history also predicts drug-taking behavior. This ongoing study examines marijuana self-administration using a modified progressive-ratio procedure as a function of marijuana use history. It is hypothesized that the reinforcing effects of marijuana will be greater in heavy users.
Methods: Sixteen healthy volunteers, classified as heavy or light users based on self-reported marijuana use (8/group) will complete an 8-session, randomized, double-blind study consisting of four 2-session test blocks. During the first session of each block, subjects receive 8 uniform puffs from a cigarette containing THC (0, 1.75 or 3.5%). During the second session of each block, subjects can earn up to 8 puffs from the previously sampled THC concentration. The first puff is earned by completing 50 responses, and the response requirement for each subsequent puff is doubled, such that 12,750 responses are required to earn all 8 puffs. Verbal-report, performance and cardiovascular assessments are completed before, immediately after, and hourly for 3 hours after smoking. Data are analyzed using ANOVA.
Results: Six light users (3.56 + 1.08 times per month) and five heavy users (17.6 + 2.54 times per month) have completed the study. Preliminary analysis indicated typical THC effects on verbal-report and performance measures. Break points increased as a function of concentration, suggesting that THC functioned as a reinforcer (0%: 3.7 ± 1.2; 1.75%: 3.9 ± 1.3; 3.5%: 5.2 ± 0.9). Group differences in break points were apparent at the 3.5% THC concentration (light users: 4.5 + 1.1; heavy users: 6.0 + 0.8) suggesting that the reinforcing effects of cannabis were greater among heavy users at this concentration.
Conclusions: These preliminary results demonstrate that the modified progressive-ratio procedure can be used to examine the reinforcing effects of marijuana and is sensitive to group differences in marijuana use history.
Financial Support: Supported by DA-05312 and RR-15592.

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DOUBLE-BLIND PLACEBO-CONTROLLED PILOT TRIAL OF MODAFINIL FOR METHAMPHETAMINE WITHDRAWAL: RESULTS OF AN AUSTRALIAN PILOT STUDY.

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Aims: Australia has one of the highest per capita uses of illicit methamphetamine in the world. However, less than 25% of dependent methamphetamine users present for treatment in Australia, and only 13% of methamphetamine treatment access is for inpatient withdrawal treatment. A number of studies have examined modafinil for cocaine and shown promising results and a limited number have examined this drug for maintenance treatment. This study aimed to examine the feasibility of a randomised trial for modafinil for methamphetamine withdrawal.
Methods: This study investigated the use of modafinil in an inpatient withdrawal setting during the first 7 days of methamphetamine withdrawal using a double-blind, randomised, placebo-controlled study design. Twenty methamphetamine dependent participants were randomised to modafinil (n=10) or placebo (n=10), with a tapering medication regime. Measures of withdrawal were taken daily for 7 days. Clinical, physiological and neurocognitive measures were taken at treatment entry, discharge and one month later.
Results: This was a feasibility study. There were no adverse events and the medication was well tolerated. There were no observable clinical effects of modafinil over placebo, but retention in treatment was better in the modafinil group. Results indicate that modafinil is linked to improvements in neuropsychological functioning when compared with placebo. There were no differences in outcomes at 1 month.
Conclusions: Modafinil is a feasible medication for methamphetamine withdrawal. With a small sample size outcomes were limited, but better treatment retention and neurocognitive functioning in the modafinil group suggest a study with a larger sample size is warranted.
Financial Support: This study was funded in part by the Australian Government Department of Health and Ageing.

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INTERACTION BETWEEN ALCOHOL AND OPIOIDS IN OPIOID-DEPENDENT HUMAN SUBJECTS.

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Aims: Concomitant use of central nervous system depressants, in particular alcohol, is identified as a risk factor for heroin overdose. We used an alcohol challenge to investigate the alcohol-heroin interaction on respiration.
Methods: 8 opioid-dependent participants receiving opioid-substitution therapy and 8 healthy controls were recruited. Participants were administered a 400ml drink containing 0.8g/kg alcohol (vodka). Measures of alcohol effect were recorded at baseline and at 15 minute intervals after alcohol consumption. Respiratory parameters (heart rate, respiration rate, oxygen saturation, nasal etCO2) were recorded. Subjects performed the Read rebreathing task to assess central chemoreflex ventilatory sensitivity to CO2, both before and after (105 minutes) following alcohol consumption.
Results: Breath alcohol concentration (BAC) significantly increased in all participants following consumption of 0.8g/kg alcohol (p<0.0001). Controlling for BAC (etCO2/BAC), nasal etCO2 significantly increased in opioid-dependent participants when compared to healthy controls (p<0.0001) with significant increases at 105, 120, 135 minutes post-alcohol consumption. At peak (105 minutes), there was a 4.51±7.6 % increase in etC02 (compared to baseline) in opioid-dependent participants, but a -6.42±9.1 % decrease (compared to baseline), for healthy controls. Heart rate significantly increased following alcohol consumption, with opioid-dependent participants heart rate significantly increased when compared to controls (heart rate/BAC, p<0.05). Respiration rate (respiration rate/BAC) and oxygen saturation (oxygen saturation/BAC) did not significantly change (p>0.05).
Conclusions: The significant increase in nasal etCO2 in opioid addicts but not controls suggests that alcohol interacts with opioids to depress respiration. This has implications when considering both heroin overdose and risk factors for opioid users.
Financial Support: MRC Programme grant (GO40075) and studentship.

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GAY-RELATED STIGMA IS PREDICTIVE OF PROBLEMATIC DRINKING AND SUBSTANCE USE IN A SAMPLE OF HIGH-RISK HIV NEGATIVE YMSM.

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Aims: Research shows that use of alcohol/drugs is an antecedent to high risk sexual behavior, which places young men who have sex with men (YMSM) at high risk for contracting HIV. Various psychosocial factors are also believed to play a role in HIV risk behavior. We examined baseline data from a randomized controlled trial testing the efficacy of a Motivational Interviewing intervention to reduce substance use and sexual risk in non-treatment seeking HIV negative YMSM and hypothesized that gay-related stigma is associated with problematic drinking and drug-related personal difficulties.
Methods: The YMSM (N=236) were HIV negative, had ≥ 5 days of drug use and ≥ 1 incident of unsafe anal sex with a high risk partner in the last 90 days. Average age was 29.6 (7.3), and 60% were non-White. We used multivariate analyses to examine the relationship between gay-related stigma and 1) problematic drinking as measured by the AUDIT, while controlling for number of heavy drinking days and 2) drug-related personal difficulties as measured by the SIP-AD, controlling for number of drug use days.
Results: Gay-related stigma emerged as a significant independent predictor of problematic drinking and drug use. Controlling for number of heavy drinking days, gay related stigma significantly predicted problematic drinking, accounting for an additional 4% of model variance ($p<.0001$). Controlling for number of drug use days, gay-related stigma significantly predicated drug-related personal difficulties, accounting for an additional 6% of model variance ($p<.0001$).
Conclusions: These findings suggest a significant and independent role of gay-stigma in problems associated with alcohol and drug use among high-risk YMSM, over and above actual patterns of use. Prevention efforts need to consider ways to attenuate the impact of gay-related stigma on one's well being, which may impact HIV risk-related behavior.
Financial Support: Research supported by NIDA grant R01DA20366.

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WHY REINFORCING DRUGS REINFORCE BEHAVIOR?

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Aims: In the first part of this paper, we review experimental evidence suggesting the hypothesis that drugs of abuse reinforce behavior because they enhance memory consolidation. In the second part, we report the results our tests of this hypothesis using heroin and amphetamine.
Methods: More specifically, male Sprague-Dawley rats were trained on two appetitive stimulus-response tasks performed in an automated 8-arm radial maze. Heroin (0, 0.03, 0.3, 1 and 3 mg/kg SC, n=8 in each dose/ group) and amphetamine (0, 0.5, 1 and 2 mg/kg SC, n=8 in each dose/group) were administered 5 min following some training sessions (i.e., post-training drug administration protocol).
Results: It was found that both heroin and amphetamine dose-dependently enhanced acquisition of the tasks, with the maximal effect found at the lowest doses. Rate of acquisition was unaltered in animals injected 4 hours post-training, suggesting that acquisition was enhanced only when the drugs were administered during a discrete time period of memory consolidation.
Conclusions: Although we found some evidence of drug-specific enhancement of particular aspects of learning, the overall conclusion is that both opiates and psychomotor stimulants enhance memory storage, and this can explain why they serve as reinforcing stimuli in drug-naïve subjects.
Financial Support: Supported by the Natural Sciences and Engineering Research Council of Canada.

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EFFECTS OF THE NICOTINIC RECEPTOR PARTIAL AGONIST VARENICLINE ON COCAINE- AND FOOD-MAINTAINED BEHAVIOR IN RATS.

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Aims: Acetylcholinergic (ACh) mechanisms are known to mediate drug-reinforcement processes. For example, both muscarinic and nicotinic ACh antagonists have been shown to attenuate cocaine self-administration (CSA) in nonhumans. The aim of the present study was to examine the effects of a nicotinic partial agonist on CSA.
Methods: The effects of the nicotinic partial agonist varenicline (VCL, 0.3 to 7.8 mg/kg, s.c., 30-min pretreatment) on CSA were examined in rats responding under a multiple fixed-ratio (FR) 5 cocaine FR 5 sucrose schedule.
Results: VCL produced a dose-dependent decrease in cocaine self-administration. A significant decrease in food intake was also observed at higher doses of VCL, but the effect was of lesser magnitude compared to that on CSA. Decreases in food intake were primarily observed during the initial component of the session when food was available in that component.
Conclusions: These results demonstrate that VCL can decrease CSA in rats. Although the selectivity of this effect was somewhat limited, the present findings suggest that further study of the ability of nicotinic partial agonists to reduce cocaine's reinforcing effects is warranted. Moreover, the present findings provide some support for examining the efficacy of varenicline in humans for the treatment of cocaine dependence.
Financial Support: Supported by NIDA grant DA020136 (M.G. LeSage). Varenicline was synthesized on NIDA grant DA12002 (F.I. Carroll).

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SIX-MONTH OUTCOMES FOR THE TARGETED ASSESSMENT WELFARE TO WORK PROGRAM.

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Aims: The Kentucky Department for Community Based Services initiated the Targeted Assessment Program (TAP) to address problems among clients that can impede transitions from welfare to work or interfere with parental responsibilities by conducting assessments, providing pre-treatment services, and making referrals.
Methods: Data was collected at baseline and 6-month follow-up on: mental health, substance use, intimate partner violence, and learning problems. Follow-up data was collected for a regional-level proportionate random sample of clients who consented to participate between January 1 & December 31, 2008 (total n=2,493). Of the 427 participants selected as the sample, 322 interviews were completed for a follow-up rate of 75%. McNemar's test for correlated proportions was used to determine significant differences between baseline and follow-up.
Results: Subjects were mostly female (93.8%) with an average age of 30.3, 84.8% were white, and 18.9% were married. Subjects self-reported significant decreases from baseline to follow-up at the .05 level or greater for: 1) feeling worried or anxious, feeling bad, or having thoughts of hurting themselves; 2) being verbally, psychologically and physically abuse by an intimate partner; and 3) using alcohol, marijuana, cocaine, depressants, amphetamines, Oxycontin®, or multiple substances.
Conclusions: Public assistance recipients can experience significant barriers to self-sufficiency. These barriers can prevent successful transitioning from welfare to work. The need for programs which facilitate this transition could be helpful. Comprehensive case management and service coordination programs, such as Kentucky's Targeted Assessment Program examined here, show promise in helping individuals who experience mental health, substance abuse, or intimate partner violence to become self-sufficient. Limitations include self-reported data and participants being reluctant to reveal information that could lose benefits or custody of their children.
Financial Support: This study was supported by the Commonwealth of Kentucky Department for Community Based Services.

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INDIVIDUAL AND CONCOMITANT INFLUENCES OF POSITIVE AND NEGATIVE AFFECT ON URGE TO SMOKE.

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Aims: Prior research has shown that low positive affect (PA) and high negative affect (NA) are associated with urge to smoke, particularly during acute tobacco abstinence. However, it is unclear whether PA and NA have unique, overlapping, or interactive influences on urge. It is also uncertain whether PA and NA differentially influence appetitive (anticipation of pleasure from smoking) and aversive (anticipation of NA relief from smoking) aspects of urge. This study examined the independent and concomitant effects of PA and NA on urge, and whether tobacco deprivation moderated these influences.
Methods: Affect was measured during a baseline session. For a subsequent experimental session, participants were randomized to one of two groups: (a) 12-hr tobacco deprivation before the session (n = 51) and (b) ad libitum smoking (n = 69). Urge was measured during the experimental session.
Results: Results showed that across deprived and nondeprived conditions, PA was inversely associated with aversive smoking urge (β = -.21, p =.007), but this effect was eliminated when controlling for NA (β = -.10, p =.20). By contrast, the influence of NA on appetitive (β = .19, p =.03) and aversive (β = .28, p =.002) smoking urge across both conditions was unique from PA. Deprivation did not moderate the effects of PA. However, deprivation significantly moderated the influence of NA on aversive smoking urge (F = 6.9, p =.01), such that NA had a robust effect on aversive urge in deprived smokers (β = .51, p =.0001), but a non-significant effect in nondeprived smokers (β = .16, p =.20). This moderational pathway was unique from PA (F = 4.6, p =.04). There were no significant interactions between PA and NA on urge. The pattern of results remained consistent after controlling for demographics and nicotine dependence severity.
Conclusions: These findings suggest that PA is not uniquely linked with urge. Alternatively, smokers with high NA may be vulnerable to aversive smoking urges, especially during acute abstinence. These results could be useful for developing cessation interventions for NA-prone smokers.
Financial Support: NIDA grant DA025041

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VARENICLINE DEMONSTRATES PARTIAL AGONIST CHARACTERISTICS BY ENHANCING RESPONDING FOR NON-PHARMACOLOGICAL REINFORCERS AND ATTENUATING THE REINFORCEMENT-ENHANCING EFFECTS OF NICOTINE.

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Aims: Data suggest that varenicline (VAR), a partial nicotinic agonist, is one of the most effective smoking cessation pharmacotherapies. Varenicline's therapeutic efficacy could be at least partly the result of substituting for the reinforcement-enhancing effects of nicotine (NIC) and/or blocking the reinforcement-enhancing effects of NIC. We addressed both possibilities by assessing the effects of VAR alone and in combination with NIC while animals lever pressed for a moderately reinforcing visual stimulus (VS).
Methods: Rats were assigned to one of eight groups [saline, NIC (0.4 mg/kg), VAR (0.1, 0.3 or 1.0 mg/kg) or NIC+VAR (0.4 mg/kg NIC+0.1, 0.3 or 1.0 mg/kg VAR)] and received drug prior to each daily 1 hr session for 14 days. A follow-up study was conducted with a broader dose range of VAR alone; rats were assigned to one of six groups [saline, NIC (0.4 mg/kg) or VAR (0.01, 0.1, 1.0 or 3.0 mg/kg)] and received 14 sessions of drug exposure.
Results: Across both studies, there was a dose-dependent effect of VAR alone on responding for the VS. The 0.1 and 1.0 mg/kg VAR groups exhibited the highest rates of responding, showing similar levels of enhanced responding for the VS as NIC-treated animals, while the 0.01 and 3.0 mg/kg VAR groups exhibited the lowest rates of responding for the VS. In the NIC+VAR groups, VAR dose-dependently attenuated the reinforcement-enhancing effects of NIC with the highest dose (1.0 mg/kg) exhibiting the greatest antagonist effects.
Conclusions: The results of these studies are consistent with the partial agonist characteristics of VAR and support the assertion that the therapeutic efficacy of VAR may be related to its ability to partially replace the reinforcement-enhancing effects of NIC at lower doses and inhibit the enhancing effects of NIC at higher doses.
Financial Support: National Institute of Health: DA10464 (Donny), DA-24801(Palmatier); Varenicline was generously donated by Pfizer, Inc.

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METHADONE PATIENTS' TREATMENT OUTCOMES: LONGITUDINAL STUDY ON THE ASSOCIATIONS BETWEEN BACKGROUND AND PROCESS VARIABLES AND RETENTION RATE, ILLICIT DRUG USE AND RISK BEHAVIOR.

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Aims: This first Israeli longitudinal study examines associations between background and process variables (methadone dosages, social network, therapeutic alliance) and outcomes (i.e., retention rate, opiate use, risk behaviors) at 6- and 12 months following admission to methadone clinics.
Major Hypotheses:1. Both process variables and outcomes will improve over time.2. Process variables will be positively associated with treatment outcomes, mainly reduction in opiate use and risk behavior
Methods: 246 of 300 (82%) consecutive patients in four (of 11) MMTP in Israel participated in three time-points: (1) first month of program admission; (2) six months (n=130) and (3) 12 months (n=137) following program admission. Face-to-face structured interviews were used, as well as computerized clinical data on methadone dosages and urine-tests.
Results: Six-month retention rate was 88% and 12-month retention was 78.4%. Opiate use decreased over time (from 79% to 32%), as well as levels of drug and sexual risk behavior (Mean= 4.76, SD=6.36 vs. Mean=1.53, SD=2.96 at admission and 12-month follow up, respectively).Therapeutic alliance decreased over time.As hypothesized- therapeutic alliance with the social worker was associated with less opiate use when both were measured at the same time-point and to a lesser degree when opiate use was measured 6 months after the measurement of therapeutic alliance.Support from social network was associated with less opiate use at a later stage.
Conclusions: Retention rate in Israel is much higher than in U.S. and Europe. Opiate use and risk behaviors of patients who remain in MMTP decrease over time. Quality of patient-social worker relationships serves a crucial role in facilitating positive outcomes of patients in MMTP.
Financial Support: Shulamit Josephitz Award, School of Social Work,Hebrew University,Jerusalem

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ESTIMATING THE INTAKE OF ABUSED METHAMPHETAMINE USING EXPERIMENTER-ADMINISTERED DEUTERIUM LABELED R-METHAMPHETAMINE: SELECTION OF THE R-METHAMPHETAMINE DOSE.

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Aims: All addictive drugs produce tolerance and addicts compensate by increasing drug exposure. Thus, the quantity of illicit drug ingestion is related to the severity of addiction. Unfortunately there are no objective methods to estimate intake for most addictive drugs. Using experimenter-administered doses of deuterium-labeled R-methamphetamine (R-(-)-MA-d3), we have developed a method to estimate the amount of abused MA intake in addicts enrolled in clinical trials. This study assessed the pharmacokinetic (PK), pharmacodynamic (PD), and tolerability of single oral doses of R-MA in healthy adults to select a dose of R-MA-d3 to be used as a biomarker for estimation the amount of MA abuse.
Methods: This was a 5-session randomized, double-blind, placebo-controlled, balanced crossover study in eight subjects. Oral R-(-)-MA was dosed at 0, 1, 2.5, 5 or 10 mg; bioavailability was estimated by slow IV dosing (30 min) of 2.5 mg of R-(-)-MA-d3, given with the 2.5 mg R-MA oral dose condition. PK and PD measures were obtained.
Results: No serious adverse events occurred during the study and all doses of R-MA were well tolerated. Linear PK was observed within our oral dose range of 1-10 mgs. Complete bioavailability and pharmacological inactivity were found for all oral doses. These characteristics indicate the advantage of a small oral R-(-)-MA-d3 dose being used as a biomarker to estimate exposure to abused MA. Based on data from this study, 5 mg of R-(-)-MA-d3 has been selected as the biomarker dose in future studies.
Conclusions: Experimenter administered oral R-(-)-MA-d3 may allow estimation of abused MA intake and exposure. Knowledge of the quantity of MA intake may allow better estimation of disease severity and treatment efficacy. Experience gained from this study also can be applied to the management of other drug dependence problems such as cocaine, cannabinoid and opiate addiction.
Financial Support: NIDA

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DELTA9-TETRAHYDROCANNABINOL ATTENUATES I.V. HEROIN SELF-ADMINISTRATION IN RHESUS MONKEYS.

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Aims: The cannabinoid receptor agonist delta9-tetrahydrocannabinol (THC) enhances the antinociceptive effects of mu opioid receptor agonists, raising the possibility of using a combination of THC and opioids for treating pain. This drug combination would be most useful if other (abuse related) effects of opioids were not increased by THC.
Methods: This study examined the effects of non-contingent and contingent THC on i.v. heroin self-administration in rhesus monkeys.
Results: Monkeys could self administer different unit doses of heroin (0.0001-0.1 mg/kg/infusion) or saline under a fixed ratio 30 schedule, generating an inverted U-shaped dose effect curve. In one experiment (n=4), non-contingent THC (0.1-1.0 mg/kg) administration (30 min prior to sessions) dose-dependently decreased the number of heroin infusions in all monkeys, shifting the heroin dose effect curve downward. In a second experiment (n=4), monkeys self-administered THC alone (0.0032- 0.032 mg/kg/infusion), heroin alone, or a mixture of THC and heroin. THC alone did not maintain responding above that obtained with saline; however, increasing the THC dose in the mixture dose-dependently decreased the number of (heroin and THC) mixture infusions.
Conclusions: Collectively, these data indicate that in rhesus monkeys, THC does not enhance the reinforcing effects of heroin. Combined with the findings that THC increases the antinociceptive effects and decreases the discriminative stimulus effects of mu opioid receptor agonists, these data suggest that a combination of THC and an opioid could be effective for treating pain with no greater, and perhaps less, abuse liability as compared with an opioid only.
Financial Support: Supported by NIDA grants DA05018 and 17918 (CPF)

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TRANSCRIPTOME PROFILING AND PATHWAY ANALYSIS OF GENES DIFFERENTIALLY EXPRESSED IN RESPONSE TO TOPIRAMATE FOR TREATMENT OF METHAMPHETAMINE DEPENDENCE.

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Aims: Several clinical investigations have indicated that topiramate would have a therapeutic effect in treating methamphetamine dependence. However, the molecular mechanisms underlying such effects are largely unknown.
Methods: In this study, we compared the genome-wide expression profiles of positive and negative responders at weeks 8 and 12 on RNA samples collected from whole blood for 50 topiramate- and 49 placebo-treated participants at three time points; i.e., baseline and the end of weeks 8 and 12.
Results: At the single-gene level, we identified 1848, 959, 675, and 741 differentially expressed genes, respectively, in the Week 8 topiramate, Week 8 placebo, Week 12 topiramate, and Week 12 placebo groups. After identification of differentially expressed genes, we performed pathway analyses using various bioinformatics tools, which revealed that 30 enriched pathways were shared at Weeks 8 and 12 in the topiramate groups. These pathways were involved in physiological functions such as neuronal activity, immune response, and cardiovascular function. Interestingly, four of these pathways; i.e., long-term potentiation, Fc epsilon RI signaling, MAPK signaling, and GnRH signaling, have been reported to play critical roles in drug addiction.
Conclusions: We conclude that topiramate treatment of methamphetamine addicts significantly modulates the expression of genes involved in multiple biological processes associated with addiction behavior as well as other physiological functions.
Financial Support: NIDA, NIH

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THE DISCRIMINATIVE-STIMULUS, SUBJECT-RATED, PERFORMANCE AND CARDIOVASCULAR EFFECTS OF COCAINE ALONE AND IN COMBINATION WITH ARIPIPRAZOLE IN HUMANS.

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Aims: The atypical antipsychotic aripiprazole is a dopamine D2 receptor partial agonist that is being evaluated as a pharmacotherapy for stimulant-use disorders. Acutely administered aripiprazole attenuates the discriminative-stimulus and other behavioral effects of d-amphetamine; however, subsequent studies indicated that maintenance on aripiprazole enhanced the effects of cocaine. The aim of the present experiment was to assess the discriminative-stimulus, subject-rated, performance and cardiovascular effects of cocaine alone and following acute administration of aripiprazole in human subjects. We hypothesized that acute aripiprazole would attenuate the behavioral effects of cocaine in a manner similar to that observed for d-amphetamine.
Methods: Eight subjects who met criteria for cocaine-use disorder participated as outpatients and learned to discriminate 150 mg cocaine from placebo. After acquiring the discrimination, the effects of cocaine (0, 25, 50, 100 and 200 mg) administered alone and in combination with aripiprazole (15 mg) were determined. Data were analyzed as peak-effect and area-under-the-curve using repeated-measures ANOVA.
Results: Significant main effects of cocaine alone were observed for the drug-discrimination task, self-report items typically associated with stimulant effects, heart rate and blood pressure. Limited effects of aripiprazole were revealed; however, planned comparisons indicated that fewer doses of cocaine were significantly greater from placebo when combined with aripiprazole, suggesting a reduction in the discriminative-stimulus, self-reported and cardiovascular effects of cocaine.
Conclusions: These data are consistent with previous studies that have tested acutely administered aripiprazole in combination with stimulant drugs and suggest that the ability of aripiprazole to modify stimulant effects is a function of the duration of treatment (acute vs. maintenance).
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THE EFFECT OF METHAMPHETAMINE ADDICTION ON METABOLITE LEVELS IN THE HUMAN BRAIN USING PROTON MAGNETIC RESONANCE SPECTROSCOPY.

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Aims: Abuse of methamphetamine has dramatically increased in recent years; it is associated with significant social and economic burdens for society, as well as negative effects on individuals. Spectroscopic studies in methamphetamine-dependent participants have reported a reduction in N-acetylaspartate (NAA) and an increase in choline-containing compounds (Cho). These changes may indicate reduced neuronal density or content and cell proliferation in response to neuronal injury respectively. This study was to determine the effect of methamphetamine addiction on metabolite levels in the brain.
Methods: Single-voxel proton MRS was performed in the anterior cingulate cortex (ACC), basal ganglia (BG) and visual cortex (VC) of eight methamphetamine-dependent participants aged 22-46, and compared with eight healthy, age-matched controls. Participants were imaged at the Centre for Advanced MRI at the University of Auckland. Spectral images were obtained on a 1.5T Siemens Magnetom Avanto System and analysed using jMRUI V4.0 software. Metabolites were expressed as ratios – NAA/creatine (Cr), Cho/Cr and Cho/NAA. Two-tailed t-tests were used to determine the significance of differences between methamphetamine-dependent and control participants ($p<0.05$).
Results: There were no significant differences in the relative ratios of these metabolites between methamphetamine-dependent and control participants in all three voxels.
Conclusions: Contrary to findings made by previous research, there was no significant change in relative ratios of these metabolites within the ACC, BG and VC of methamphetamine-dependent participants. However, unlike comparative trials the participants were not abstinent. Therefore, it is likely that these changes only occur following methamphetamine withdrawal.
Financial Support: School of Pharmacy, The University of Auckland

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ACCEPTANCE AND COMMITMENT THERAPY FOR METHADONE DETOXIFICATION: IDENTIFYING MECHANISMS OF CHANGE.

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Aims: Acceptance and Commitment Therapy (ACT) is an innovative behavioral treatment that represents a significant shift in philosophy and perspective. A primary tenet of ACT involves the notion that avoidance or behavioral inflexibility regarding negative emotions, thoughts, or bodily sensations results in and perpetuates maladaptive behavior (e.g., drug use).
Specific aim is to assess the proposed mechanisms of change in ACT; thereby testing whether:
(1) Experiential avoidance mediates treatment outcome.
(2) Experiential avoidance moderates the relation between drug use outcomes and detoxification fear.
Methods: Methadone patients (N = 54) were randomized to receive either 24 individual therapy sessions of ACT (n=28) or Drug Counseling (n=26) in the context of a 6 month linear dose reduction program.
Mechanisms of change included detoxification fear, inflexibility, and mindfulness. Experiential avoidance, the primary proposed mechanism of ACT assessed the patient's ability to accept undesirable thoughts and feelings while still pursuing self-identified goals.
Primary outcome data was the number of opiate negative urine screens. To test the hypothesized moderator effect for each independent variable across the five study time points, repeated measures ANOVA was used.
Results: Results indicated that in the ACT condition only,
AAQ and AIS scores decreased significantly over time. In response to our primary aim of identifying mechanisms of change, significant interactions were found in the ACT condition in relation to fear of withdrawal and experiential avoidance.
Conclusions: From these results we are able to begin to identify specific mechanisms of change to understand how ACT therapy for opiate detoxification works. This study helps provide good estimates of the proximal ACT variable effects and reasonable estimates of the more distal opiate use and relatively permanent change effects.
Financial Support: NIDA R01DA019436 (PI: Stotts)

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BELIEFS AND TREATMENT OUTCOME.

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Aims: We examined the association between participants' beliefs and treatment outcome in a subset of participants in a recent out-patient treatment trial for methamphetamine dependence.
Methods: Data were analyzed from 40 individuals randomized to an active treatment or a placebo. All participants received 5 intravenous infusions over a 3-week period, oral medications for 40 days, and weekly cognitive behavioral treatment for the duration of the 106-day trial. After the study ended, participants were asked whether they believed they had received active medication or placebo and the results were examined for the relationship between what participants believed they had received, what they did receive, and urine test results.
Results: Of the 40 participants, 24 believed they had received active medication although only 13 actually did while the other 11 received placebo. At the end of the study the 13 participants who received the active treatment provided 55% MA-free urine samples while the 11 who received placebo provided 62% MA-free samples—no significant differences between the two groups. Of the 16 participants who believed they'd received placebo 11 actually received active treatment and they returned 29% MA-free urine samples while the remainder provided 22% MA-free urine samples.
Conclusions: These findings suggest that participant beliefs played an important role in treatment outcome; those who believed they were given the active medications were twice as likely to be abstinent at the end of the study compared to those who believed that they were receiving the placebo no matter what they actually received.
Financial Support: Hythiam, Inc.

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PATHOLOGICAL LEARNING IN SMOKERS: A CONDITIONING EXPERIMENT UTILIZING ERP MEASUREMENTS.

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Aims: Substance use disorders are characterized by cognitive processing biases, such as automatically detecting and orienting attention towards drug-related stimuli. Up to now it is unclear how, when, and what kind of attention (i.e., implicit, explicit) interacts with the processing of these stimuli. In addition, it is unclear whether smokers are hypersensitive to emotionally significant cues in general or to smoking-related cues in particular.
Methods: The present study aimed to enhance insight in drug-related processing biases by manipulating attention for smoking cues and other motivationally relevant (emotional) cues in 27 smokers and 27 non-smokers in a visual oddball task. Both groups were presented with a rapid and continuous stream of frequent animal (22), garbage (22) and smoking pictures (22). Each of these three categories served in separate blocks as target (explicit attention; counting) or non-target (implicit attention; oddball) category. ERPs were recorded to all stimuli. Afterwards, participants rated the pictures on their arousal and valence properties.
Results: Compared to non-smokers, smokers' P300 (350-600 ms) was enhanced to smoking pictures under both attention conditions. P300 amplitude did not differ between groups in response to positive, negative, and neutral cues.
Conclusions: It can be concluded that attention manipulation affects the P300 differently in smokers and non-smokers. Smokers display a very specific bias to smoking-related cues, and this bias is present in both explicit and implict processing.
Financial Support: This work was supported by a VIDI grant funded by the Netherlands Organization for Scientific Research (NWO; grant number 016.085.322)

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EFFECT OF CHRONIC TREATMENT WITH ARIPIPRAZOLE ON THE WAKING AND POSTPRANDIAL URGES TO SMOKE IN CHINESE HEAVY SMOKERS.

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Aims: The central dopaminergic system plays a critical role in the reinforcing effects of nicotine, which are key determinants in the urge to smoke. Previous study has demonstrated that acute administration of 10 mg aripiprazole significantly decreased various subjective responses to smoking. The present study investigated whether 2 week treatment with 10 mg aripiprazole could attenuate waking and postprandial urges to smoke in Chinese male and female heavy smokers.
Methods: A randomized and placebo-controlled pilot clinical study was conducted to assess the effect of aripiprazole on various responses to smoking. The primary outcomes were subject's ratings on questionnaires of smoking urge, withdrawal syndromes, and cigarette evaluation. All participants were administered either placebo or 10 mg aripiprazole for two weeks. Throughout the experiment, participants were required to self-report (1) smoking urge and nicotine withdrawal symptoms before their first cigarette after awakening and after lunch and (2) subjective responses to the first cigarette smoked of the day and after lunch.
Results: Aripiprazole was associated with significantly decreased waking and postprandial urges to smoke. Aripiprazole failed to produce a significant effect on overall nicotine withdrawal symptoms after awakening and after lunch. However, waking, but not postprandial, withdrawal craving and syndromes was significantly reduced by aripiprazole. Aripiprazole had no effect on the overall subjective responses to the first cigarette of the day and after lunch.
Conclusions: The attenuating effects of aripiprazole on waking and postprandial urges to smoke demonstrate the promising effect of aripiprazole in the treatment of nicotine dependence.
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EXTINCTION OF ATTENTIONAL BIAS TO COCAINE-RELATED STIMULI: DIFFERENCE BETWEEN NON-TREATMENT-SEEKING AND TREATMENT-SEEKING COCAINE-DEPENDENT SUBJECTS.

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Aims: In recent studies, cocaine-dependent subjects showed attentional bias to cocaine-related stimuli. Furthermore, non-treatment-seeking and treatment-seeking cocaine-dependent subjects responded to cocaine-related stimuli differently. Whether attentional bias to cocaine-related stimuli is sustained over repeated measures has never been studied. The aim of the current study was to investigate changes in attentional bias to cocaine-related words using a repeated-measures design.
Methods: We used a cocaine Stroop task, which included 4 blocks with cocaine-related words and 4 blocks with neutral words in an alternating order, in 32 control subjects, 22 non-treatment-seeking and 15 treatment-seeking (before treatment start) cocaine-dependent subjects. Attentional bias was defined as longer reaction time to respond to cocaine-related words than neutral words.
Results: We found that compared with control subjects, both non-treatment-seeking and treatment-seeking cocaine-dependent subjects showed attentional bias to cocaine-related words for the first block. This attentional bias disappeared thereafter for non-treatment-seeking cocaine-dependent subjects but remained in the second and third blocks for treatment-seeking cocaine-dependent subjects.
Conclusions: The results suggest that attentional bias was extinguished by repeated measures and may last longer over repeated measures in treatment-seeking than in non-treatment-seeking cocaine-dependent subjects. Higher addiction severity in treatment-seeking cocaine-dependent subjects may be related to this difference, but further research is needed to explore the mechanisms involved in this effect.
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PROTON MAGNETIC RESONANCE SPECTROSCOPY DETECTS PUTAMEN GLUTAMATE CHANGES DURING CHRONIC COCAINE EXPOSURE IN SQUIRREL MONKEYS.

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Aims: Chronic cocaine exposure alters brain structure and function. Studying cocaine's brain effects prospectively in humans is difficult, and it is impossible to conduct studies including baseline (pre-cocaine) assessments. Accordingly, we developed a squirrel monkey model to study the brain effects of chronic cocaine exposure prospectively.
Methods: At baseline, 4 adult male monkeys underwent right putamen MRS on a Varian 9.4T scanner under isofluorane (2%) anesthesia. A STEAM sequence was used with parameters: TE/TM/TR of 9.7/7/4000 ms, 128 averages, voxel size=6x6x6 mm (0.216 mm3). Monkeys subsequently were administrated cocaine intramuscularly 3 times/day, 5 days/week, at 1 mg/kg for 1 week, 2 mg/kg for 1 week, and 3 mg/kg, for 8.5 months. Scans were repeated after 1, 3, 6 and 9 months. Spectral data were processed and fitted with a customized, automated Matlab script, and LCmodel. Metabolite ratios were calculated using total creatine (Cr) as the denominator. One-way within-subjects ANOVAs were run for each ratio to test for exposure time effects.
Results: Only the glutamate (Glu)/Cr ratio was significant ($F_{4,12}=75$, $P<0.000001$). Post-hoc tests revealed that Glu/Cr ratios decreased and increased from baseline, respectively, after 1 ($t=6.85$, $p<0.01$) and 9 ($t=8.9$, $p<0.003$) months cocaine. The early Glu/Cr decrease is consistent with reduced anterior cingulate Glu/Cr levels reported in human chronic cocaine users (Psychiatry Res. 174:171, 2009). The late Glu/Cr increase also is consistent with that study, which noted a positive correlation between cocaine use duration and Glu/Cr levels.
Conclusions: Thus, this prospective squirrel monkey model may be suitable for studying some of cocaine's chronic effects, as well as for testing novel treatment medications.
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LATIN AMERICAN PSYCHIATRISTS DEVELOP BIOLOGICAL PROTOCOLS TO CONTROL CRAVING AND PREVENT RELAPSE IN COCAINE DEPENDENCE.

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Aims: Cocaine hydrochloride, coca paste and crack are industrial derivatives of the Andean coca leaves designed for recreational and addictive purposes.
Methods: In Peru, in the 1980s were introduced psychosurgery and agonist therapy with oral cocaine to control craving and maintain abstinence in cocaine dependent patients.
Results: Results were presented and explained at several medical meetings including NIDA/CPDD. Bilateral anterior cingulotomy surgery was performed in 33 patients. More than a hundred Peruvian patients were treated with agonist protocols using oral cocaine alkaloid contained in coca tea infusions, coca tablets, coca powder or coca leaf. There is a report in Bolivia about the use of coca leaves used as chewing (chacchado) for control craving, and a study in Peru with Valerian root, and anecdotal comments in Argentina, Brasil and Paraguay of use of the weak stimulant alkaloid mateine containing in yerba mate plant for reduce anxiety in cocaine-dependent patients. In the Andean regions, where coca products developed a worldwide uncontrollable cocaine dependence, psychiatrists are currently seeking an effective biological schedules to control craving, avoid relapse and maintain long-term abstinence (FDA currently do not approve any protocol for treatment).
Conclusions: We show the results of twenty years' use of these biological methods.
Financial Support: Private

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PSYCHOATIVE DRUG USE AND ASSOCIATED RISK BEHAVIORS IN BRAZIL.

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Aims: To identify typologies of alcohol, tobacco, and other drug use among high school students and to estimate associations linking types to other risk behaviors.
Methods: A self-report questionnaire was applied in 2,691 students selected by a probability sampling of private schools in Sao Paulo, Brazil. The instrument assessed patterns of drug consumption such as alcohol, tobacco and the illegal drugs (marijuana, inhalants, amphetamines, benzodiazepines and ecstasy) in the preceded month as well as risk behaviors: riding motorcycle without helmet, carrying a weapon, involvement in fights, unprotected sex, and using pills for a diet without prescription. Cluster analysis identified typologies, followed by a Chi-square test to search for associations.
Results: Four groups were identified: the first is characterized by non-use of drug (46%); the second by lower level use of alcohol (1 to 5 days; 14%); the third by the use of tobacco and alcohol (1 to 5 days) in heavy episodic pattern (21%); the fourth by the use of alcohol, tobacco and use of any other illegal drug (20%). Risk behaviors were associated with membership in the fourth group ($p<0.05$): 18-19% with motorcycle riding without helmets, 11-12% with weapon carrying; 22-23% with fighting; 20-21% with unprotected sex; 6-7% with using pills for dieting. Corresponding estimates for the non-user group were: 5-6% for riding motorcycle helmetless; 3% for weapon-carrying; 5-6% for fighting; 1-2% for a diet pill use.
Conclusions: As observed in research on students in other places, Brazil's school attending youths exhibit problem behavior syndromes, with drug use woven into a fabric that includes other risk behaviors.
Financial Support: Fapesp, AFIP and Capes.

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EFFICACY OF CONTINUING MEDICAL EDUCATION FOR PROMOTING PHYSICIAN PRACTICES AIMED AT DECREASING BUPRENORPHINE MISUSE AND DIVERSION.

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Aims: Office-based opioid dependence treatment (OBOT) with buprenorphine (BUP) has expanded greatly. Post-marketing surveillance data indicate BUP is misused and diverted in Appalachia. It is important that doctors understand BUP clinical pharmacology and engage in best practices to decrease risk of BUP diversion and misuse. The hypotheses are that continuing medical education (CME) will improve knowledge and promote positive changes in physician practices.
Methods: All DEA X-licensed doctors in a 50-mile radius of Big Stone Gap, VA (n=123) were invited to a CME, entitled "Buprenorphine Diversion and Misuse: How to Protect Your Office-based Practice," and to complete 4 surveys (1 before, 1 on-site after, and 1- and 3-months post-CME). Surveys evaluated physician characteristics, practice behaviors, and BUP pharmacology and legislative knowledge.
Results: Of 28 doctors attending the CME, 22 had medical board certifications; one completed an Addiction Psychiatry/Medicine fellowship. BUP pharmacology and legislative knowledge significantly improved immediately after the CME, and was retained 3 months later ($p<0.05$). Significant ($p<0.05$) practice behavior changes from baseline to 3 months post-CME included: increased examination of patients for track marks/intranasal erythema, random urine testing, use of objective markers of treatment progress to guide frequency of doctor visits and days of medication prescribed, engagement of pharmacies in treatment, registration for a Physician Clinical Support System mentor, and decreases in prescribed maintenance dose (mg).
Conclusions: Physicians significantly improved practice behaviors that should enhance the overall quality of OBOT and may decrease risk of BUP misuse and diversion from their practices. Given the expansion of OBOT and many new physicians with limited addiction training, more CME activities targeting this new provider group could have positive patient and public health outcomes.
Financial Support: Investigator-initiated research study funded by Reckitt Benckiser Pharmaceuticals

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SUBSTANCE USE DISORDER RISK AND INHIBITORY CONTROL ON AN ANTI-SACCADE TASK.

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Aims: Adolescents with disruptive behavior disorders (including conduct disorder and oppositional defiant disorder) exhibit high levels of impulsivity and disinhibition and are considered to be at higher risk for the development of SUDs. In this preliminary study, we compared adolescents with and without disruptive behavior disorders on performance of a behavioral measure of disinhibition, including reward and neutral conditions.
Methods: Thirteen high risk subjects (those having a diagnosis of CD or ODD) were compared with 74 low risk subjects (those not having a diagnosis) who were similar on age. The measure of disinhibition and impulsivity used was the anti-saccade task. Subjects were required to inhibit a prepotent response by directing their gaze toward the opposite side of the screen from the stimulus presented. We predicted that high risk subjects will have a lower percentage of correct responses than low risk subjects.
Results: Compared with the low risk group, the high risk group had significantly lower percentages of correct responses on the anti-saccade task, regardless of condition. Males had a lower rate of correct reponses than females. Males were also significantly more likely than females to have a disruptive behavior disorder diagnosis. No significant interaction between sex and task performance was found. When a diagnosis of ADHD was added to the regression model, it was found that this diagnosis did not account for significant variance.
Conclusions: These preliminary results indicate that high risk adolescents exhibit greater levels of impulsivity and disinhibition as measured by a behavioral anti-saccade task than low risk adolescents. Future studies with larger samples are needed to elucidate the associations among CD, ODD, and performance on the anti-saccade task. These results could inform the development of prevention and intervention strategies for SUDs by targeting these problematic behaviors.
Financial Support: NIAAA R21 AA017312-02

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PREDICTORS OF NON-MEDICAL PRESCRIPTION STIMULANT USE AMONG COLLEGE STUDENTS.

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Aims: To examine impulsivity, positive and negative expectancies, and evaluations of potential positive and negative consequences as predictors of nonmedical prescription stimulant use in a college population.
Methods: Data were collected from 203 college students (19.4 years of age, *SD* = 1.6; 56% female) regarding their use of prescription stimulants for non-prescribed purposes and up to three good and three bad consequences they expected to occur from use. Participants rated the likelihood that those consequences would occur from use (Expectancies) and how good or bad those consequences would be if they were to occur (Evaluations) using 7-point Likert scales. Impulsive personality traits (i.e., lack of premeditation, sensation seeking, lack of perseverance, positive urgency, and negative urgency) were assessed using the UPPS-P.
Results: Prescription stimulant use for non-prescribed purposes during the past year was reported by 26% of the sample. Significant bivariate correlations were found between (a) lack of premeditation (failure to plan) and Positive Expectancies, (b) Sensation seeking (preferences for novel or unique experiences) and Positive Evaluations, (c) Lack of Perseverance (failure to persist at frustrating/difficult tasks) and Negative Evaluations, and (d) between these three personality traits and self-reported use. Positive Expectancies, Negative Expectancies, and Negative Evaluations were all significantly related to self-reported use in the expected directions. Hierarchical logistic regression analysis found that stronger Positive Expectancies were associated with an increased likelihood of use (OR=1.52; 95%CI=1.1,2.1) whereas stronger Negative Evaluations were associated with a decreased likelihood of use (OR=.71, 95%CI=.54,.92). Expectancies and Evaluations were found to mediate the association between personality traits and self-reported use.
Conclusions: This study extends prior research on non-prescribed use of prescription stimulants by demonstrating the role of impulsive personality, outcome expectancies, and evaluations of expected consequences in predicting use.
Financial Support: This study was conducted without financial support.

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INDIVIDUAL DIFFERENCES IN IOWA GAMBLING TASK: POSSIBLE ROLE OF EARLY PUNISHMENT INTENSITY.

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Aims: Initial intensity of punishment is an important determinant of behavioral suppression. The Iowa Gambling Task (IGT) examines individual differences in decision-making. Individual differences have been associated with differences in prefrontal lobe function. Subjects make a series of 100 choices from four decks of cards associated with varying amounts of hypothetical rewards and punishments. In two decks (risky decks) higher-value short-term rewards are combined with larger-intensity intermittent punishments, while in the other decks (safe decks) lower-value short-term rewards are combined with lower-intensity punishments. Subjects are instructed to earn as much money as possible and that some decks are more advantageous. We hypothesize that some individual differences in risky choice in the IGT may result from differences in initial intensity of punishment.
Methods: IGT was administered to 12 cigarette smokers. We plan to study 30 subjects. The IGT was completed under ad-lib smoking. Number of choices from the risky decks in trials 1-20 was compared to choices made in trials 81-100 to establish learning. Subjects were divided into high- and low-risk choosers using a median split in number of risky choices made in trials 81-100. Individual differences in intensity of initial punishment was examined by comparing high- and low-risk choosers on amount of money lost in the first two punishments.
Results: Number of risky choices decreased between blocks 1 and 5 (13 ± 1.15 vs. 7 ± 1.43, $p < .05$). The median split on risky choices in block 5 resulted in significant differences in number of risky choices between high- and low-risk groups (11.17 ± 0.83 vs. 2.83 ± 1.67, $p = .001$). Money lost through initial two punishments among high- and low-risk groups differed in the hypothesized direction ($\$1,175 \pm \$394$ vs. $\$383 \pm \$183$, $p = .12$), although not significant, this is likely due to the small number of subjects studied to date.
Conclusions: Initial intensity of punishment experienced may contribute to individual differences in IGT performance.
Financial Support: NIDA T32 DA007242 and R01 DA008076

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CORTICO-CEREBELLAR ABNORMALITIES IN ADOLESCENTS WITH MARIJUANA DEPENDENCE.

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Aims: Aims: One prior fMRI study utilizing a finger-tapping paradigm, found that adult MJ users had reduced activation in Brodmann's area (BA) 4 (primary motor cortex), BA6 (supplementary motor area) and cingulate (CG) compared to healthy controls (HC).3 The current study aimed to evaluate whether there were activation differences in the cerebellum in addition to previously reported cortical regions between MJ using adolescents and HC on a fMRI bilateral finger-tapping task.

Methods: Methods: Nineteen adolescents (aged 17.9±1.0 years), with DSM-IV MJ Dependence and 19 HC, matched for age (17.6±1.3), had MRI scans on a 3T Siemens scanner, including a standard bilateral fMRI finger tapping sequence. Image data was analyzed using general linear model and the SPM5 software package in Matlab. Regions of interest (BA4, BA6, CG and cerebellum) were selected and significant clusters of activity were thresholded at $p<0.05$, corrected. Linear regressions were performed for age of MJ onset and lifetime MJ use.

Results: Results: Marijuana users reported their age of first MJ use and average frequency of MJ use was 14.9 ±1.3, and 10.4±8 times/week respectively. Healthy controls had greater activation than MJ for BA 4 (max T =2.89,154 voxels), BA 6 (Tmax=3.12, 49 voxels), CG (Tmax=2.75, 179 voxels) and cerebellum (Tmax=3.96, 3263 voxels). Activation of the cerebellum (Tmax=5.45) and BA6 (Tmax=5.64) were found to negatively correlate with age of onset in MJ users. Activation of the cerebellum (Tmax=4.54) and CG (Tmax=3.64) correlated with lifetime MJ smokers.

Conclusions: Conclusion: This is one of the first studies to evaluate cortico-cerebellar circuits in adolescents with heavy MJ use utilizing a bilateral finger tapping fMRI task. Our results are consistent with a previously reported study in adults1. The findings provide evidence for cerebellar dysfunction in MJ abuse and that age of first use and lifetime MJ use may impact the developing brain.

1. Pillay SS, et al: Exp Clin Psychopharmacol. 2008;16:22-32

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DIFFERENCES IN DRUG USE AMONG WHITE AND AFRICAN-AMERICAN WOMEN WHO USE METHAMPHETAMINE.

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Aims: To compare mode of methamphetamine (meth) use and consumption of ancillary drugs among white and African American (AA) female meth users. There is limited knowledge about women who use meth, particularly AA women.

Methods: A chain referral sample of female meth users was interviewed in San Francisco from 2007-2009. Eligibility criteria included meth use past 30 days. We compared use of meth and other drugs among AA (n=147) and white (n=105) women. Participants from other racial/ethnic groups (n=70) were excluded from this analysis.

Results: Mean number of days meth used in the past month was 15, and did not differ significantly by race. Injection of meth in the past 30 days was more common among white women than AA women (63% vs. 33% $p<.01$), while non-injection use (smoking or snorting) did not differ by race. In logistic regression analysis, white women had higher odds of injecting meth than AA women (adjusted odds ratio=2.92; 95% confidence interval 1.69, 5.05), controlling for age, homelessness, and years since first meth use. Nearly all (91%) of participants used ≥1 illicit drug in addition to meth. Crack was most common, with 67% of AA and 50% of white women smoking crack in the past 30 days ($p<.01$). Injection of heroin (alone or mixed with cocaine or meth) was reported by 37% of white and 18% of AA participants ($p<.01$). Among injectors, 21% reported receptive syringe sharing in the past 6 months and 11% distributive sharing, with no significant differences by race. Daily alcohol use was higher among AA women (27% vs. 11%, $p<.01$). Drug treatment in the past 6 months was reported by 29% of AA women and 44% of whites ($p=.01$), reflecting more methadone treatment among whites.

Conclusions: While AA and white women used meth with similar frequency, injection was far more common in whites. Use of meth and opiates by injection may put white women at higher risk for hepatitis C virus and HIV infection. The drug treatment needs of meth-using women may vary by race with respect to the ancillary use of crack, alcohol and/or heroin.

Financial Support: NIDA grant #R01DA21100.

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ATTENTIONAL CONTROL BRAIN REGIONS INVOLVED IN ATTENTIONAL BIAS IN SMOKERS.

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Aims: Smoking is associated with biases in the processing of smoking-related stimuli. Attentional bias is one of the processing biases in addiction and is the tendency of addicted substance users to automatically direct their attention to substance related cues in the environment. Attentional bias is known to influence addictive behaviors and relapse. However, little is known about the neural mechanisms behind attentional bias. The current study aims to elucidate which brain regions are involved in attentional bias in smokers.

Methods: Nineteen smokers and twenty non-smoking matched controls performed a newly developed attentional bias line-counting task during fMRI scanning. This task measures stimulus driven attention for smoking and neutral pictures as well as top-down attention involved in a simple line counting task while distractive pictures are presented.

Results: Smokers, as compared to controls, showed more activation while counting lines in smoking pictures, relative to neutral pictures in the dorsal anterior cingulate cortex (dACC), the right intraparietal sulcus (r-IPS) and the left superior temporal gyrus (l-STG). Amongst other regions, the rostroventral zone of the ACC (rvACC) showed hypoactivation in smokers, as compared to controls, during line counting in both smoking and neutral pictures. The increase in craving during attentional bias correlated with left insula and right putamen activation. All p's <0.001 uncorrected.

Conclusions: It can be concluded from this study that attentional control regions (the dACC and the r-IPS) are involved in attentional bias. It seems that smokers need more attentional control to perform a simple cognitive task when distracting smoking stimuli are present. Also, the hypoactivation in smokers in the rvACC during this emotional salient task, suggest differential salience attribution as compared to non-smoking controls.

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TESTING THE ABILITY OF ORAL THC TO BLOCK THE DISCRIMINATIVE STIMULUS EFFECTS OF MARIJUANA IN CANNABIS-DEPENDENT INDIVIDUALS.

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Aims: This ongoing study is designed to evaluate whether oral THC blocks the discriminative stimulus effects of marijuana in order to validate drug discrimination as a model for assessing potential treatment medications.

Methods: Cannabis dependent participants first were trained to discriminate marijuana (2.70% THC) from placebo (0.02% THC) cigarettes. Dose-response functions then were generated to determine whether different THC concentrations (0.02, 1.70, 2.70%) occasioned marijuana-appropriate responding (i.e., demonstrating pharmacological sensitivity). Next, different pretreatment doses of another cannabinoid (oral THC: 0, 10, 20 mg) and a drug from a different class (d-amphetamine: 0, 5, 10 mg) were administered in combination with placebo (0.02% THC) marijuana cigarettes to determine whether they occasioned marijuana-appropriate responding (i.e., demonstrating pharmacological selectivity or substitution). In each session, participants consumed an acute pretreatment dose of oral THC (0, 10, 20 mg) prior to smoking a marijuana cigarette (0.02, 1.70, 2.70% THC), to determine whether oral THC altered the discriminative stimulus effects of marijuana.

Results: Preliminary data from subjects who have completed the study indicated that 2.70% THC was reliably discriminated from 0.02% THC marijuana cigarettes, and that 1.70% THC occasioned marijuana-appropriate responding. None of the doses of d-amphetamine or oral THC substituted for marijuana. Finally, oral THC did not appear to block the discriminative stimulus effects of marijuana.

Conclusions: These data suggest that higher pretreatment doses of oral THC might be necessary to attenuate marijuana's discriminative stimulus effects in cannabis dependent individuals.

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AEROBIC EXERCISE BLOCKS INCUBATION OF COCAINE-CRAVING AND ITS ASSOCIATED NEUROADAPTATIONS.

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Aims: Recent work using rat models of cocaine addiction has shown that wheel running, a form of aerobic exercise that is reinforcing in rats, can decrease cocaine self-administration during a maintenance phase. It is not yet known whether exercise may be useful as a treatment option during relapse. Thus, the goal of this study was to determine whether exercise may block incubation of cocaine craving, an animal model of relapse, and neuroadaptations associated with the incubation effect.
Methods: Once rats acquired self-administration, they were given 24/hr access to cocaine (1.5 mg/kg/infusion) under a discrete trial procedure (4 infusions/hr) for a total of 10 days. Rats then began a 14 day abstinence period, with no access to cocaine. During this period, 9 male rats were given access to a running-wheel for 2 hours each day while another 7 male rats did not have access to a running wheel (these sedentary rats were placed in similar boxes but the wheel was locked at all times). Cocaine-seeking, as assessed under a cued-induced reinstatement paradigm, and markers of ERK signaling in the medial prefrontal cortex, which has been shown previously to be positively associated with incubation of cocaine craving, were then examined in rats after abstinence from extended access cocaine self-administration (i.e., following 2 weeks of abstinence, when cocaine seeking is known to be high).
Results: Results showed that wheel running modestly, but significantly, reduced lever presses during extinction, and dramatically reduced drug seeking in response to the cues formerly associated with cocaine. Although total ERK levels did not differ between groups, phosphorylated levels of ERK were decreased in the medial prefrontal cortex of exercising rats as compared to sedentary rats.
Conclusions: Taken together, these results suggest that aerobic exercise blocks incubation of cocaine craving and its associated neuroadapations.
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PROBABILISTIC FIBER TRACKING OF WORKING MEMORY PATHWAYS IN COCAINE-DEPENDENT SUBJECTS.

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Aims: Previously we have used diffusion tensor imaging (DTI) to demonstrate that the microstructure in the midsagittal corpus callosum (CC) is regionally compromised in cocaine dependent subjects (CD) compared to non-drug-use control subjects (NC), predicting that transcallosal white matter pathways, including those crucial to working memory (WM), are compromised in CD. In this study, we aim to extend our work by testing this hypothesis.
Methods: DTI images were acquired from 10 CD and 10 age-matched NC. Left (L) and right (R) dorsolateral prefrontal (DLPFC) cortex, 2 crucial regions of WM system, were chosen as ROIs based on an anatomical atlas. For each subject, the probabilistic fiber tracking algorithm as implemented in FSL was used to determine the white matter tracts connecting the 2 ROIs (from L DLPFC to R DLPFC, and from R DLPFC to L DLPFC respectively). For each tract and each subject, the volume and the mean value of the fractional anisotropy (FA) on the whole tract and on the midsagittal slice were quantified. Group difference was evaluated using Student t test.
Results: For both tracts, CD had lower mean values on all 3 measures. For example, for the tract from L to R, volumes are 23434+/-10474 cubic mm (CD) and 28854+/-12920 cubic mm (NC), p=0.32. FAs on the whole tract are: 0.39+/-0.02 (CD) and 0.40+/-0.02 (NC), p=0.70; FAs on the midsagittal slice are: 0.44+/-0.06 (CD) and 0.47+/-0.04 (NC), p=0.22.
Conclusions: The lack of statistical significance may be due to 3 factors: (1) partial volume effect of the tracts; (2) small number of subjects; (3) large variance for the volume measurement. More subjects will be recruited in this ongoing project in order to increase the statistical power. In addition, other ROIs, e.g., posterior parietal cortex, will be added. Other DTI measures such as axial, radial, and mean diffusivities will be examined.
Financial Support: This study was funded by NIDA Grants #P50 DA009262 and K02 DA00403 (FGM).

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IDENTIFICATION OF CLINICAL RESPONDERS TO TOPIRAMATE IN A RANDOMIZED CLINICAL TRIAL FOR TREATMENT OF METHAMPHETAMINE DEPENDENCE.

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Aims: In a 12-week, multi-center, randomized, placebo-controlled clinical trial, 140 eligible methamphetamine-dependent subjects were randomly assigned to receive either topiramate (200 mg/day) (N=69) or placebo (N=71). Besides the primary outcome of negative methamphetamine use, there were six binary outcome measures for 12-week treatment/follow-up period.
Methods: We applied latent class analysis (LCA) to these six correlated binary outcomes, adjusting for age, sex, and other baseline measures.
Results: Our LCA revealed that 47 subjects were responders and 93 non-responders. Compared with non-responders, responders were more likely to reach 21+ consecutive days of abstinence (28% vs. 16%), to achieve 50% reduction in the proportion of positive use days from baseline (45% vs. 16%), and to achieve 50% reduction in the median urine concentration at weeks 1-12 from baseline (100% vs. none). Interestingly, we found that the responders were more likely to have received topiramate treatment than placebo (OR=2.135; p=0.037). Separate LCA on the six outcomes from weeks 6-12 yielded similar results.
Conclusions: We conclude there indeed exists a subset of subjects who respond to topiramate treatment better than others and methamphetamine users responded to treatment of topiramate differently, with various response patterns based on the six secondary outcome measures. Our findings strongly indicate that the LCA is a powerful tool to identify those participants who responded better to topiramate treatment than others according to multiple secondary outcome measures collected from each participant.
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PSILOCYBIN-OCCASIONED MYSTICAL EXPERIENCE PREDICTS INCREASES IN THE NEO-PI PERSONALITY TRAIT OF OPENNESS.

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Aims: The goal of this study was to explore the effects of psilocybin-occasioned mystical experience on changes in trait personality measures of Neuroticism, Extroversion, Openness to experience, Agreeableness, and Conscientiousness.
Methods: Fifty-two hallucinogen-naïve volunteers (28 F; 24 – 64 years) participated in Study 1 (N = 35) and Study 2 (N = 17). After extensive preparation, volunteers received a high dose of psilocybin (30 mg/70 kg oral). After drug effects resolved, volunteers completed 3 questionnaires. The States of Consciousness Questionnaire (SOCQ) and the Hood Mysticism Scale (M-Scale) assessed mystical experience, and the Hallucinogen Rating Scale (HRS) assessed hallucinogen-related psychological and somatic effects. The NEO Personality Inventory, a 240-item measure of the 5 major personality factors, was administered at study screening (*pre*) and at 2 months (Study 1) or 3 weeks (Study 2) after the psilocybin session (*post*).
Results: There were significant increases in Openness from pre (M = 135.8) to post (M = 140.6; t = 2.34, p = .02). Further, changes in Openness were correlated with strength of mystical experience (SOCQ: *rho* = .47, p < .001; M-Scale: *rho* = .40, p = .003). Changes in other personality factors were not significant (p > .10). A linear regression model including drug intensity (HRS item) and mystical experience predictors (scores on both the SOCQ and M-Scale) explained significantly more variance in Openness than a model excluding mystical experience predictors (R^2 change = .14, p = .002). Thus, mystical experience significantly predicted changes in Openness after controlling for drug intensity.
Conclusions: Results demonstrate that under supportive conditions psilocybin can lead to increases in Openness to experience, a trait linked to creativity and fluid intelligence. Moreover, mystical experience significantly predicted changes in Openness, suggesting an independent role for mystical experience on changes in a core personality trait.
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EVALUATING MULTIPLE BUPRENORPHINE TREATMENT APPROACHES.

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Aims: APT Foundation offers an integrated system of buprenorphine treatment composed of three levels of care. Services include treatment in a primary care unit, a program embedded in an open access outpatient program(clients select the frequency of groups attended) and a program integrated into a methadone treatment program. The aims of the research are to compare these three buprenorphine approaches within a single agency on: 1) Client outcomes; 2) Client satisfaction, progress, and performance improvement feedback, and; 3) Operational pros and cons.
Methods: 1) Client (n=176) outcome differences between the three approaches will evaluate medical record information(days in treatment, dosing, service use, urine results)and the BASIS-24,a self-report symptom measure administered to clients at admission and follow-up. 2) Client feedback (n=95) will be analyzed from client questionnaires on treatment satisfaction, perceived progress, and program responsiveness. 3) Operational pros and cons will consider client questionnaire feedback, questionnaires completed by program staff (n= 17),and program costs.
Results: 1) Clients in the outpatient program report 70% program satisfaction, MTP based clients report 10% and primary care clients report 45%. 2) Program retention at 1 month is 100% in both MTP and outpatient compared to 91.5% in primary care. At three months retention is 84% in outpatient compared to 72% in MTP and 68% in primary care. 3) Urine drug screens show clients testing postive for illicit opioids to be lowest for primary care at month 1 and lowest for outpatient at month 3. 4)BASIS-24 data indicate that all groups make similar gains in treatment though MTP clients have higher depression scores and higher substance abuse scores at admission.
Conclusions: Clients prefer a balance of structure and autonomy in buprenorphine treatment as shown by higher levels of treatment utilization, satisfaction, postive self comments and retention and lower levels of illicit drug use per urine screens in the outpatient program.
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METHAMPHETAMINE MODULATES AXONAL GUIDANCE MOLECULES IN MOUSE HIPPOCAMPUS.

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Aims: Methamphetamine (METH) users are at high risk for addiction, cognitive impairment and neurotoxicity, partly manifest by pruning or losses in monoaminergic axons and impaired hippocampal function and neurogenesis. Axon growth promotion and attenuation is guided by diverse receptors and ligands, designated as axonal guidance molecules (AGMs). During neurodevelopment, AGMs are critical for axon guidance and pruning. In the adult brain, they contribute to neuroadaptive processes (neurogenesis, synaptic plasticity, dendritic morphology, promotion/blockade of axonal repair). Psychostimulants directly or inferentially are linked to AGM modulation, via monoamine signaling. We hypothesized that METH alters mRNA expression of these critical proteins in hippocampus.
Methods: We used real-time PCR to detect mRNA expression levels of AGMs in adult mouse brain and compared mRNA expression of AGM expression in 5 control and 5 METH treated male and female mice. Saline or 5.0 mg/kg METH was administered once daily in the morning for 6 consecutive days, followed by a no treatment day.
Results: RT-PCR revealed robust mRNA expression of the AGMs semaphorin3e, semaphorin5a, neuropilin-1, ephrinA2, ephrinB3, EphB3, EphA4, EphB4, EphB6 in whole mouse brain. rt-PCR on hippocampal extracts detected reduced mRNA expression levels of two AGMs in METH treated mice compared with saline controls: semaphorin5a and EphB3. Semaphorin5a is an AGM implicated in axonal guidance and development of brain vasculature; EphB3 is implicated in maintaining mature neuronal connections, re-arrangement of synaptic connections, and in hippocampal axon defasciculation. mRNA expression of Dusp6, an extracellular signal regulated kinase (ERK) phosphatase was increased in the same subjects.
Conclusions: These results suggest that METH may alter hippocampal morphology and function by changing expression levels of axonal guidance molecules, raising the possibility that AGMs contribute to METH-induced neurotoxicity and offering new leads for medications development.
Financial Support: DA 15305

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EFFECTS OF A BRIEF BEHAVIORAL ACTIVATION TREATMENT ON SUBSTANCE ABUSE TREATMENT DROPOUT, DEPRESSION, AND ACTIVATION AMONG LOW-INCOME SUBSTANCE USERS.

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Aims: Depression is prevalent among substance users and is associated with substance abuse treatment dropout. One treatment approach that has been suggested to be useful in this context is behavioral activation (BA); Daughters et al. (2008) adapted BA to meet the needs of low-income substance users with depression. In an initial study, the Life Enhancement Treatment for Substance Use (LET'S ACT) was associated with reductions in depressive symptoms and increases in reinforcement. However, several extensions to this study are necessary, including a contact time-matched control and examination of the effect of LET'S ACT on substance use outcomes.
Methods: This study compared LET'S ACT to Supportive Counseling (SC) among 58 substance users with elevated depressive symptoms (BDI ≥ 12) or MDD who were in residential substance abuse treatment in Washington, DC. Assessments were at baseline, post-treatment, and 2-week follow up on measures of depression, behavioral activation, and dropout.
Results: A logistic regression demonstrated LET'S ACT to be significantly associated with treatment dropout (OR = 11.74, CI = .01-.81, $p < .05$). Further, cox proportional hazards survival analyses indicated that SC was significantly associated with higher likelihood of treatment dropout each given day (hazards ratio = 10.49, CI = 1.27-86.86, $p < .05$). Repeated measures ANOVAs showed a significant group x time interaction at post-treatment with behavioral activation; individuals in LET'S ACT demonstrated greater increases in behavioral activation compared to SC ($F(1, 45) = 5.39$, $\eta 2 = .10$, $p < .05$). Repeated measures ANOVAs also revealed a significant group x time interaction at the 2-week follow up with clinician-rated depressive symptoms; individuals in LET'S ACT demonstrated greater improvements compared to those in SC ($F(1, 18) = 4.78$, $\eta 2 = .21$, $p < .05$).
Conclusions: These findings provide initial evidence for the effect of LET'S ACT in reducing substance abuse treatment dropout and provide further evidence of the effects of LET'S ACT on behavioral activation and depression.
Financial Support: None

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HEROIN-DEPENDENT OFFENDERS' EXPERIENCES WITH BUPRENORPHINE VS. METHADONE MAINTENANCE.

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Aims: To determine how similar offenders treated in jail with either methadone or buprenorphine experienced and assessed these treatments.
Methods: The parent study voluntarily randomly assigned male heroin-dependent inmates at the Rikers Island jail in New York City to be maintained in jail with methadone, the standard of care at Rikers (n=56), or buprenorphine - SuboxoneR (n=60). Subjects completed an exit interview at release (98% response), which provides the data for this analysis.
Results: Hispanic (63%); African-American (25%); age (mean=39 yrs); high school grad/GED (42%); lifetime arrests (mean=22); heroin use in last 30 days before arrest (mean=28 days). Methadone patients were more likely to report feeling uncomfortable the first few days, having side/withdrawal effects during treatment, disliking the methadone treatment delivery process in jail and being concerned about continued dependency on medication after release. In contrast, buprenorphine patients' main issue was the bitter taste. All of the buprenorphine patients stated that they would recommend buprenorphine to others, with almost all preferring it to methadone because of its perceived lesser addictive potential, fewer side effects, faster treatment effect and availability of prescriptions, among other reasons. 93% of buprenorphine vs. 44% of methadone patients intended to enroll in those respective treatments after release, with an added 25% of the methadone patients intending to enroll in buprenorphine maintenance instead. Actual post-release enrollment was correlated with these intentions.
Conclusions: There are distinct differences in how methadone and buprenorphine maintenance are perceived by heroin-dependent offenders, which cannot be explained by their background characteristics or treatment preferences, since the subjects were randomly assigned to these treatments. The results reinforce the importance of increasing access to buprenorphine treatment in the community for indigent heroin-dependent offenders.
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SEROTONIN TRANSPORTER POLYMORPHISMS AND ATTENTIONAL BIAS IN COCAINE DEPENDENCE.

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Aims: Animal studies have shown that behavioral responses to cocaine-related cues are altered by serotonergic medications. Human studies have shown that cocaine-related cues are associated with an attentional bias in cocaine users. The purpose of this study was to examine whether attentional bias to cocaine-related stimuli in cocaine- dependent subjects was associated with the serotonin-transporter-linked polymorphism region (5-HTTLPR), which has been shown to affect serotonin transporter expression.
Methods: The serotonin transporter polymorphism was genotyped by PCR and enzyme digestion for the trialleic L_A, L_G and S alleles in healthy control and cocaine-dependent subjects. The high expressing L_A allele was designated L' and the low expressing L_G and S alleles were grouped as S'. The cocaine Stroop task was used to measure attentional bias to cocaine-related words, which was defined as the mean reaction time to cocaine-related words minus the mean reaction time to neutral words.
Results: As previously reported, cocaine users had higher attentional bias scores than non-drug using controls. When analyzed by genotype (L'L' plus L'S' versus S'S'), there was a significant association with attentional bias ($F = 4.48$, $p < 0.05$). However, only a trend was found when the allele frequency was analyzed for its association with attentional bias ($F = 3.71$, $p = 0.06$).
Conclusions: This study implies that the serotonin transporter may be involved in modulating attentional bias in cocaine-dependent and control subjects. It also provides insight into the regulation of cue reactivity in cocaine addiction.
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DISPENSING OF METHADONE AND BUPRENORPHINE BY PHARMACISTS. CROSS-SECTIONAL SURVEY, BAYONNE, FRANCE.

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Aims: 1)to describe patients treated by buprenorphine and methadone in community pharmacies of the metropolitan area of Bayonne in October 2008; 2)to assess pharmacists practices, their relationship with patients and pharmacists' involvement; 3)to compare with local and national data.
Methods: This was a two-part-questionnaire-based cross-sectional survey. The first part of the questionnaire was sent to all 142 pharmacies of the area. It gathered the number of patients concerned, pharmacists' practice, quality of pharmacist-patient relationship and involvement in training and networking with other professionals and especially with GPs. The second part of the questionnaire was sent to pharmacists for each declared patient to collect individual patient information: dosage, dispensing modalities, other prescriptions and potential problems.
Results: 129 (91%) pharmacists replied to the first questionnaire and reported 470 patients: 135 treated by methadone and 335 by buprenorphine. Pharmacists involved in networking trained more, had higher scores on the pharmacist-patient relationship. 400 patient's questionnaires were returned:127 methadone patients (average dose 55.9 mg (SD=27,0) and 273 buprenorphine (average dose 9,9 mg (SD=5.6). Mean age was 39.8 (SD=5,9), 70% were male. Problems were related for 19.6% of patients (N=71). 25% (N=92) had benzodiazepine dispensed in the same pharmacy.
Conclusions: As in the previous survey, patient-pharmacist relationship was positively related to pharmacists' involvement in networking and training. Within these surveyed pharmacies,30% of patients were treated with methadone. During the same time 87 patients received methadone in a Treatment Center in the same area. In October 2008, 43% of opiate maintained patients in this area were receiving methadone. These results (as in the 2006 survey)show the diversity and quality of care access in this area.
Financial Support: Charles O'Brien

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ANTIDEPRESSANT-LIKE EFFECTS OF ECSTASY.

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Aims: Improved mood and other positive subjective effects of ecstasy due to increased synaptic serotonin (5-HT) levels may indicate a potential antidepressant-like action. Such an effect may be more prominent in subjects with a pre-existing mood disturbance who may use ecstasy more frequently as a 'self-medication'. This study compared depressive symptoms and the immediate effects of ecstasy on mood in subjects with and without a predisposition to depression.
Methods: Ecstasy users (mean±SEM age 22.2±0.73y) were assessed using the Profile of Mood States (POMS) and Beck Depression Inventory (BDI) when drug-free, and at a party session, when 20 subjects voluntarily consumed ecstasy (ecstasy group) and 20 abstained from ecstasy (controls). Predisposition to depression was determined by the Brief Symptom Inventory. At the party session, POMS and BDI were administered 60 min after ecstasy consumption, or at matched time for controls. MDMA was detected in saliva samples of all subjects in the ecstasy group collected 60 min after pill ingestion. All subjects were genotyped for two 5-HT transporter gene polymorphisms.
Results: There was no difference in demographic and genetic background or patterns of ecstasy use between subjects with (WD) and without (ND) a predisposition to depression. The WD subjects had greater mood disturbance scores and depressive symptoms at baseline than the ND group (POMS Total mood Disturbance (TMD) scores: ND 5.85±1.63, WD 14.5±2.82, $p<0.05$, BDI scores: ND 4.9±0.86, WD 11.2±1.65, $p<0.01$, mean±SEM). At the party session, the mood of ND subjects improved irrespective of their choice of ecstasy consumption (TMD: controls -1.4±2.1, ecstasy -2.6±3.0), whereas the mood of WD subjects improved only after taking ecstasy (TMD: controls 11.8±5.1, ecstasy -1.7±4.8). A trend to a decrease in depressive symptoms after ecstasy ingestion was observed only in WD subjects ($p=0.053$).
Conclusions: Mood enhancing effects of ecstasy were observed only in subjects predisposed to depression. This was also associated with a decrease in depressive symptomatology. This effect of MDMA may influence patterns of ecstasy use.
Financial Support: The authors thank NHMRC for financial support.

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PATTERNS OF ALCOHOL ABUSE AND DEPENDENCE SYMPTOMS AMONG MALE YOUTHS IN THE UNITED STATES: A LATENT CLASS ANALYSIS.

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Aims: Classifying youths into more homogenous groups of alcohol users with varying levels of alcohol problem severity is an important research goal that may lead to more accurate diagnosis, more precise determination of prognosis, and ultimately, to more effective treatment and prevention programs. The study aims were to empirically classify adolescent male drinkers into groups based on their pattern of DSM-IV Alcohol Abuse and Dependence symptoms and examine the validity of classes with respect to demographic characteristics and a set of criterion variables.
Methods: This study uses data from the 2005-2007 National Survey on Drug Use and Health a nationally representative household survey of the entire United States. Latent class analysis was used to examine the pattern of DSM-IV Alcohol Abuse and Dependence symptom reporting in 4594 male drinkers aged 15-17. Associations between the classes and demographic and criterion variables were examined via two-sided Fisher's exact tests, t-tests, and latent class regression analyses.
Results: Results suggested that a four class solution best fit the data. The low severity class (65.6% of the sample) endorsed relatively few symptoms. The moderate-low severity class (29.2% of the sample) had moderate to high reporting of many symptoms. The moderate-high severity class (3.0% of the sample) was distinguished from the moderate-low severity class by having higher estimated probabilities of three Abuse symptoms and one Dependence symptom. The high severity class (2.3% of the sample) had high estimated probabilities of almost all symptoms. The classes were shown to be valid in that they were distinct from one another with respect to many of the criterion variables examined.
Conclusions: This study has implications for the diagnosis of DSM-IV Alcohol Abuse and Dependence among older adolescent males and targeting youths to treatment and selected and indicated prevention programs.
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DISULFIRAM FOR METHAMPHETAMINE DEPENDENCE: AN OPEN-LABEL PILOT STUDY.

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Aims: Treatment-seeking methamphetamine dependent individuals were enrolled in this 8-wk, open-label, pilot clinical trial examining tolerability and preliminary efficacy of disulfiram at 250 mg/day in this population.
Methods: Participants attended clinic every weekday during week 1 of the trial in order to receive disulfiram under observation and complete assessments. Subjects then received weekly blister packs of medication and attended clinic thrice weekly during weeks 2-6. Subjects no longer took disulfiram and were monitored during weeks 7-8, then referred to treatment elsewhere, if interested. Supervised urine samples were obtained and a disulfiram side-effects checklist was completed thrice-weekly. Self-reported drug use, mood, amphetamine withdrawal, craving and mood ratings were also completed at least weekly. All subjects underwent cognitive behavioral therapy. Adjunctive contingency management procedures were utilized to enhance attendance.
Results: Thus far, 9 methamphetamine-dependent volunteers (6 males/3 females; 6 Cauc/1 AA/1Other) with a mean age of 30.4 yrs entered the study proper. Participants completed a mean of 3.3 weeks, with 3 completing at least the 6 week disulfiram maintenance period. Baseline mean MSSA score was 49.2 +/- 22.4. Eight adverse events that were at least possibly related to disulfiram were reported, including nausea/vomiting (n=4), confusion (n=1), headache (n=1), metallic taste (n=1), and elevated BP (n=1). All were mild and resolved without intervention. Preliminary analyses indicate that there was a significant decrease in the HAM-A (t= -5.61, p=0.0004) and HAM-D (t= -3.96, p<0.0001) scores over time. There is also a trend toward a decrease in methamphetamine positive urines over time (t= -1.79, p=0.07).
Conclusions: These preliminary results suggest that disulfiram is tolerated and may facilitate reductions in methamphetamine use in the methamphetamine dependent population.
Financial Support: NIDA grant P50 DA12762, R01 DA13441, and UAMS Psychiatry Dept. Pilot Funds

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PREVALENCE OF HEPATITIS B IN A GROUP OF FRENCH ALCOHOL ABUSERS.

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Aims: Aims: Update epidemiology of hepatitis B among alcohol abusers, known for their poor access to vaccine. Recent studies more likely focus on hepatitis C (HCV) in this group.
Methods: Methods: Between 1998 and 2005, 714 patients were admitted in the addiction medicine healthcare unit of our general hospital in Saint Dizier, Champagne-Ardennes, France. Each of them was proposed to test serology for HBV, HCV & HIV.
Results: Results: Sex ratio of our study group (n= 714) is three male (n=537) for one female (n=177). For 24 patients (14 men, 10 women) test were not completed. 6.7% (35/523) of men and 7.8% (13/167) of women did already meet HBV. 5 patients tested viremic for (PCR +).Liver biopsy revealed 2 cirrhosis, and 3 severe fibrosis (Metavir F3; n=1 / Metavir F2; n=2)
Conclusions: Conclusions: Among the study group, 7% (n=48) were chronically infected and among them, one sixth (n=8) showed criteria of severity. If that level frequency is confirmed in this population, a screening of HBV in alcohol abusers have to figure in future guidelines.
Financial Support: none

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ASSOCIATIONS BETWEEN IMPLICIT AND EXPLICIT DRUG-RELATED COGNITIONS AND RELAPSE: AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY.

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Aims: Relapse is a central problem in drug addiction. Studies using ecological momentary assessment (EMA) have shown that drug craving plays a role in relapse. Recent laboratory studies have reported that performance on the drug Stroop task, which assesses attention captured by drug cues, and the Implicit Association Test (IAT), which assesses implicit attitudes to drugs, is associated with relapse. We extended this research by examining whether implicit and explicit cognitions assessed using EMA can predict relapse.
Methods: Participants were 64 heroin dependent inpatients undergoing detoxification at an addiction treatment center. They carried around a handheld computer (PDA) for 1 week during detoxification. They responded to up to four random assessments (RAs) per day. Participants were also instructed to press a "temptation assessment" (TA) button on the PDA whenever they felt a strong urge to use drugs. At each assessment (RA, TA), participants responded to items assessing craving and explicit attitudes to drugs, and they subsequently completed either a drug Stroop task or an IAT. The primary outcome measure was relapse/drop-out during the first week of detoxification.
Results: Using linear mixed models, relapsers (n=10) reported higher levels of craving and more positive explicit attitudes to drugs than non-relapsers (n=54) at TAs (but not at RAs). Similarly, relapsers exhibited larger Stroop and IAT effects than non-relapsers at TAs (again, not at RAs). The associations between implicit cognitions and relapse at TAs persisted when controlling for drug craving and explicit attitudes. Analyses of trends over time revealed that the drug Stroop effect increased in the days before relapse in TAs.
Conclusions: Implicit cognitions assessed during EMA may help to identify individuals at risk of subsequent relapse. Implicit cognitions also provide information on relapse risk beyond that gained from self-reported craving.
Financial Support: This study is supported by a ZonMw/NIDA grant (31180001)

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COST OUTCOMES WITH EXTENDED-RELEASE NALTREXONE IN INSURED ALCOHOLICS.

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Aims: To examine utilization and cost outcomes of insured patients treated with psychosocial treatment alone or prescribed one of four different FDA-approved alcoholism medications.
Methods: This naturalistic, retrospective analysis examined MarketScan® insurance claims data across many states. Patients had a claim for either psychosocial treatment alone, extended-release naltrexone (XR-NTX) or an oral medication between July 2006 and Dec 2008. Patients were ≥18 yrs, continuously enrolled for ≥6 months pre- and post-index and had claims for ≤1 oral agent in the 3 months before index. Patient differences on demographic, clinical and service utilization variables were controlled for with propensity-score matching.
Results: During the 6 month pre-period, XR-NTX patients (N=295) were more likely to have a diagnosis of an alcohol or drug use disorder, bipolar disorder or depression, a psychiatrist visit, a detox or alcoholism-related admission than patients treated with oral naltrexone (N=2,064), disulfiram (N=2,076) or acamprosate (N=5,068). Mean refill persistence on XR-NTX was ~81 days vs. ~73 days for oral agents. A greater pre-post reduction in detoxification days and alcoholism-related inpatient admission days was observed among patients treated with medication. Among these, XR-NTX was associated with significantly lower costs (per 1000 patients) versus oral naltrexone, disulfiram and acamprosate (Detox: $0.60-million vs. $1.48-million, $1.08-million, $1.40-million; respectively; P<0.01 for XR-NTX vs. naltrexone and acamprosate).
Conclusions: In the largest real-world sample to date, patients prescribed medication had significantly and substantially less intensive medical service utilization. Of the approved medications, XR-NTX was associated with more persistence and larger reductions in alcoholism-related health care utilization.
Financial Support: Sponsored by Alkermes, Inc; and by the National Institute on Alcohol Abuse and Alcoholism grant K24 AA13736 (Dr. Kranzler's participation)

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ADOLESCENT CANNABIS USE DISORDERS AND LATER DEPRESSION: EFFECTS OF PSYCHOSOCIAL MEDIATORS.

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Aims: Aim: Although several studies have reported that cannabis use disorders (CUDs) in adolescence predict later major depression, the reason for this association remains unclear. The goal of this study was to investigate one possible explanation for this link: that psychosocial correlates and consequences of heavy cannabis use—specifically, educational failure, crime, and unemployment—mediate the link between adolescent CUDs and depression during the transition to adulthood.
Methods: Methods: Participants were drawn from the Minnesota Twin Family Study, a community-based sample. They were first assessed at age 17, then followed-up at ages 20 and 24 (n=1253). Diagnoses (cannabis abuse and dependence and major depression) and life events (educational failure, crime, and unemployment) were assessed via structured interviews. Two composite "consequences" variables were created: one dichotomous (coded 1 if one or more of these three consequences was present and 0 if not), and the other ranging from 0-3 (the number of consequences experienced). Analyses adjusted for the presence of correlated observations (two adolescents per family).
Results: Results: Consistent with other studies, the results indicated that CUDs in adolescence (by age 17) predicted depression during the transition to adulthood (between ages 17 and 24), even after adjusting for the effects of depression prior to age 17. The psychosocial consequences measures were correlated with CUDs at 17 and with depression between 17 and 24. However, the association between early CUDs and later depression was not mediated by the either of the composite "consequences" variables. Follow-up analyses examining each consequence (educational failure, crime, and unemployment) separately indicated that none of these specific consequences mediated this association either.
Conclusions: Conclusion: The link between CUDs in adolescence and later depression cannot be accounted for by the occurrence of these psychosocial correlates/consequences of heavy cannabis use.
Financial Support: Supported by NIDA and NIAAA.

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MODAFINIL EFFECTS ON SMOKING CESSATION: A CLINICAL TRIAL.

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Aims: Previous research has demonstrated that modafinil administration was associated with decreases in hunger during acute nicotine withdrawal in nicotine dependent smokers. This observation prompted the current Clinical Trial examining the impact of modafinil (300 mg, po daily) on smoking cessation, nicotine withdrawal symptoms, and appetite and weight gain in nicotine-dependent smokers motivated to stop smoking.
Methods: We conducted a randomized, double-blind placebo controlled study investigating the effects of modafinil on smoking cessation. Subjects included treatment-seeking adults, age 18-55, who smoked 10 or more cigarettes per day, had a CO (carbon monoxide) reading of 10 ppm or greater at intake, were medically stable, and were not receiving psychotropic medications. After completing a medical screen, subjects were assigned to an active (300 mg) or placebo group with randomization stratified by gender and smoking level (low: 10-19 cigarettes/day and high: > 20 cigarettes/day). Assessments of CO levels, nicotine withdrawal and drug effect measures, including vital signs, weight, Visual Analogue Scale, Minnesota Nicotine Withdrawal Scale, and Continuous Performance Task, occurred weekly for 8 weeks on drug, and at 1 and 12 weeks after drug. Cotinine and personality measures (Beck Depression Inventory, Conner's Adult ADHD Rating Scale, Sensation Seeking Scale, and Weight Concerns Scale) were collected at intake, weeks 4 and 8 during intervention, and again post drug at weeks 9 and 20.
Results: An interim analysis was conducted on a subset of key variables and indicated significant modafinil-induced decreases in CO (-4.34 ppm; p-value 0.041) and body weight (-.91 kg; p value 0.008) relative to placebo.
Conclusions: Preliminary evidence demonstrates that modafinil could be effective as an adjunct in smoking cessation, particularly for smokers who are concerned about or experiencing weight gain.
Financial Support: R21DA023049, RR-15592, Cephalon, P20 RR15592

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ABSTINENCE AND DRINKING PATTERNS AMONG WOMEN IN AFRICA.

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Aims: This study aims to describe patterns of alcohol use among women in 20 African countries, and to determine sociodemographic factors associated with current drinking among women by country.
Methods: Data were collected as part of the WHO World Health Survey between 2002 and 2004 in 20 African countries. Single respondents were randomly selected per nationally representative household. In total 41, 420 (53.6%) women aged 18 years and older were included. Standardized questionnaires collected household and individual data. Alcohol measures included lifetime abstinence, current use (1+ drink past week), high consumption (15+/wk) and heavy drinking (5+ in one day). Country-specific descriptives of alcohol use were calculated, and regression models fitted for each country to identify factors associated with current drinking.
Results: Overall 34,450 (83 %) African women from 20 countries report being lifetime abstainers, ranging from 55% in Mauritius to 99% in Comoros. Current use ranges from 1.5% in Malawi to 26.3% in Burkina Faso. Rates of high consumption vary between 5.2% in Ghana to 43.3% in Chad. Heavy drinking rates range from 3.3% in Ghana to 55% in Chad. Age and income are associated with current use for nearly all countries. Working for pay is associated with current drinking for 6 countries, while the remaining covariates are associated with drinking in varying directions between countries.
Conclusions: Abstinence levels are generally high among women in Africa. However, there is a range in current use, high consumption and heavy drinking by country. The consistently positive association between working for pay and current use suggest increased drinking with trends of societal modernization and wealth growth. The low levels of current drinking and especially high risk drinking present an opportunity to maintain healthy patterns of no or moderate alcohol use among the majority of women in Africa. However, this window of opportunity may diminish in the future if proactive measures, such as culturally appropriate alcohol education for African women, are not undertaken.
Financial Support: The Norwegian Center for Addiction Research supported this work.

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DIFFERENTIAL RECRUITMENT OF THE ORX/HCRT SYSTEM BY COCAINE VS. PALATABLE NATURAL REWARD.

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Aims: Orexins are hypothalamic peptides that regulate a range of physiological processes and have also been implicated in processes related to reward and incentive motivation. This study compared neuronal activation within Orx/Hcrt cell groups in the lateral hypothalamus (LH) produced by a cocaine-related stimulus vs. a stimulus conditioned to a palatable conventional reinforcer, sweetened condensed milk (SCM).
Methods: Male Wistar rats were trained to associate a discriminative stimulus SD with the availability of cocaine or SCM (S+) vs. saline or non-reward (S-). Following conditioning, both the cocaine and SCM groups were placed on extinction conditions in daily 30 min sessions during which the reinforcers and SD were withheld until a criterion of ≤ 4 responses/session for 3 consecutive days was reached. Fos-positive Orx/Hcrt neurons in the LH then were counted following COC or SCM S+ presentation and compared to Fos-positive counts obtained following the final extinction session.
Results: Although the stimuli conditioned to cocaine and conventional reinforcer were equally effective in eliciting reinstatement, only the cue conditioned to cocaine recruited a larger number of Fos-positive Orx/Hcrt cells in the LH. To clarify the behavioral significance of the differential activation of Orx/Hcrt neurons in the LH by cocaine vs. SCM S+, the effect of Hcrt-r1 antagonist SB334867 on reinstatement elicited by a cocaine or SCM S+ was tested. SB334867 (1–20 mg/kg; IP) dose-dependently reduced reinstatement induced by the cocaine S+, with significant effects at a dose as low as 3 mg/kg, but did not interfere with behavior induced by the SCM S+, except at the highest dose (20 mg/kg).
Conclusions: The results show that blockade of Hrct-r1 receptors fails to interfere with the motivating effects of a stimulus conditioned to potent natural reward, but effectively reverses the motivating effects of the same stimulus when conditioned to cocaine. These findings further support a differential role of the Orx/Hcrt system in compulsive-like drug-seeking vs. normal motivated behavior.
Financial Support: NIDA DA08467 (FW)

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TRENDS IN PRESCRIPTION DRUG USE DISORDERS SECONDARY TO NON-MEDICAL USE IN ADOLESCENCE.

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Aims: Prevalence of drug use disorders due to nonmedical use of prescription drugs (NMPD- opioids, stimulants, sedatives, tranquilizers) might vary across different subgroups of drug users, increases can lead to worse outcomes for adolescents. This study aims to explore past-year prevalence changes across time in prescription drug abuse and dependence among adolescents, based on their use of other substances during the same time period.
Methods: Secondary analysis of adolescent data from the National Survey of Drug Use and Health (NSDUH) years 2002 to 2007 (n=17,709-18,678). Past-year substance use groups were defined as: 1- no alcohol, tobacco or illegal drug users, 2- alcohol/tobacco users, 3- illegal drug users. Data were analyzed separately for early (12-14 year olds) and late (15-17 year olds) adolescence through basic contingency tables and weighted logistic regression models comparing prevalence across years adjusting for sex, race, insurance, mental health and substance use treatment, deviant behaviors, and sensation-seeking.
Results: Adolescents that used illegal drugs had the higher prevalence of prescription drug abuse and dependence, followed by alcohol/tobacco users and by those that didn't use other substances. Among NMPD users, prevalence of abuse was comparable over time in both age groups except there were three-fold increases in 2006 among 12-14 year olds that didn't use other substances (AOR:2.9[1.1,7.6]) and in 2004 among 15-17 year-old alcohol/tobacco users (AOR:3.8[1.4,10.3]). Prevalence of dependence remained relatively stable across time and only increased in 2004 among 12-14 year-olds that didn't use other substances (AOR:7.9[1.6, 39.4]) and in 2007 among 15-17 year-old illegal drug users (AOR:1.6[1.0-2.5]).
Conclusions: Prevalence rates of PD abuse and dependence among adolescents need to be monitored, particularly among younger adolescents that still do not use other substances.
Financial Support: NIDA grant DA023434 (P.I. Martins).

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EXTENDED ACCESS TO INTRAVENOUS METHYLPHENIDATE LEADS TO ESCALATION OF SELF-ADMINISTRATION IN RATS.

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Aims: Methylphenidate (MPH) is a widely prescribed drug for ADHD, but it has abuse potential in humans. Only a few studies have examined the reinforcing effect of MPH in laboratory animals. Previous research with rats using a fixed ratio (FR) schedule of daily MPH self-administration has been conducted using sessions limited to 1 or 2 hr per day. Longer sessions (e.g. 6 hrs) may be required to characterize more fully the abuse liability of MPH.
Methods: Male Sprague-Dawley rats were trained to lever press for MPH through the method of autoshaping. Subjects were then assigned randomly to either a short access (ShA; 1 hr sessions) or long access (LgA; 6 hr sessions) group. Half of the subjects in each of these groups were given access to 0.1 mg/kg/infusion MPH and the other half were given access to 0.3 mg/kg/infusion MPH for 21 consecutive sessions. MPH was available on an FR 1 schedule of reinforcement.
Results: All rats acquired lever pressing for MPH without prior training to lever press for food or another drug. Subjects in both of the LgA groups administered significantly more MPH over the course of the 21 sessions, whereas subjects in the ShA groups did not change in the amount of MPH intake. The escalation in self-administration was more pronounced for subjects in the 0.1 mg/kg/infusion group than in the 0.3 mg/kg/infusion group. When the time course of MPH self-administration within a session was examined across sessions, subjects in the 0.1 LgA group showed a significant difference in time course of self-administration, whereas subjects in the 0.3 LgA group did not.
Conclusions: The results demonstrate that rats given long access to MPH self-administration will escalate in the amount of MPH intake, indicating that MPH use can be become dysregulated similar to the use of other drugs of abuse.
Financial Support: USPHS Grants P50 DA05312 and T32 DA007304.

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EXCITED DELIRIUM, TASERS AND SUDDEN DEATH.

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Aims: Excited delirium is a serious medical condition associated with acute onset of agitated violent behavior that often culminates in sudden unexplained death. Our aim was to conduct a mortality review for a case series of excited delirium deaths to identify its occurrence and associated risk factors. Because there is a need for biomarkers to assist medical examiners with identifying these cases at autopsy, we also conducted quantitative analyses of the dopamine transporter (DAT) and heat shock protein 70 (Hsp70).
Methods: A total of 97 deaths were taken from routine medical examiner investigation of sudden unexpected deaths, most in police custody. We reviewed the circumstances surrounding the death, available records from emergency departments, forensic autopsy and toxicology findings. Quantitative assays of the DAT and Hsp70 were validated for specificity and interindividual variation.
Results: Force measures used by police included empty hand control for combative subjects, application of mechanical restraints, chemical agents or electrical incapacitation (TASERs). Psychostimulants (cocaine, meth) were detected in 94% of the cases; five subjects had no drugs or alcohol measured at autopsy. Mean core body temperature where recorded was 40o C. Quantitative PCR demonstrated elevated expression of the heat shock protein HSPA1B transcript. Elevated Hsp70 confirms that hyperthermia is an associated symptom in these cases. DAT levels were significantly below the range of values in drug-free controls or cocaine abusers who died due to cocaine intoxication.
Conclusions: In excited delirium, there is no anatomic cause of death, which adds to the confusion and controversy surrounding these cases. Our studies demonstrate that there are network-level changes in DAT and Hsp70 that can reliably serve as biomarkers to identify and confirm the occurrence of the syndrome at autopsy.
Financial Support: Supported by NIDA RO1 DA006227

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HEALTHY VOLUNTEERS FEEL "HIGH" AND "LIKE" THE SUBJECTIVE EFFECTS OF ZOLPIDEM BUT DO NOT CHOOSE IT OVER MONEY.

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Aims: Recent case reports suggest that non-drug-abusing individuals may be vulnerable to abuse of and/or dependence on the benzodiazepine-like hypnotic zolpidem, particularly at doses higher than those recommended for treating insomnia. The present study measured zolpidem-induced subjective effects in drug-naïve volunteers in order to study the constellation of effects that may contribute to the abuse-related properties of this commonly prescribed sleep-aid.
Methods: Eleven healthy male (6) and female (5) non-smoking volunteers were recruited as part of a larger fMRI study. Participants received oral zolpidem (0, 5, 10, or 20 mg) in a double-blind, placebo-controlled design, and answered computerized questionnaires assessing drug-induced subjective effects periodically over the course of a 7-hr experimental session.
Results: When rating "How high do you feel right now?", participants reported significant increases relative to placebo at a number of time points following administration of the 20 mg dose ($p=0.01$). Across time, the 5 and 20 mg doses increased ratings of "How much do you like the drug you took?" ($p=0.04$), while the therapeutic dose (10 mg) did not. A questionnaire administered at the end of the session indicated that all three doses increased ratings of "Drug Strength" ($p<0.001$), but only the 20 mg dose increased ratings of "Drug Liking" ($p=0.008$), "Good Effects" ($p=0.006$), and "Willingness to Take Again" ($p=0.055$). While 20 mg and 10 mg ($p=0.021$) also increased ratings of "Bad Effects", no dose of zolpidem was chosen over money ($0.35 - $10) at any time point when participants made hypothetical choices between the two.
Conclusions: These results suggest that zolpidem-related ratings of high, drug liking, and a willingness to take the drug again may be not be powerful enough to facilitate the abuse of and/or dependence on this drug.
Financial Support: NIDA grants T32 DA015036 (SEL), K05 DA000343 (SEL), and K01 DA023659 (SCL).

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MENTAL HEALTH, SCHOOL PROBLEMS, AND SUBSTANCE USE AMONG URBAN ADOLESCENTS: THE MEDIATING EFFECT OF SOCIAL NETWORK QUALITY.

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Aims: We hypothesized that social network quality would mediate the effects of school problems, accounting for internalizing problems and parental relations, on alcohol, marijuana, and tobacco use with a primary care sample of 301 urban adolescents.
Methods: Adolescents presenting for a routine medical check-up were self-assessed for substance use, social network quality, mental health, and school problems.
A series of path models were tested using AMOS- SPSS structural equation modeling program to examine our hypotheses on each substance.
Results: Results show that all three models provided very good fits to the data and demonstrated the mediation effects of social network quality on alcohol and marijuana, and partial mediation effects on tobacco.
The effect of school problems on alcohol use was mediated through social network quality by a 3-fold reduction in the regression coefficient and rendered it non-significant.
About one half of effect of school problems on marijuana use was mediated through social network quality, and rendered it non-significant.
About one third of effect of school problems on tobacco use was partially mediated through social network quality, although it remained significant.
Conclusions: These findings contribute to the literature of social networks by illuminating processes of school problems, and associated mental health issues, on substance use among urban adolescents, particularly with youth living in chronic environmentally stressed conditions.
Protective social networks matter and can be targeted and tested as an intervention point for urban youth.

The independent effect of social network quality on a robust composite variable such as school problems supports our hypothesized socially driven model of urban adolescent substance use.
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HIV/AIDS "CONSPIRACY BELIEFS" AMONG RACIAL/ETHNIC MINORITY DRUG USERS.

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Aims: Examine the prevalence of HIV/AIDS "conspiracy beliefs" (beliefs about HIV/AIDS that reflect deep-seated mistrust of the health care system) among racial/ethnic minority drug users DUs.
Methods: 287 DUs were recruited from community-based programs for structured interviews (n = 192) or focus groups (n = 95). Survey data included demographics; HIV/HCV status; drug & sex risks; and agreement with statements about HIV/AIDS conspiracy theories. A logistic regression model controlling for recruitment site, gender, age, educational level, homelessness, insurance status, HIV status, examined factors associated with HIV/AIDS conspiracy beliefs. Fourteen focus groups of either African-American or Latino(a) DUs elicited perceived barriers to HIV services, including experiences of racial discrimination. Themes were identified through content analysis of focus groups.
Results: DUs' beliefs differed markedly by race/ethnicity. For example 32% of African Americans, 30% of Latino(a)s, and 11% of non-Hispanic whites agreed that "AIDS is a form of genocide against people of my race/ethnicity." Regression modeling revealed that conspiracy beliefs were more prevalent among racial/ethnic minorities than non-Hispanic whites ($p < 0.05$). Focus group results suggested that for some DUs HIV/AIDS conspiracy beliefs may be barriers to HIV treatment engagement.
Conclusions: Conspiracy beliefs about HIV/AIDS are not uncommon among ethnic minority DUs, particularly African Americans. HIV prevention and treatment programs may need to address conspiracy beliefs generally as part of multicomponent interventions to enhance engagement in care among high-risk groups of racial/ethnic minorities.
Financial Support: NCMHD, CA HIV/AIDS Research Program (ID06-SF-198), and NIDA Grants (R01DA20781, R01DA02084, P30DA011041, P50DA09253 & U10DA15815).

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BEYOND SANCTIONS: IS THERE A NEED TO TREAT FIRST-TIME DUI OFFENDERS?

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Aims: Driving Under the Influence (DUI) enforcement can be a screening mechanism for alcohol and other drug problems. The current response to DUI is focused on using mechanical means to prevent inebriated persons from driving, with little attention directed towards underlying substance abuse problems. To lessen recidivism, the justice system, as part of the DUI response, should identify and treat substance abuse problems.
Methods: This is a secondary analysis of the Texas DSHS BHIPS administrative dataset of over 345,000 individuals who entered Texas substance abuse treatment between 2005 and 2008. Of these, 36,372 were either on probation for driving under the influence (DUI), referred to treatment by DUI probation, or had been arrested for DUI in the past year. The DUI offenders were compared on demographic characteristics, substance use patterns, and levels of impairment with those who were not DUI offenders and first DUI offenders were also compared with those with more than one past-year offense. T tests and chi square tests were used to determine significance.
Results: DUI offenders were more likely to be employed, to have a problem with alcohol, to report more past-year arrests for any offense, to be older, and to have used alcohol and drugs longer than the non-DUI clients who reported higher ASI scores and were more likely to use daily. Those with one past-year DUI arrest were more likely to have problems with drugs other than alcohol and were less impaired than those with two or more arrests based on their ASI scores and daily use. Non-DUI clients reported higher levels of mood disorders than DUIs but there was no difference in their diagnosis of anxiety. Similar findings were found between those with one or multiple DUI arrests.
Conclusions: Although first-time DUIs were not as impaired as non-DUI clients, many were dependent and they also presented with co-morbidity issues. Thus, screening and assessment at the time of arrest for all DUI offenders and yoking treatment with justice sanctions may prove an effective method to reduce future recidivism.
Financial Support: Center for Substance Abuse Treatment. Type: UD1 TI13423)

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A CROSS-NATIONAL VIEW OF SOCIALLY MALADAPTIVE BEHAVIOR AND DRUG USE: EVIDENCE FROM SEVEN LATIN AMERICAN COUNTRIES.

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Aims: With local community characteristics held constant, early socially maladaptive behavior (SMB) may be an individual-level cause of later drug involvement. This 'causes of cases' perspective can be contrasted with a 'causes of incidence' perspective such that areas with higher mean SMB levels might be expected to have higher levels of drug involvement. Here, the aim was to study country-level associations that link SMB levels with levels of drug involvement.
Methods: Data are from the NIDA PACARDO research consortium, with nationally representative surveys of school-attending youths in Panama, Central America, and Republica Dominicana (n>1500 in each country). Self-report questionnaires covered SMB and drug involvement.
Results: After exploratory factor analysis, a multi-group confirmatory factor analysis approach disclosed that Costa Rica had a much higher mean level of youthful SMB, as compared to the other six countries in the PACARDO project. On this basis, we predicted that Costa Rica might be exceptional with respect to estimated cumulative occurrence of youthful tobacco smoking, cannabis smoking, and alcohol beverage consumption. The cross-national estimates support this prediction (for Costa Rica: tobacco, 47%; cannabis, 9.5%, alcohol 72%), with generally lower estimates for the other six countries.
Conclusions: Epidemiology offers two ways of studying causes. One approach is focused on the causes of cases at the individual level; the other approach has a focus on the causes of incidence at the population level. Shifts in the population means for SMB levels might be followed by shifts in the population means for drug involvement. An alternative possibility is that Costa Rica continues to school its students with drug use and correlated SMB, whereas these students drop out of school or are expelled in the other countries of the region. This topic remains an open issue for future research.
Financial Support: NIDA award K05DA015799 & MSU OVPRGS funds.

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EFFECT OF COCAINE ON BUPRENORPHINE OR METHADONE PHARMACOKINETICS: CLINICAL IMPLICATIONS.

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Aims: The effect of chronic cocaine use on buprenorphine or methadone pharmacokinetics was investigated to identify drug interactions and potential toxicities. We now compare previously presented data on the effect of cocaine on buprenorphine to new data on the effect of cocaine on methadone.
Methods: In a retrospective analysis, buprenorphine (dose: buprenorphine/naloxone 16/4 mg/d) pharmacokinetics were compared in 16 study participants who regularly used cocaine and 74 participants who used cocaine rarely or not at all. Methadone (dose range: 40-120 mg daily) pharmacokinetics were compared for those who were either regular cocaine users (n=16) or with intermittent or no cocaine use (n=23). All participants were maintained on a stable dose of buprenorphine/naloxone or methadone for at least 2 weeks prior to study and were taking no other medications.
Results: Buprenorphine-maintained participants who used cocaine regularly had lower buprenorphine exposure (AUC 34% lower; Cmax 27% lower and C24 37% lower; p£0.001 for all comparisons). Regular cocaine users were younger (p=.0007), and reported more heroin (p=.004) and cocaine (p<.0001) use at study entry. Similarly, methadone pharmacokinetics analyses showed a significant decrease in Cmin (p=.04) and a trend for decreased AUC (p=0.09) with more rapid methadone clearance (p=0.08) in those methadone-maintained individuals who were also regular cocaine users. No opiate withdrawal symptoms were observed in any participant.
Conclusions: Regular cocaine use may result in lower opioid plasma concentrations with the effect greater for buprenorphine than methadone. These findings indicate that cocaine may induce cytochrome P450 3A4 and may alter absorption of these medications with potential for adverse clinical outcomes particularly for patients prescribed other medications that may also induce methadone or buprenorphine metabolism.
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ADOPTION OF BUPRENORPHINE IN TWO HEALTH PLANS.

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Aims: The FDA approved buprenorphine in October 2002. We assessed change over time (2000 to 2008) in buprenorphine prescriptions in two health plans (one purchased methadone maintenance, one did not). The methadone maintenance health plan was expected to adopt buprenorphine earlier and more rapidly.
Methods: Individuals with two or more diagnoses of opioid dependence were extracted from the health plans' electronic health records. The number and percent of individuals receiving buprenorphine or enrolled in methadone were calculated each year.
Results: Over the nine study years, the number of individuals with two or more diagnoses of opiate dependence increased 260% (2000 = 1,829; 2008 = 4,772). Use of buprenorphine began slowly – one health plan treated 45 individuals in 2003. The percent of opioid dependent patients receiving buprenorphine increased slowly: 2003 = 2%, 2004 = 7%; 2005 = 8%; 2006 = 14%; 2007 = 23%; 2008 = 30%. The health plan with methadone maintenance experience, adopted sooner and a higher portion of patients used buprenorphine. The percent of patients receiving methadone declined from 60% in 2001 to 29% in 2008 while the use of burpenorphine increased from 6% in 2003 to 34% in 2008. In the comparison health plan buprenorphine use increased gradually with a substantial uptick in 2007 and 2008: 2004 = 2%, 2005 = 3%, 2006 = 9%, 2007 = 19%, 2008 = 28%.
Conclusions: Buprenorphine is changing treatment for opioid dependence in two integrated health plans. The proportion of patients receiving methadone has declined in the health plan with a history of methadone maintenance. Changes in federal legislation eliminating the 30 patient limit on each health plan and permitting authorized physicians to treat up to 100 patients at a time appears to have facilitated implementation.
Financial Support: The National Institute on Drug Abuse supported the analysis (R01 DA016341).

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EFFECTS OF SEROTONIN TRANSPORTER INHIBITORS ON COCAINE-PRIMED REINSTATEMENT IN RHESUS MONKEYS.

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Aims: One of the most challenging aspects in treating cocaine addiction is the high incidence of relapse following a period of drug abstinence. The reinstatement paradigm is a frequently used preclinical model of drug relapse in laboratory animals. Pretreatments with drugs that inhibit the serotonin transporter can attenuate cocaine self-administration; however the effects of serotonin transporter inhibitors on cocaine-induced reinstatement are not well characterized. The present study characterized the reinstatement effects of cocaine and the selective DAT inhibitors, RTI-113 and RTI-336, in rhesus monkeys (n=5) previously maintained under a second order schedule of i.v. cocaine (0.03-0.1 mg/kg/infusion) self-administration.
Methods: Following saline extinction, non-contingent priming injections of cocaine (0.03-1.0 mg/kg), RTI-113 (0.01-0.1 mg/kg), and RTI-336 (0.1-1.0 mg/kg) were administered and their effectiveness to reinstate cocaine self-administration was assessed. In subsequent experiments, the effects of pretreatments with the selective serotonin transporter inhibitors, citalopram (0.3-5.6 mg/kg) and fluoxetine (0.3-5.6 mg/kg), on reinstatement induced by cocaine, RTI-113, and RTI-336 were examined.
Results: Priming injections of cocaine, RTI-113, and RTI-336 induced robust reinstatement in all subjects. Furthermore, pretreatments with fluoxetine and citalopram dose-dependently attenuated the reinstatement effects induced by cocaine and the dopamine transporter inhibitors.
Conclusions: The findings indicate that cocaine-induced reinstatement is mediated by the inhibition of the dopamine transporter, and suggest that a direct interaction between dopamine and serotonin underlies the effectiveness of the SERT inhibitors to attenuate cocaine-induced reinstatement.
Financial Support: Supported by USPHS grants DA010344, DA000517 and RR00165.

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THE EFFECTS OF VARENICLINE ON SMOKING IN A BRIEF ABSTINENCE MODEL.

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Aims: Evidence is mounting which suggests that one mechanism by which varenicline aids in smoking cessation is to reduce the rewarding effects of smoking. This in turn may reduce the likelihood of relapse following a slip or lapse episode during a quit attempt. The current study investigated prospectively the effect of varenicline on smoking behavior during a brief structured-cessation attempt.
Methods: Smokers not wanting to quit immediately were randomly assigned to receive varenicline or placebo during a 5-week practice quit attempt. Smokers underwent 24-hours of abstinence (last 7 hours monitored) after which they smoked two cigarettes in the laboratory to model a clinical lapse occurring early in a quit attempt. Smoking behavior was then assessed for 4-weeks, with financial incentives provided during the first week to enhance motivation to abstain.
Results: Smoking decreased during the 4-week follow-up period for both placebo (n=13) and varenicline (n=13) groups, but was lower upon completion of the study for those receiving varenicline compared with placebo. Specifically, at the last study visit, mean urinary cotinine levels were 829 ng/mL vs. 1561 ng/mL, mean breath CO levels were 6 ppm vs. 11 ppm, and mean self-reported cigarettes smoked per day were 3 vs. 7 in the varenicline and placebo groups respectively. However, complete abstinence from smoking in either group was rare.
Conclusions: Findings suggest that varenicline improved smokers' ability to cut down their smoking dramatically in a context where they were motivated to achieve abstinence. This may reflect reduced rewarding effects of smoking as one mechanism of varenicline's previously demonstrated efficacy as a smoking cessation aid.
Financial Support: This work was supported by Pfizer, Inc. and NIDA grant T32DA07209.

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A RANDOMIZED CONTROLLED TRIAL EVALUATING THE EFFICACY OF A PERFORMANCE IMPROVEMENT SYSTEM IN OUTPATIENT SUBSTANCE ABUSE TREATMENT PROGRAMS.

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Aims: To evaluate the efficacy of a semi-automated performance improvement system ("Patient Feedback") via a randomized, controlled multi-site trial implemented in non-methadone maintenance outpatient substance abuse treatment programs.
Methods: Initiated in 2006, the randomized controlled trial was conducted at 20 community-based, outpatient substance abuse treatment programs in the northeast United States. Patients in group therapy sessions completed anonymous surveys on a weekly basis evaluating treatment satisfaction and therapeutic alliance with their group counselors. Surveys were processed and generated into two types of feedback reports, Caseload Reports (clinician-level data) and Clinic Reports (clinic-level data), for clinicians to view via a password-protected website. Overall, 118 clinicians across 20 clinics participated in the study. Ten clinics received 12 weeks of the Patient Feedback performance improvement intervention and ten clinics received no intervention during the 12 weeks. Over 1500 patients provided anonymous ratings of therapeutic alliance and drug/alcohol use. Clinicians provided assessments of organizational functioning and job satisfaction.
Results: There was no evidence of an intervention effect on the primary drug and alcohol use scales, on secondary measures of therapeutic alliance, nor on clinician-rated measures of organizational functioning and job satisfaction.
Conclusions: These negative findings will be discussed in light of baseline and staff-level qualitative and quantitative data regarding participants' reactions to the use of the performance improvement system. Recommendations for alternative methods of utilizing feedback reports to enhance clinical outcomes are proposed. Limitations such as ceiling effects and the utilization of self-report measures of drug and alcohol use are also addressed.
Financial Support: NIDA grants R01 DA020809-01(NYU) and R01 DA020799(U of P)

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THE DEVELOPMENT OF A NEW MODEL FOR INTERNATIONAL COLLABORATIVE RESEARCH AND EDUCATION.

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Aims: To begin a dialogue toward the development a new model for international collaborative research and education in drug abuse.
Methods: Programs to create and strengthen an infrastructure for international interdisciplinary collaborative research and education on drug abuse, its origins and consequences are needed. This requires a partnership between governmental, non-governmental and educational institutions in the participating nations. Through such collaboration a contribution to the knowledge base of drug abuse can be made as well as a determination of factors common to most nations as well as aspects unique to individual countries. By working together it will be possible to train young scientists from many countries to become outstanding investigators in the international field of drug abuse.

Collaborative international training and research on the global epidemic of drug abuse will provide extensive education and training opportunities that are quickly translatable from science to societal application. By engaging scientists with other professionals who are responsible for preventing and intervening with this far-reaching epidemic that reaches into homes and streets, and disrupts major economic, legal, health and other socio-cultural conditions, the scientific knowledge base will be enriched and applied to better cope with this epidemic. Drug use has often been explained through the medical model yet many other forces converge in the migration and use of illicit substances. Numerous theories from diverse disciplines have attempted to explain drug abuse but none have fully addressed the economic, legal, cultural, and social structures which are involved in its origin and spread.
Conclusions: A new cohort of scientists need to be trained in international research. The cooperation and collaboration between medical experts and social scientists would allow for a synergistic exchange of ideas that contribute to a more holistic approach to drug abuse.
Financial Support: Supported by the Comprehensive Drug Research Center, University of Miami

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SPECIFIC PREDICTORS OF SUICIDE ATTEMPTS IN A HIGH RISK COMMUNITY CORRECTIONS POPULATION.

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Aims: Determination of rates and unique risk factors for suicide attempts in a community corrections population with high rates of substance dependence.
Methods: Self-report data was collected from 20,858 enrollees in community corrections with 10.9% (N=2279) reporting a history of suicidal ideation (ideators) and 7.7% (N=1608) reporting a past suicide attempt (attempters). A comparison group of respondents without a suicide history (N= 1969) was randomly selected. The three groups (no suicide, ideators, and attempters) were compared using Chi-square or ANOVA procedures. Logistic regression analyses were conducted to determine predictors of ideation and attempt.
Results: Suicidal ideation and attempts were most strongly predicted by the same seven variables: prior psychiatric hospitalization, physical/emotional abuse, sexual abuse, prior counseling for depression or anxiety, feeling "out of control" in absence of intoxication, hallucinations, and cocaine dependence diagnosis. Among substances of abuse, alcohol dependence diagnosis was a significant independent predictor for suicidal ideation while only cocaine dependence predicted both suicidal ideation and attempts. Receiving disability, education attainment less than high school, female gender, and a history of violent offenses were significant independent predictors of suicide attempts. Among those with suicidal ideation, predictors of suicide attempts included being female, young, white race, cocaine dependence, history of violent offenses, living with family members, higher than high school education, sexual abuse history, history of counseling for depression or anxiety and history of psychiatric hospitalization.
Conclusions: Participants in community corrections had high rates of suicide attempts with unique predictors of suicide attempts. Specifically, cocaine dependence and history of violent offenses stand out as unique and addressable risk factors for suicide attempts.
Financial Support: Internal support, Department of Psychiatry, UAB

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CANNABINOID RECEPTOR GENE POLYMORPHISM AND MARIJUANA'S PHARMACOLOGIC EFFECTS ON NEGATIVE AND POSITIVE AFFECT.

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Aims: Models that integrate biological and behavioral factors are important to understanding the mechanisms by which genetic variability influences marijuana dependence and sensitivity to its acute effects. The cannabinoid receptor type 1 (CB1), a G-coupled receptor encoded by the CNR1 gene, primarily mediates the psychoactive effects and rewarding actions of marijuana. Several polymorphisms in the CNR1 gene have been associated with cannabis dependence and cannabis-related intermediate phenotypes, but those related to acute changes in affect have not been studied.
Methods: In a 2 X 2, instructional set (told delta-9-tetrahydrocannabinol (THC) vs. told no THC) by drug administration (smoked marijuana with 2.8% THC vs. placebo) between-subjects design, we examined the pharmacologic effect of marijuana on changes in negative and positive affect (measured by the POMS) with weekly marijuana smokers (mean age = 21.3; 32% female; 73% Caucasian).79 participants were genotyped, with frequencies of the rs2023239 SNP consistent with previous reports: T/T (n = 59) and T/C (n = 20).
Results: Regression models with baseline values as covariates, two main effects of drug administration and genotype, and the drug X CNR1 genotype interaction revealed significant interaction effects on the following POMS subscales post-smoking: on depression-dejection (sr2 = .06, p = .04), on anger-hostility (sr2 = .08, p = .02), and on vigor-activity (sr2 = .03, p = .05). In follow-up models with marijuana smokers who received THC (n = 35), medium to large effects of the CNR1 SNP were confirmed for depression-dejection (sr2 = .07), for anger-hostility (sr2 = .12), and for vigor-activity (sr2 = .18).
Conclusions: Preliminary data for the individual differences in CNR1 genotype in responses to acute marijuana are promising and may explain some of the variability observed in marijuana's acute effects on negative affect.
Financial Support: R01 DA021403 from NIDA to Jane Metrik

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AMYGDALAR VOLUME AND MOOD RATINGS IN ADOLESCENT MARIJUANA USERS.

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Aims: Mood alterations have been documented in long-term marijuana (MJ) users, and amygdalar volume reduction has been reported in depression and MJ smokers. However, there is limited data examining the association between mood changes, MJ use, and amygdalar volume in adolescents. This study examines the association between amygdalar volume and depression in MJ-abusing adolescents compared to healthy controls (HC) to assess whether there are differences in self-reported measures of depression on amygdalar volumes.
Methods: Eighteen adolescents with current chronic heavy MJ use and no other current Axis I disorder (aged 17.8±0.9 years) and 18 age-matched HC (aged 17.3± 0.8 years) had a 3T MRI. Volumetric segmentation was performed with Freesurfer and amygdalar volumes were corrected for total brain volume. Subjects completed a diagnostic interview, Hamilton Rating Scale for Depression (HAM-D), and Profile of Mood States (POMS).
Results: Compared to HC, MJ users reported significantly higher levels of depression (HAM-D; p = .02) and a trend for lower right amygdalar volume (p = .076). For MJ users, right amygdalar volume correlated significantly with cognitive inefficiency (POMS-C, p = .04), and low energy (POMS-F, p = .05). The correlation between depression and right amygdalar volume trended toward significance (HAM-D, p = .066). There was no significant correlation between lifetime MJ use and amygdalar volume. Healthy controls evidenced no reduction in amygdalar volume and no correlation between amygdalar volume and measures of depression or mood.
Conclusions: MJ users reported significantly more depressive symptoms than age-matched HC, which appeared to be associated with reduced right amygdalar volume. For HC, there was no association between mood measures and amygdalar volume. These findings suggest that reduced amygdalar volume may be a predisposing risk factor for MJ use. Further investigations into the impact of depressive symptoms and amygdalar volume in association with MJ use will need to be performed.
Financial Support: Supported by funding from NIH 1R01 DA020269

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TREATMENT OUTCOMES FOR METHAMPHETAMINE DEPENDENCE: FINDINGS FROM THE METHAMPHETAMINE TREATMENT EVALUATION STUDY.

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Aims: To determine the impact of community-based drug treatment on methamphetamine dependence and related harms.
Methods: A prospective cohort study. Participants were 400 methamphetamine treatment entrants from community-based drug treatment services in Australia and a comparison group of 101 out-of-treatment dependent methamphetamine users. Participants were assessed at entry to treatment and at 3 and 12 months post treatment (81% and 75% f/up respectively). Outcome measures included methamphetamine use (DSM-IV diagnosis of dependence, abstinence), polydrug use, crime, HIV risk, psychotic symptoms (BPRS), disability (SF-12) and psychological distress (K10). Measures of treatment exposure were: (a) treatment vs. no treatment; (b) treatment duration; (c) modality of treatment (detoxification, counseling, residential); and (d) treatment completion. Treatment effects were established using propensity scores to adjust for differences ($p < 0.05$) between treatment groups.
Results: Treatment increased the probability of abstinence at both 3 and 12 month follow-up ($p < 0.01$) and was associated with significant reductions in polydrug use, crime, psychotic symptoms, psychological distress and disability due to poor mental health ($p < 0.05$). Abstinence was more likely with counseling or residential treatment (cf. detoxification) and with longer treatment exposure, although these effects were attenuated at 12 months. Abstinence was more likely for lighter non-injecting methamphetamine users and those with high readiness to change.
Conclusions: Community-based drug treatment can significantly reduce methamphetamine use and related harms.
Financial Support: Australian National Health and Medical Research Council (Project Grant 350974) and the Australian Government Department of Health and Ageing.

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KAPPA OPIOID MEDIATION OF STRESS-INDUCED BEHAVIORS.

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Aims: Exposure to chronic stressors activates the kappa opioid receptor (KOR), contributing to maladaptive behavioral responses such as the increase of cocaine-seeking behavior. The aim of this study was to determine if a stress-induced endogenous activation of KOR signaling might mediate other stress-related behaviors, specifically the potentiation of ethanol reward and self-administration and the impairment of learning and memory performance.
Methods: C57Bl/6J and prodynorphin gene-disrupted (Dyn -/-) mice were exposed to repeated forced swim stress (FSS). Ethanol conditioned place preference (CPP) and two-bottle free choice (TBC) assays were then used to measure the effects of stress-induced KOR signaling on ethanol reward and self-administration, respectively. Moreover, the effect of stress-induced KOR signaling on learning and memory performance was assessed with tasks of novel object recognition and activity in the Barnes maze. To determine KOR mediation in all resulting behaviors, additional subjects were pretreated with the KOR antagonist nor-binaltorphimine (nor-BNI, 10 mg/kg). Data were then compared to saline-treated, unstressed control mice.
Results: Mice exposed to repeated FSS demonstrated a 4.4-fold potentiation of ethanol-CPP and increased the consumption of 10% (v/v) ethanol by 19.3% in the TBC assay in a nor-BNI sensitive manner. In contrast, mice exposed to FSS displayed significant performance deficits in novel object recognition and increased escape latencies in the Barnes maze when compared to unstressed animals. Pretreatment with nor-BNI prevented all stress-induced impairments in learning and memory performance. Finally, Dyn -/- mice did not demonstrate significant either stress-induced increases in ethanol consumption or impairments in learning and memory performance.
Conclusions: These data demonstrate a stress-induced potentiation of the rewarding effects and self-administration of ethanol mediated by endogenous KOR signaling. However, stress-induced endogenous activation of the KOR paradoxically impaired novel object recognition and spatial memory performance.
Financial Support: Supported by R03-DA0164515 and R01-DA023924.

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ORAL INTACT EXTENDED-RELEASE OXYMORPHONE HAS FEWER SUBJECTIVE AND COGNITIVE EFFECTS THAN EQUIANALGESIC CONTROLLED-RELEASE OXYCODONE.

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Aims: To assess relative potential for abuse and cognitive impairment, we compared subjective and cognitive measures for controlled-release oxycodone (OC) and extended-release oxymorphone (OM).
Methods: 40 healthy nondependent recreational opioid users received oral intact OC (30 and 60 mg), oral intact OM (15 and 30 mg), and placebo in a randomized, double-blind, placebo-controlled, 5-way crossover, exploratory study. Subjective measures included Addiction Research Centre Inventory Morphine Benzedrine Group (MBG), Drug Liking Visual Analog Scale (VAS), Good Effects VAS. Cognition measures included the Divided Attention (DA) test.
Results: 35 subjects completed the study. OM showed less effect than equianalgesic-dose OC (OM 15 mg vs OC 30 mg; OM 30 mg vs OC 60 mg, respectively) on MBG (3.0 [3.43] vs 5.3 [4.64], P=0.01; 4.1 [4.45] vs 6.6 [4.45], P<0.001), Drug Liking VAS (59.4 [14.31] vs 81.9 [15.62], P<0.001; 71.7 [17.01] vs 91.3 [11.67], P<0.001), Good Effects VAS (49.5 [31.61] vs 84.4 [24.36], P<0.001; 66.7 [31.59] vs 93.9 [10.21], P<0.001. Results were similar for other subjective measures and pupillometry. During the DA test, less cognitive impairment was observed with OM compared with equianalgesic-dose OC: reaction time (mean msec [SD]) was shorter for OM vs OC (569.9 [79.59] vs 590.6 [75.46], P=0.03; 574.5 [88.36] vs 605.4 [92.62], P<0.001); tracking accuracy (mean % [SD]) was greater for OM vs OC (70.3 [12.81] vs 64.3 [16.69], P=0.007; 69.0 [16.20] vs 58.9 [15.40], P<0.001), as was target accuracy (79.4 [17.01] vs 72.3 [20.03], P=0.02; 79.2 [17.48] vs 64.8 [24.52] P<0.001).
Conclusions: Oral intact OM had fewer subjective effects and produced less cognitive impairment compared with equianalgesic OC in this exploratory study.
Financial Support: Endo Pharmaceuticals Inc.

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IDENTIFICATION OF INTERNET DISCUSSION AIMED AT DEFEATING ABUSE DETERRENT FORMULATIONS.

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Aims: Over the past few years, pharmaceutical companies have devoted considerable effort to develop so-called "abuse deterrent" formulations (ADFs) for the purpose of decreasing the levels of abuse of prescription opioid medications, particularly abuse by alternate routes of administration (i.e., snorting, injecting). Some ADFs employ physical barriers that resist common methods of tampering (e.g., crushing) in order to extract the active ingredient, whereas other formulations incorporate antagonist-agonist combinations, aversive stimulus (e.g., capsaicin) or prodrugs. While these formulations may create barriers to extraction, the concern remains that some abusers will be dedicated to defeating the tamper resistant qualities of these formulations. It is generally believed that these efforts will take the form of "recipes" that will be disseminated via the Internet.
Methods: We have developed a systematic process of identifying messages (i.e., "recipes") aimed at defeating new ADFs on Internet-based recreational drug abuse forums. NAVIPPRO's proprietary Web Informed Services (WIS™) Internet monitoring archive contains over 4 million messages from recreational drug abuse forums.
Results: Data explorations were conducted to establish a standard operating procedure for identifying messages containing recipes. Identification of recipes required: (1) creation of a drug-related dictionary, (2) text disambiguation, (3) evaluation of recipe-related word frequencies, (4) identifying key word groupings (i.e., "filters"), and (5) sensitivity/specificity evaluation of recipe identification. Recipe-specific filters were created to identify all messages pertaining to a recipe profile in order to evaluate dissemination of the recipe within the online recreational drug abuse forums.
Conclusions: Results suggest that systematic filtering of messages from recreational drug abuse forums increases the ability to identify a recipe in a timely manner which may be an essential component of post marketing surveillance for ADF products.
Financial Support: King Pharmacueticals

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STRESS AND CUE-ELICITED CRAVING IN MARIJUANA-DEPENDENT INDIVIDUALS.

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Aims: Cue-elicited craving and stress responses have been identified as predictors of relapse, but little research exists on the contribution of these factors to marijuana use specifically. The aims of the present study were to (1) evaluate responses to a psychological stressor, (2) evaluate responses to marijuana-related cues, and (3) evaluate if exposure to a psychological stressor augments craving subsequently elicited by marijuana-related cues in marijuana-dependent individuals.
Methods: Subjects were marijuana-dependent men and women between the ages of 18 and 65 years. Subjective (craving, stress) and neuroendocrine (ACTH, cortisol) responses to the presentation of neutral and marijuana cues were assessed after randomization to a psychological stressor (Trier Social Stress Task; TSST) or no-stress condition. Outcome measures were assessed at baseline, post-stressor, post-neutral cue, and post-marijuana cue. A repeated measures ANOVA framework was used to test for differences in response.
Results: 87 participants completed procedures (stress group, n=45; non-stress group, n=42). The mean ± SD age of participants was 25.8 ± 8.6 and 67% were males. The stress group had a significant increase over the non-stress group in stress ($p<0.001$), craving ($p=0.028$), cortisol ($p<0.001$), and ACTH ($p<0.001$) after completing the TSST. Following the TSST or no-stress condition, an increased craving response for all participants was seen following presentation of the marijuana cues ($p=0.005$), largely due to the response of the non-stress group. The non-stress group had a mean (SE) increase of 3.7 (1.2) in craving to marijuana cues as compared to neutral cues ($p=0.002$); the stress group did not have a significant increase in craving (M (SE): 0.9 (1.1); $p=0.404$).
Conclusions: A social stressor increased craving and elicited a neuroendocrine response in marijuana-dependent individuals; however, after the stressor condition, the response to subsequent marijuana-cue exposure was attenuated relative to the non-stress group.
Financial Support: Supported by R21DA22424 (McRae-Clark) and K24DA00435 (Brady).

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HEPATITIS C VIRAL LOAD: A COMPARATIVE STUDY BETWEEN CAPILLARY MICRO SAMPLE AND VENOUS BLOOD.

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Aims: Rational of the study: Prevalence of HCV is high among drug users, and there are multiple screening and management obstacles, such as for instance the blood test issue. Screening is carried out using capillary samples as an alternative to venous sampling. Beyond screening, it seems justified to assess the interest of such method to confirm chronic C hepatitis and assess its severity on one same sample. The results might allow a better definition of the prospect in terms of patient management and recovery.
Methods: *Main purpose:* To assess the sensitivity and specificity of the viral load calculation by Real Time PCR quantification from a capillary sample compared to a standard venous sample. *Secondary purposes:* To assess the sensitivity and specificity of the serological results of both samples. To assess the sensitivity and specificity of the genotype of both samples. To describe the correlation between both methods for patients with high viral load (> 800.000 UI/ml). To describe the correlation between both methods for patients with low viral load (< 800.000 UI/ml)
Results: Drug users followed up in education consultation are consecutively included for a 6-month period. Each patient's viral load and genotype are determined from both venous and capillary samples. A centralized analysis of the samples is carried out by RT-PCR in real time (detection limit > 15 UI/ ml, Taqman Roche). Twenty patients had a negative venous viremia with the capillary sample. Hence, such method has a 100% sensitivity and specificity. Thirty patients had a positive viral load. Capillary viremia was lower than the venous one, except for one patient. There was a good correlation in low viral loads and significant differences in high viral loads.
Conclusions: In 50 patients, capillary viremia always allowed chronic load screening. When combined with genotype, it allowed recovery assessment. Such method is much interesting in drug users and should become widespread in drug-addicts.
Financial Support: none

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THE EFFECTS OF THE OPIATE NEUTRAL ANTAGONIST 6β-NALTREXOL IN OPIATE-DEPENDENT SUBJECTS.

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Aims: Complications of prescription opioids include abuse and constipation. The molecular pharmacology of 6β-Naltrexol (6βN), a neutral opioid antagonist, suggested it might attenuate μ-agonist effects without precipitating opiate withdrawal (OWD), decreasing abuse liability if co-formulated with μ-analgesics, and reverse opiate constipation, without compromising analgesia.
Methods: In this proof-of-concept, placebo-controlled, blinded study 4 (3F, 1M) opiate-dependent subjects (on 19-70 mg/day methadone) received ascending doses of 6βN (0.05, 0.15, 0.50 & 1.0 mg, over 15 mins IV). The primary endpoint was precipitated OWD; all subjects were screened with naloxone 50 μg IV before 6βN exposure to assure tolerability of OWD. Measures included vital signs (HR and BP), Visual Analog Scales (VAS) of 'any' 'good' and 'bad' drug effect; 'opiate withdrawal'; 'sickness'; the Objective and Subjective OWD Scales (SOWS, OOWS), oral-cecal transit time (OCTT, measured by expired H2 after 10 gm po lactulose), and laxation. Dose escalation was terminated for VAS OWD >25. PK profiles were obtained with the 1.0 mg dose in two subjects.
Results: Three subjects (all F) received the maximal 1.0 mg of 6βN; the one M reached stopping criteria at 0.5 mg. No subject would have been advanced beyond 1 mg due to significant abdominal distress. Although 6βN produced abdominal discomfort and withdrawal symptoms no significant changes in VAS measures of OWD, total SOWS and OOWS scores, or HR and BP occurred. 0.15 mg 6βN accelerated OCTT in 2 subjects; >0.5 mg produced laxation within 20 minutes in 3/4 subjects; naloxone did not produce laxation.
Conclusions: 6βN acts as a neutral opiate antagonist, is less potent than naloxone in precipitating OWD and produces laxation. These features suggest that a combination formulation of 6βN with an opioid analgesic could attenuate opiate-induced constipation and decrease abuse of μ-opioids.
Financial Support: Supported by AIKO Biotechnology, Portland ME

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THE ROLES OF NICOTINIC AND MUSCARINIC CHOLINERGIC RECEPTORS IN COST-BENEFIT DECISION MAKING.

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Aims: Risky and impulsive decision making are common in drug-addicted individuals. Although the role of several neurotransmitter systems in such behavior has been thoroughly investigated, little is known about the involvement of the cholinergic system. The overall goal of these experiments was to determine how cholinergic signaling is involved in cost-benefit decision making.
Methods: Male Long-Evans rats were trained in a "probabilistic discounting" task, in which they chose between small guaranteed and large probabilistically delivered food rewards. A separate group of rats were trained in a "delay discounting" task, in which they chose between small immediate and large delayed food rewards. Once stable performance was achieved, the effects of acute administration of nicotinic and muscarinic receptor agonists and antagonists were tested in each task.
Results: In the probabilistic discounting task, acute administration of the inhibitor donepezil decreased choice of the large risky reward in "risk-taking" rats and increased choice of the large reward in "risk-averse" rats. Acute administration of nicotine increased choice of the large risky reward in both groups, whereas administration of the nicotinic receptor antagonist mecamylamine decreased choice of the large risky reward in "risk-taking" rats. In the delay discounting task, donepezil had no effects, but nicotine decreased choice of the small immediate reward in "impulsive" rats. Choice preference in both tasks was not significantly altered following acute administration of either a muscarinic agonist or antagonist.
Conclusions: These experiments suggest that the cholinergic system is involved in cost-benefit decision making. Given that drugs targeting the cholinergic system are already in use for treatment of a variety of clinical conditions, the results suggest that these drugs may prove useful for treatment of decision-making deficits present in addiction.
Financial Support: Supported by MH65728 (IAM), AG02942 (JLB) and DA024671 (BS)

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PERCEPTIONS OF IMPAIRED HEALTH PROFESSIONALS REGARDING PARTICIPATION IN A STATE MONITORING PROGRAM.

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Aims: The aims were: 1) to understand the experiences of substance-impaired health professionals participating in a state monitoring program (SMP), 2) to identify the components of the SMP that were deemed most beneficial by the participants, and 3) to explore potential areas for improvement.
Methods: Data from 2 studies were included. First, 80 physicians (85% male) in a SMP completed an anonymous online survey regarding their substance use and experiences in the SMP. Next, 110 health professionals (54 physicians, 94% male; 33 pharmacists, 73% male, and 23 allied health professionals, 61% male) under contract with a SMP participated in anonymous focus groups (n = 18).
Results: In study 1, 78.4% of respondents reported being satisfied with the SMP, with 92.5% indicating they would recommend it to others. The aspects of the SMP deemed most beneficial included peer fellowship/support (26%) and advocacy related to legal or licensure concerns (26%). Communication, individualization of contract requirements, and convenience were identified as areas for improvement. In study 2, the primary themes that emerged concerning benefits of the SMP included peer fellowship/support, as well as advocacy. Professionals noted that monitoring provided a vehicle through which they could implement a Recovery lifestyle, because abstinence was mandatory. Non-physician professionals reported more concerns regarding the cost of the program, which some experienced as burdensome.
Conclusions: State monitoring programs provide health professionals with added incentive to initiate and sustain sobriety, allowing them to take advantage of programs that encourage a Recovery lifestyle. Though monitoring may be experienced as burdensome by some professionals, the majority appreciate the opportunity for peer support and advocacy.
Financial Support: This research was sponsored in part by NIDA research grant R01-DA20791 (PI: Cottler). The first author is supported in part by NIDA training grant T32-DA-07313-10 (PI: Cottler).

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EFFECT OF PRENATAL COCAINE EXPOSURE ON CHILDHOOD GROWTH.

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Aims: Limited research exists on how prenatal cocaine exposure affects childhood growth. We examined the effect of prenatal cocaine exposure on trajectories of childhood growth by gender through age 14. It was hypothesized that prenatally cocaine exposed children would be lighter and shorter throughout childhood versus non-exposed.
Methods: A total of 9,132 growth data points from the Miami Prenatal Cocaine Study (MPCS) (N = 476, 53% prenatally exposed to cocaine, 48% female) were analyzed. We longitudinally compared anthropometric measures (height, weight, body mass index [BMI]) from birth to age 14 among term (≥37 weeks gestation) African American children/adolescents who were/were not prenatally exposed to cocaine. Heights and weights were converted to BMI z scores and %iles for age and sex to generate longitudinal growth curves. Repeated measures analyses compared exposure group growth at ages birth, three, five, seven and 12-to-14 years.
Results: Prenatally cocaine exposed girls were significantly lighter (P =0.014) and shorter (P =0.004) at birth versus boys but by age 6 years were heavier and taller. Children born both LBW and prenatally exposed to cocaine remained shorter and lighter than their non-exposed LBW counterparts through age 14. By age 14 33% of the prenatally exposed group and 42% of all females were overweight (BMI >85th %ile for age and sex).
Conclusions: Children born both LBW and prenatally exposed to cocaine may be at particularly high risk for future onset cardiometabolic disease due to the combination of being born small and later development of overweight. Although the influences that impair fetal development and program adult chronic disease remain to be defined, our findings here suggest that prenatal exposure to cocaine may permanently alter structure, physiology and metabolism as children grow and consequently put them at high risk for later onset chronic disease.
Financial Support: National Institute on Drug Abuse, Grants K01 DA026993-01, P50 DA024584, R01DA006556

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ACUTE EFFECTS OF MARIJUANA SMOKING ON NEGATIVE AND POSITIVE AFFECT.

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Aims: Human studies and animal experiments present a complex, often contradictory picture of the acute impact of cannabis on emotions. Some studies find increases in negative affect following THC administration and some find reductions; although, there is a dearth of human studies that assess acute changes in negative and positive affect.
Methods: In a 2 X 2, instructional set (told delta-9-tetrahydrocannabinol (THC) vs. told no THC) by drug administration (smoked marijuana with 2.8% THC vs. placebo) between-subjects design, we examined the pharmacologic effect of marijuana on subjective measures and changes in negative and positive affect with 97 weekly marijuana smokers (mean age = 21.4; 32% female; 75% Caucasian). Individuals were first tested under a baseline/no smoking condition and again under experimental condition.
Results: Relative to placebo, THC significantly increased feelings of tension and anxiety (sr 2 =.07, p < .01), fatigue (sr2 =.03, p < .05), and arousal (sr2 =.08, p < .01), and increased confusion-bewilderment (sr2 = .09, p =.001). Significant expectancy X drug interaction effect (sr2= .05, p <.01) revealed that either expecting placebo regardless of actual drug content (sr2 =.15, p =.001) or receiving placebo regardless of the instructional set (sr2=.11, p <.01) was associated with an increase in negative affect. Significant pharmacologic effects were also evident for self-reported physical reactions to marijuana (sr2= .35, p <.001), increased food craving (partial $\eta 2$ =.17, p <.001), and ratings of satisfaction (partial $\eta 2$ =.23, p <.001), liking (partial $\eta 2$ = .12, p <.001), and positive affect (partial $\eta 2$ =.14, p <.001). Expectancy main effects were also significant on these measures demonstrating the additive effect of expectancies on affective reactions to marijuana. Individual differences characterizing marijuana users most sensitive to these effects are also examined.
Conclusions: Results demonstrate that expectancy and pharmacology play largely independent roles in the effects of marijuana.
Financial Support: Grant R01DA021403 from NIDA to Jane Metrik

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NEVER HIV TESTED: RESULTS OF SCREENING DATA FROM 12 DRUG TREATMENT PROGRAMS IN THE CTN 0032 HIV RAPID TESTING AND COUNSELING STUDY.

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Aims: The Centers for Disease Control and Prevention recommends persons between the ages of 13 and 64 be HIV tested. Drug users are at higher risk for HIV infection compared with the general population, but little is known about the proportion of drug treatment patients that have never tested for HIV infection.
Methods: From January – May, 2009, we collected screening data as a part of the HIV Rapid Testing and Counseling Randomized Controlled Trial sponsored by NIDA's Clinical Trials Network (CTN 0032). Individuals (n=2,453) 18 years and older in 12 community based drug treatment programs throughout the U.S. were interviewed face-to-face about their past HIV testing histories.
Results: 41% women, 10% Hispanic, 27% African American; 46% reported having injected drugs in the past 12 months. Age of patients was: 26% between 18 – 29, 23% between 30 – 39, 31% between 40 – 49 and 19% over 50 years of age. One fifth of the study participants (20.3%) have never tested for HIV. Men (26%) were more likely than women (12%) to never have tested. African Americans (12%) were less likely to have never tested compared with Hispanics (20%) and Whites (25%). Individuals 29 years or less were more likely to report no prior HIV tests (31%) than individuals 30 years or older (15%). Multivariable analysis suggested that African American patients (vs. White patients) were less likely to have never tested for HIV, after controlling for Hispanic ethnicity, gender, age, and injection drug use status. Similarly, injectors (vs. non-injectors) and persons older than 30 years of age were more likely to have been tested for HIV. There was an interaction between race/ethnicity and gender with Hispanic males, Non-Hispanic males, and Hispanic females (vs. white females) being more likely to never have tested for HIV.
Conclusions: Results suggest that strategies are needed to improve the uptake of HIV testing for persons in drug abuse treatment.
Financial Support: National Institute on Drug Abuse

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"YOUTHFUL EPIDEMIC" OR DIAGNOSTIC BIAS? DIFFERENTIAL ITEM FUNCTIONING OF DSM-IV CANNABIS USE CRITERIA IN AN AUSTRALIAN GENERAL POPULATION SURVEY.

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Aims: The first aim of this study is to examine the differences in endorsement rates of the cannabis use disorder criteria in younger (i.e., 18-24) and older (i.e., 25+) adult age groups using general population data. The second aim of this study is to investigate whether there is any age-related differential item functioning in the DSM-IV diagnostic criteria for cannabis use disorders using an item response theory approach.
Methods: The sample consisted of 10641 participants in a population-based survey of Australian adults aged 18 years and older. DSM-IV cannabis use disorders were assessed in all respondents who had used cannabis more than five times in the previous twelve months (n=722). Age-based differential item functioning was assessed in each of the DSM-IV criteria for cannabis use disorders.
Results: Age-based differential item functioning was only detected in the Hazard criterion of the DSM-IV cannabis use disorders. The Hazard criterion was found to be more discriminating for those aged 18-24 when compared with those aged 25 and over.
Conclusions: The DSM-IV criteria for cannabis use disorders appear to function similarly across age groups. Differential item functioning was only detected in the α parameter for the Hazard criterion. These results are discussed with regard to implications for future editions of the DSM system.
Financial Support: Univerisity of NSW, Faculty of Medicine, Postgraduate Research Support Sceme

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MALE-FEMALE AND AGE-OF-ONSET VARIATIONS IN RISK OF CLINICAL FEATURES ASSOCIATED WITH COCAINE DEPENDENCE.

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Aims: In this study, we estimate male-female and age-of-onset variations in the occurrence of clinical features associated with cocaine dependence, with a focus on very recent onset cocaine users, all of whom had started to use cocaine within 90 days of assessment (VROCU-90d).
Methods: Data are from the 2004-2007 National Surveys on Drug Use and Health (NSDUH), which are cross-sectional sample surveys conducted each year in the United States. A total of 222,221 individuals completed computer-assisted self-interviews; 1,343 VROCU-90d were identified; assessment of clinical features associated with cocaine dependence was guided by DSM-IV-TR criteria. Estimation takes complex survey design into account.
Results: Among the VROCU-90d, an estimated 9-10% had experienced tolerance; an estimated 1-2% had used more cocaine than they had intended to use. Estimates for the other clinical features were intermediate in value. There is no male-female variation in the occurrence of the clinical features ($p>0.05$), but adolescent-onset cocaine users and those older than 26 years were at excess risk, as compared to young adult VROCU ($p<0.05$).
Conclusions: In these data, we found variations in occurrence of clinical features associated with cocaine dependence, with tolerance experienced most often. There was no male-female variation in occurrence of these clinical features soon after onset of cocaine use, but there was interesting variation associated with age at onset of cocaine use.
Financial Support: NIDA award K05DA015799 & T32DA021129.

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EFFECT OF NOVEL NICOTINIC RECEPTOR ANTAGONIST R-B3,5L/3PIDDB ON NICOTINE- AND FOOD-MAINTAINED SELF-ADMINISTRATION.

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Aims: Smoking is one of the most preventable causes of death. Currently there are several treatments for smoking cessation available. However, with limited efficacy of available pharmacotherapies and high relapse rates, alternative novel therapeutics for smoking cessation are warranted. The current study investigated the effects of r-b3,5L/3PiDDB, a bis-tertiary amine that has nicotinic antagonist activity at $\alpha6\beta2$-containing receptors, on nicotine self-administration and food-maintained responding.
Methods: Sprague Dawley rats (N = 12) were first trained to self-administer nicotine intravenously (0.03 mg/kg/infusion). Upon stable responding, rats were then pretreated with r-b3,5L/3PiDDB (19.4, 58.3, 109 or 194 μmoles/kg; SC) to assess the acute dose response. To investigate the selectivity of effect on nicotine self-administration, a separate group of rats (N=6) were trained to lever press for food pellets and then were pretreated with r-b3,5L/3PiDDB (19.4, 58.3, 109 or 194 μmoles/kg; SC). The effects of repeated administration of r-b3,5L/3PiDDB were also investigated. In this latter experiment, rats (N=12) were trained to self-administer nicotine (0.03 mg/kg/infusion) and then were pretreated on 7 consecutive days with r-b3,5L/3PiDDB (109 μmoles/kg; SC).
Results: r-b3,5L/3PiDDB dose-dependently decreased nicotine self-administration acutely, with no significant effects of r-b3,5L/3PiDDB on responding for food pellets. The 109 μmoles/kg dose also maintained a decrease in nicotine self-administration across repeated sessions.
Conclusions: Results from these experiments suggest a potential new lead in the development of a novel therapeutic for smoking cessation.
Financial Support: Supported by NIH grant U19 DA17548.

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WITHDRAWAL SYMPTOMS AS A PREDICTOR OF MORTALITY IN PATIENTS HIV-INFECTED THROUGH DRUG USE AND RECEIVING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY.

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Aims: Even in the highly active antiretroviral therapy (HAART) era, individuals HIV-infected through injecting drug use (IDUs) are at increased risk of death due to the burden of competing events such as liver disease, overdose and suicide. The objective of this study was to explore the role which life events' experience, in particular drug-related events such as detoxification or withdrawal symptoms, may play on the risk of death in HIV-infected IDUs.
Methods: Our analysis was based on longitudinal data of 296 HIV-infected IDUs from when they started HAART. Data collection included medical records and patient's self-reports detailing, among other information, life events including drug-related problems.
Multiple imputation for missing data in the explanatory variables together with Cox models were used to identify predictors of death.
Results: During HAART follow-up, 26 deaths occurred, corresponding to 1.8 deaths per 100 person-years.
The majority (N=8) were attributable to liver disease while 5 were from unknown causes (found deceased at home or in a car). After adjustment for age and time-dependent viral load (>10,000 cp/ml) individuals experiencing withdrawal symptoms had a 5-fold increased risk of death with respect to the others.
Conclusions: Withdrawal symptoms in IDUs living with HIV reflect physicians' difficulties in managing their patients' opioid dependence. Early detection and increasing substitution dosages or switching to a more adequate treatment could prevent possible drug-related deaths.
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PHARMACODYNAMIC AND PHARMACOKINETIC PROFILE OF CRUSHED INTRANASAL SUBOXONE® AND SUBUTEX® IN SPORADIC OPIOID ABUSERS.

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Aims: Sublingual buprenorphine (Subutex®; BUP) and BUP/naloxone (Suboxone®; BUP/NX) are efficacious opioid dependence pharmacotherapies, but there are concerns about their diversion and misuse by the intranasal (IN) route. The study objectives were to examine and compare the IN pharmacodynamic and pharmacokinetic profiles of both agents with regard to abuse liability.
Methods: Healthy sporadic opioid abusing (n=8) adults with IN opioid experience completed this inpatient randomized, double-blind, crossover study. Six sessions (72 hrs apart) were conducted to examine five IN doses [0/0 mg, crushed Subutex® (2, 8 mg), crushed Suboxone® (2/0.5, 8/2 mg)] and one IV dose (0.8 mg BUP/0.2 mg NX to assess bioavailability). Plasma samples, subjective, observer-rated and physiological measures were collected before and up to 72 hrs after drug administration.
Results: Both drugs produced time- and dose-dependent increases on mu opioid agonist effects (e.g., "liking," "high"). However, the time to onset of effects for BUP/NX was delayed compared to BUP, particularly after 8 mg (e.g., miosis, "high"). Subjective ratings were higher for 8 mg BUP than 8/2 mg BUP/NX. Subjects reported they would pay 25-30% more for BUP than BUP/NX at both doses. No differences in peak plasma BUP concentration or time course were observed between Subutex® and Suboxone® (Cmax= 3 & 9 ng/mL after 2 & 8 mg, respectively). Mean Tmax occurred between 35-40 min after all IN doses.
Conclusions: These data suggest that IN Suboxone® may have reduced abuse liability compared to IN Subutex® in non-dependent opioid users at higher doses. This is not attributable to differential absorption of BUP. The observed delay in onset of pharmacodynamic effects, a factor known to alter abuse liability, after Suboxone® may be due to the IN absorption of naloxone.
Financial Support: NIDA R01 DA016718 (SLW), NIDA T32 DA016176 (LSM) and Reckitt Benckiser for analytic support (DEM)

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GENDER DIFFERENCES IN THE RELATIONSHIP BETWEEN NEIGHBORHOOD ENVIRONMENT AND CHILDHOOD DEPRESSION: RESULTS FROM A COMMUNITY EPIDEMIOLOGIC STUDY OF PREDOMINANTLY AFRICAN-AMERICAN URBAN CHILDREN.

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Aims: Rates of depression in early childhood are generally similar among boys and girls, with some evidence that boys are slightly more likely to be depressed. By late adolescence, however, rates of depression are nearly two times higher among girls and this gender difference continues through the lifespan. Explanatory theories include those related to pubertal changes, variations in coping skills and stress response, and gender differences in social roles. Little work has focused on the importance of the neighborhood environment in explaining gender differences in rates of depression from childhood through adolescence. This study seeks to address this gap in the literature by examining gender differences in the association between neighborhood environment and depression in a community-based sample of predominately African American urban school children.
Methods: Environmental measures included observational assessments of drug, alcohol, and violence related environmental hazards. Depression was assessed using the Achenbach Youth Self Report(YSR).
Results: Environmental characteristics were similar among boys and girls, however, depression was greater among boys. For every increase in the number of environmental alcohol and other drug indicators, there was an estimated 1.17 increase in the odds of being depressed for girls (OR=1.17, p=0.05); there was no difference in depression by neighborhood environment among boys.
Conclusions: These preliminary findings suggest that while primary school-aged boys are more likely to be depressed, girls are more negatively impacted by deleterious environments.
Financial Support: This research was supported by NIAAA R01AA015196, NIDA R01DA018318, and CDC 1U49CE000728

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CM TREATMENT OUTCOMES FOR COCAINE-DEPENDENT HOMELESS AS A FUNCTION OF AGE.

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Aims: Although America's population is aging and epidemiological data show cocaine heavy users tend to be older, few studies have examined treatment response for cocaine dependence as a function of age. This is particularly true for cocaine dependent homeless at high risk for multiple health problems and risks associated with poverty and incarceration. We report abstinence outcomes for a cohort of 206 cocaine dependent homeless persons randomly assigned to two Contingency Management (CM) interventions, where both reduced drug use measured for 12 months post admission (Milby et al 2005). We predicted abstinence outcomes would improve as a function of age.
Methods: For analysis, we divided subjects into four 10-year epochs: 20-29; 30-39; 40-49; 50-59. Graphical and descriptive data summaries suggested that abstinence increased with age regardless of treatment through age 40 with limited age-related change thereafter. Mean (standard deviation) abstinence levels ignoring treatment were 8.8 (13.0), 13.7 (14.4), 19.2 (14.3), and 20.2 (14.8) for the 4 respective epochs.
Results: General linear model analyses that allowed for different age effects on abstinence after controlling for treatment showed a significant age effect prior to age 40 (slope of 0.7 added consecutive weeks abstinent per additional year of age, p=0.007) but no evidence of an effect after age 40 (slope of 0.1 added consecutive weeks abstinent per additional year of age, p=0.7). These significant differences held after controlling for baseline characteristics of previous treatment attempts, education, employment status, cocaine use over the prior 30 days, and gender.
Conclusions: Results are consistent with the Maturing out Hypothesis (Winnick,1962) with caveats that drug use, as measured, covered only 12 months of age effect to be manifested, and study subjects do not include users who died before study recruitment.
Financial Support: Supported by NIDA R01 DA11789-04

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THE FATTY ACID AMIDE HYDROLASE INHIBITOR, URB597, MORPHINE, AND THE CB1 AGONIST, CP55940 IN ASSAYS OF PAIN-ELICITED, PAIN-SUPPRESSED, AND SCHEDULE-CONTROLLED BEHAVIOR.

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Aims: It is well established that opioid and cannabinoid receptor agonists possess antinociceptive effects. Recently, modulators of endogenous cannabinoid signaling, such as fatty acid amide hydrolase (FAAH) inhibitors, have also revealed antinociceptive effects. The present studies compared the effects of a FAAH inhibitor, URB597, with morphine and the CB1 agonist CP55940 in assays of pain-elicited behavior (hotplate and acetic acid-induced writhing), pain-suppressed behavior (acetic acid-suppressed feeding) and schedule-controlled behavior.
Methods: A range of doses [URB597 (0.32-17.0 mg/kg), morphine (0.1-32.0 mg/kg), and CP55940 (0.01-0.32 mg/kg)] was examined in C57BL/6J mice. Hotplate: response latencies were measured at 56°C. Acetic acid-elicited writhing and -suppression of feeding: 0.6% acetic acid was injected intraperitoneally (ip) and writhing responses and consumption of liquid food were measured over 30 m. Schedule-controlled behavior: responses were maintained under a fixed ratio 4 schedule of reinforcement.
Results: Morphine and CP55940 produced dose dependent increases in hotplate latencies, but URB597 was not effective in this assay. All three compounds inhibited acetic acid-elicited writhing, but only URB597 attenuated the suppression of feeding by acetic acid injection. Finally, morphine and CP55940 dose dependently decreased rates of schedule-controlled behavior, but URB597 did not alter response rates in this assay.
Conclusions: These data are consistent with previous research demonstrating that inhibition of anandamide catabolism by FAAH produces antinociception, but does not produce the disruption of other behaviors that is seen with administration of cannabinoid agonists. Further, these data support the notion that assays of pain-suppressed behavior can be used to complement more traditional assays of pain-elicited behavior.
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IS EXPOSURE THERAPY FOR POSTTRAUMATIC STRESS DISORDER EFFICACIOUS AMONG PEOPLE WITH SUBSTANCE USE DISORDERS? RESULTS FROM A RANDOMISED CONTROLLED TRIAL.

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Aims: To evaluate the efficacy of an integrated treatment for PTSD (incorporating imaginal and in vivo exposure) among people with SUD
Methods: 103 participants were recruited from SUD treatment services and community referrals in Sydney, Australia (83% response rate). Participants were randomly assigned to receive either i) integrated treatment (IT) for SUD and PTSD (n=55); or ii) treatment as usual (TAU) for their SUD (n=48). Components of the IT included psychoeducation, CBT for SUD and PTSD, imaginal and in vivo exposure. Participants completed interviews at baseline, 6-weeks, 3- and 9-months follow-up. Over 70% of the sample were re-interviewed at each time point. Intention-to-treat analyses were conducted comparing the outcomes of those who received the IT versus TAU.
Results: The mean age of the sample was 35.7 years and 62% were female. The most commonly used substances were benzodiazepines (73%), cannabis (69%), alcohol (67%), heroin (45%) and amphetamines (42%). All participants met DSM-IV criteria for substance dependence and PTSD. The most commonly reported traumas involved physical or sexual assault. Over 75% had experienced childhood trauma; 55% reported childhood sexual abuse. Over the 9-month follow-up period, both the IT and TAU group evidenced reductions in their substance use, however, these were more pronounced in the IT group. The IT group also demonstrated substantial improvements in relation to the frequency and severity of PTSD symptoms, whereas the TAU group demonstrated little change in relation to these outcomes.
Conclusions: Contrary to popular belief, exposure therapy for PTSD is safe and effcacious among individuals with SUD
Financial Support: Funded by the Australian National Health and Medical Research Council

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ATTENTION AT 12 YEARS IN PRENATALLY COCAINE-EXPOSED CHILDREN.

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Aims: To assess differences in attention abilities between prenatally cocaine exposed (PCE) and non cocaine-exposed (NCE)at age 12 years.
Methods: Two hundred and ninety six (148 PCE) and 148 (NCE) primarily African American, low socioeconomic status children participated in a prospective longitudinal study. Attention was assessed using the Continuous Performance Test (CPT). Number of omissions (NO)and commissions (NC) errors, hit reaction time (HRT), hit reaction time standard error (HRTSE), variability of standard error (VSE) and an inattentiveness summary score (ISS) were assessed. The Behavior Rating Inventory of Executive Function (BRIEF) caregiver report (inhibitory control) was also evaluated. Multiple regression analyses for continuous variables and logistic regression for dichotomous variables were used to assess the effects of PCE on attention, controlling for covariates.
Results: Greater inhibitory control problems were reported on the BRIEF for PCE females compared to NCE females (16.17(.64) vs 14.07(.56); p<.02). PCE was not associated with increased attention problems any CPT scales. Higher average 1st trimester prenatal alcohol exposure increased the odds of NC errors in the clinical range (OR=1.44, CI 1.09-1.93, p<.01). Better caregiver vocabulary was associated with lower odds of HRT (OR=.97, CI .96-.99, p<.02). Higher child IQ was associated with better attention scores on all scales. Blood lead measurements taken at two or 4 years were not associated with lower attention. The percentage of children with 2 or more t scores above 60, indicating attention problems, was CE 23.65 vs NCE 25.68,(p>.05).
Conclusions: Although caregiver report of inhibitory control indicated more attention problems among prenatally cocaine exposed females, performance data on the CPT did not corroborate these findings. 1st trimester alcohol exposure was associated with impulsive responses on the CPT. Children of women who used cocaine and alcohol prenatally should be considered at risk for problems of attention and should be screened early to reduce associated problems.
Financial Support: This reseach was supported by NIDA R01 07957.

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ACUTE EFFECTS OF AMBIEN CR™ ON COGNITIVE PERFORMANCE AND SLEEP IN HEALTHY MALE VOLUNTEERS AFTER CHRONIC NIGHTLY USE.

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Aims: Ambien CR™ (AMB), an extended-release formulation of zolpidem (a non-benzodiazepine hypnotic that binds at the ω_1 benzodiazepine receptor subtype), is prescribed commonly for insomnia. Acutely, zolpidem impairs psychomotor and cognitive performance. We sought to examine acute effects of AMB on performance and sleep following 28 nights of AMB use. Based on studies in chronic benzodiazepine users, we hypothesized that tolerance would not develop to AMB's acute impairing effects.
Methods: Fifteen healthy male volunteers (aged 20-41) with normal sleep patterns completed four overnight experimental sessions (in fixed order) involving double-blind capsule administration [placebo (PL) or 12.5 mg AMB; 30 min before bedtime], performance testing, and polysomnographic sleep monitoring: 1. baseline phase/PL, 2. baseline phase/AMB, 3. chronic phase/AMB (after 28 nights of at-home AMB), and 4. chronic phase/PL (after 7 more nights of at-home AMB).
Results: Analysis of Variance indicated a significant main effect of drug such that performance was significantly ($p < 0.05$) worse for AMB relative to PL during the peak effects battery (after forced awakening approximately 50 min post-bedtime) across all measures (psychomotor, attention, memory, metacognition), with no differences for AMB between the baseline and chronic phases. Memory for words shown at peak and tested the next morning was impaired by AMB, but no other next-morning effects were found. Initial sleep latency and Stage 1 sleep decreased, and sleep efficiency and Stage 2 sleep increased for AMB relative to PL. For PL, psychomotor and working memory performance and slow-wave sleep decreased in the chronic phase relative to baseline.
Conclusions: Tolerance did not develop to Ambien CR™-induced acute performance impairment. This result may have significant implications for patients when circumstances necessitate nighttime awakening and functioning. Discontinuation of nightly Ambien CR™ use may be associated with acute abstinence effects that impact both sleep quality and performance.
Financial Support: R01DA11936; M01RR02719; T32DA07209

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ACUTE ADMINISTRATION OF DRUGS OF ABUSE MODULATES RISKY DECISION MAKING.

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Aims: People are faced with daily decisions among competing alternatives, some of which may be accompanied by adverse consequences. Most people are able to accurately assess the risks and rewards of such alternatives and decide accordingly; however, drug users often display maladaptive decision making, such that choices are biased toward risky options. This type of decision making is commonly studied in laboratory tasks in humans (e.g. the Iowa Gambling Task). There have been few attempts using animal models to determine how risks of adverse consequences (punishment, as opposed to reward omission) influence decision making. Our lab has recently developed such a task, in which rats choose between small "safe" rewards and large rewards that are accompanied by varying risks of punishment. Previous work in our lab showed that amphetamine decreased risk taking in this task, whereas cocaine rendered rats insensitive to changes in the risk of punishment. The purpose of this study was to extend our investigation of the effects of drugs of abuse on risky decision making, using acute administration of nicotine, morphine, and ethanol.
Methods: Male Long-Evans rats were trained in the risky decision making task in standard operant chambers, in which they were given choices between pressing one of two levers, one of which resulted in a small, "safe" reward and the other which resulted in a large, "risky" reward; the choice of the large reward was accompanied by the possibility of a mild footshock, the probability of which increased over the course of the session in consecutive blocks of trials (0, 25, 50, 75, 100%).
Results: Nicotine caused a dose-dependent decrease in risk taking (fewer choices of the large risky reward). Morphine increased risk taking, whereas ethanol had no effect on choice behavior. Finally, as found previously, amphetamine dose-dependently decreased risk taking.
Conclusions: These results suggest that acute intake of drugs of abuse can modulate risk taking in a drug-specific manner, either increasing or decreasing choices of highly rewarding, but risky, options.
Financial Support: R01 DA024671 (BS)
F31 DA023331 (NWS)

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THE ANTICONVULSANT LEVETIRACETAM CAN POTENTIATE ALCOHOL CONSUMPTION IN NON-TREATMENT-SEEKING HEAVY DRINKERS: CONTRIBUTION OF DRD2 POLYMORPHISMS.

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Aims: Levetiracetam (Keppra) is an atypical anticonvulsant that has been shown to attenuate alcohol consumption in treatment-seeking alcohol dependent subjects (Sarid-Segal et al., 2008). The mechanism by which Keppra decreases alcohol consumption is as yet unclear. However, Keppra inhibits activity at N-type calcium channels (Lukyanetz et al., 2002; Pisani et al., 2004) and recent animal data suggest that N-type calcium channel inhibitors attenuate acute intoxication induced by ethanol (Newton et al., 2008).
Methods: We evaluated the effects of Keppra on alcohol consumption in non-treatment seeking heavy drinkers receiving either a low (500-1000g/day) or moderate (1000-2000g/day) dose of Keppra during a 42-day placebo controlled double-blind randomized crossover trial.
Results: In contrast with previous data, we found that subjects drank on average slightly more on Keppra (121% of placebo drinking), regardless of dose. Additionally, there were significant positive correlations between the AUDIT ($p = .043$; $R = .30$) and DUSI ($p = .037$; $R = .31$) scores of drinking severity and treatment effect, such that greater alcohol misuse indicated greater increased drinking on Keppra. We also examined polymorphisms of candidate genes associated with alcohol consumption and found that the DRD2 polymorphism (rs1800497) significantly predicted Keppra treatment efficacy ($n = 44$; $p = .004$): GG individuals ($n = 28$) drank significantly more than both AA ($n = 3$; $p = .046$) and AG individuals ($n = 13$; $p = .014$) during Keppra treatment.
Conclusions: Our data suggest that Keppra is not an appropriate treatment strategy for non-treatment seeking heavy drinkers with the DRD2 GG allele, as they drink even more, possibly in an effort to compensate for attenuated alcohol induced intoxication. However, Keppra may be of benefit to heavy drinkers with two copies of the DRD2 AA allele.
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CHANGES IN INJECTION- AND SEX-RELATED HIV RISK BEHAVIORS FOR IN- AND OUT-OF-TREATMENT OPIATE-DEPENDENT INDIVIDUALS.

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Aims: To compare changes in self-reported injection- and sex-related HIV risk behaviors for opiate-dependent individuals either in- or out-of-treatment over a 12 month period of time.
Methods: The Texas Christian University AIDS Risk Assessment (ARA) was administered to 314 newly-admitted methadone treatment program patients and 139 out-of-treatment opiate-dependent individuals recruited from the streets who were not seeking treatment at baseline and at 6- and 12-months post-study entry. Generalized estimating equations were conducted for all items on the ARA to examine group differences in reported risk behaviors over time.
Results: Significant Group X Time interactions were found for 7 of the injection-risk items and 2 of the sex-risk items. The in-treatment participants reported injecting drugs (in the past 6 months and past 30 days) less often and injecting with other people in the last 30 days less often (all $ps < .01$) than did the out-of-treatment participants. In the past 30 days the in-treatment participants also reported using dirty needles and sharing cookers, cotton or rinse water less often, and sharing works with fewer people than did the out-of-treatment participants (all $ps < .05$). At the 6 months assessment, both groups reported decreasing their number of sex partners within the past 6 months as well as the number of times they had had sex in the past 30 days (both $ps < .01$). Reported condom use with someone other than a spouse/primary partner did not change over time.
Conclusions: Methadone treatment participation is associated with decreases in numerous HIV risk behaviors over the course of 12 months, most notably those behaviors associated with drug use. Many sex-related risk factors did not change over time for those in treatment, including condom use with main or casual partners. Methadone programs need to emphasize to their patients the need to change their HIV sexual risk behaviors.
Financial Support: NIDA RO1 DA 0158420

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FMRI OF THE SELECTIVE ADENOSINE A2A ANTAGONIST SYN115 IN COCAINE-DEPENDENT SUBJECTS.

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Aims: To examine effects of a single 100 mg dose of the selective adenosine A2A antagonist (SYN115, Synosia Therapeutics, 4-Hydroxy-4-methyl-piperidine-1-carboxylic acid-(4-methoxy-7-morpholin-4-yl-benzothiazol-2-yl)-amide) in cocaine dependent individuals using fMRI.
Methods: Scans were acquired from 8 cocaine dependent subjects performing the IMT/DMT working memory task with 3, 5 and 7 digits per stimulus. All subjects were administered placebo and SYN115 prior to each of 2 fMRI sessions. Activation was defined as BOLD signal during delayed minus immediate memory and analyzed using SPM8 Random Effects.
Results: SYN115 was well tolerated with no serious side effects or significant changes in vital signs. During 7-digit load, SYN115 resulted in significantly increased activation compared to placebo (FDR-corrected cluster $p<0.002$) in right superior, middle, and inferior frontal gyrii, and bilateral anterior cingulate and caudate. These regions had significantly less pre-treatment activation in unmedicated cocaine-dependent subjects compared to controls in a previous study (Moeller et al, In Press). SYN115 also resulted in significantly increased activation in right insula, superior orbital gyrus, rectal cortex, and putamen, bilateral mid-orbital gyrus, and left olfactory cortex.
Conclusions: These preliminary findings support SYN115 at well-tolerated doses produces changes in brain activation in cocaine dependent subjects. Many of the regions that showed increased activation after SYN115 showed lower activation in unmedicated cocaine dependent subjects compared to controls in a separate study, possibly related to SYN115's augmentation of dopamine function.
Financial Support: This study was supported by NIDA grant P50DA009262 and K02DA00403 (Moeller). SYN115 was provided by Synosia Therapeutics.

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PSYCHOLOGICAL BENEFITS OF EXERCISE IN THE TREATMENT OF CHEMICAL DEPENDENCY.

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Aims: This study examined whether a walking exercise program can enhance the psychological benefits in chemically dependent clients and whether the effects of a walking intervention program can be utilized in the treatment of drug dependence.
Methods: Forty-eight males and females from an inner city Mid-western substance abuse treatment program were randomly assigned to either engage in the weekly walking program or to engage in the regular low level recreation activities group session. Participants completed the Coping Inventory for Stressful Situations (CISS), Rosenberg's Self-Esteem Inventory (SEI) and Profile of Mood States (POMS) Questionnaires prior to and following a 6-week walking exercise program.This program consisted of an experimental and control group.
Results: Analyses (ANCOVA) revealed significant differences between groups on task-oriented coping ($F(1, 43) = 7.60$, $p < .01$) and total mood states ($F(1, 43) = 11.19$, $p < .01$) after a 6-week walking exercise program. Adjusted mean scores for emotion-oriented coping and self-esteem showed a positive trend toward a significant difference ($p < .05$) in the experimental group relative to the control group. Results from the follow-up questionnaire at 4 weeks indicated that exercise may have lasting psychological effects.
Conclusions: In addition, walking exercise appears to have a positive effect on minimizing dropout rates (8.4 % versus 33 %). These results suggested that an exercise program may be beneficial during treatment for substance dependence. Future research should focus on extending the frequency and duration of the exercise program in order to determine sustainability of these benefits.
Financial Support: Once my abstract is approved, I will be able to apply for a $400.00 travel allowance from our Student Senate (KU). I will fund the rest of the conference expenses.

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THE EFFICACY OF MOTIVATIONAL ENHANCEMENT THERAPY FOR AFRICAN-AMERICAN SUBSTANCE USERS.

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Aims: The low retention rates among African Americans in substance abuse treatment combined with the limited number of treatments with demonstrated efficacy for African American substance users are both public health concerns. The two aims of this study were (1) to examine the extent to which Motivational Enhancement Therapy (MET) improved retention and substance abuse outcomes in an African American sample and (2) to determine whether the relationship between treatment type (MET vs. control) varied for specific subgroups.
Methods: The study was a secondary analysis of a randomized clinical trial of MET conducted across 5 treatment sites by the NIDA Clinical Trials Network (CTN). The sample for the study included 194 African American adults randomly assigned to receive either 3 sessions of MET prior to standard treatment or 3 additional sessions of standard treatment. Retention was defined as the number of days between the day of enrollment and the last day that the participant received services at the clinic. Substance use was assessed by both urine screens and self-report. OnTrak TesTcups (urine screens) were collected weekly during the 4 weeks of the active phase of the study. The Substance Use Calendar was used to collect self- report information about drug use weekly throughout the entire 16 week study.
Results: African Americans in MET and standard treatment did not significantly differ on either substance use or retention outcomes. However, time-to-event analyses revealed that African American females in MET had significantly better retention at 12 weeks than females in standard treatment (Log-rank test $p = .05$). However, no treatment differences were evident for males (Log-rank test $p = .86$). In addition, a trend was evident suggesting that African American MET participants who were alcohol users had better retention than alcohol users in standard treatment (Log-rank test $p = .08$) at 13 weeks.
Conclusions: These findings suggest that the efficacy of MET for African Americans may vary by subgroup.
Financial Support: NIDA CTN

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A STUDY OF INITIAL RIBOFLAVIN LEVELS IN 2,738 TREATMENT-SEEKING SUBSTANCE USERS.

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Aims: A common approach to determining medication adherence is to add riboflavin to medication preparations. Riboflavin levels are then semi-quantitatively assessed and compared to a threshold or cutoff value. Relatively little is known about urine riboflavin levels in the general population of substance users. The goal of this presentation is to better characterize initial riboflavin levels in substance users seeking participation in pharmacotherapy trials.
Methods: We used a data set (N = 2,738) collected from October 1994 to October 2004. Participants provided a urine sample that was submitted to spectrophotoflurometry to obtain a semi-quantitative level of riboflavin using a Model 4-8202 Aminco-Bowman spectrophotofluorometer (American Instrument Co., Silver Springs, Maryland). Riboflavin levels range from 0 to 99 fluorescence units (FU). Urine creatinine (mg/mL) levels and the presence of 90 prescription and illicit drugs were also determined.
Results: The sample characteristics were as follows: Age (M = 38.0 years, SD = 7.8), 72.2% male, Race (40.3%, White; 51.3%, Black; 8.4%, Hispanic), and weight (male, M = 184.8 lbs., SD = 39.7; female, M = 158.6, SD = 41.2). Riboflavin levels (fluorescence units) were generally low (M = 15.1, SD = 14.5, Median = 11.0). In a multivariate regression, riboflavin levels were higher in Whites than Blacks ($p<.05$), and lower in those not testing positive for cocaine use ($p<.0001$).
Conclusions: n a population of treatment-seeking substance users, relatively low levels of riboflavin were detected. Levels used to classify medication adherence in the published literature (e.g., >20-35 FU) were rarely observed.
Financial Support: This research was supported by the NIDA grants P50-DA-009262. Dr. Mooney is supported by a NIDA Career Development award K01-DA-019446.

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IMPROVEMENT IN PSYCHOPATHOLOGY AMONG OPIOID-DEPENDENT YOUTH DURING BEHAVIORAL-PHARMACOLOGICAL TREATMENT.

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Aims: To examine changes in behavioral and emotional problems among opioid-dependent youth during combined behavioral and pharmacological treatment.
Methods: We examined scales of behavioral and emotional problems using the Youth Self Report (YSR) at the time of substance abuse treatment intake and changes in scale scores post treatment. Participants in the first study were 36 adolescents (ages 13-18) who met DSM-IV criteria for opioid dependence. Participants received a 28-day outpatient, medication-assisted withdrawal with either buprenorphine or clonidine as part of a double-blind, double-dummy comparison of the medications. All participants received a common behavioral intervention, composed of three individual counseling sessions per week, and incentives contingent on opioid-negative urine samples. In a second study, we are examining these same changes in behavioral and emotional problems using the YSR in another sample of youth (n=56) who met criteria for opioid dependence (ages 13-24), randomly assigned to either a 28-day or 63-day buprenorphine-assisted withdrawal. We will present results from both trials.
Results: Significant reductions were observed post treatment on YSR Syndrome grouping scales: Internalizing Problems, Externalizing Problems, and Total Problems. All three of the Syndrome grouping scale scores changed from borderline clinical ranges to non-clinical ranges. On the Competence/Adaptive scales, no significant differences were observed; however, scores shifted from the borderline clinical range to the non-clinical range for the Activities Scale, and from the clinical range to the non-clinical range for the Total Competence scales. Among those retained in treatment, no significant differences were observed across medication condition on any of the scales.
Conclusions: Youth demonstrated substantive improvements in a number of clinically meaningful behavioral and emotional problems, irrespective of the pharmacotherapy provided to them.
Financial Support: R03 DA 14570
1 R01 DA018297

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ACCEPTABILITY OF A GUIDED COMPUTERIZED HEALTH SCREENING IN PRIMARY CARE.

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Aims: Screening, brief intervention, and referral to treatment (SBIRT) is an evidence-based approach to the delivery of early interventions for persons at risk for substance use disorders. Efforts to incorporate SBIRT into primary care settings have proven difficult. A proactive, computer-guided health screening and assessment program was implemented for the detection of smoking, alcohol and drug use behaviors in primary care patients. The pilot data evaluating the acceptability of the computer-guided program is presented here.
Methods: A computer-delivered SBIRT program was developed and piloted in 123 patients, the majority attending an urban, academic medical center primary care clinic. A minority of patients were females from an inpatient substance abuse treatment center. Participant acceptability data were collected via the computerized program itself and through focus groups.
Results: Participants were African American (53%) and Caucasian (37%) men (35%) and women (65%) with an average age of 45 years. The computerized screening program was satisfactory to a majority of participants with 78% identifying it as "very acceptable" with only 8% classifying it below "acceptable". Working with the program was identified as "very easy" by 85% of participants. Of the 49 participants using the narrator to guide them through the assessment part of the program, 78% felt that it was "very acceptable". Focus groups were conducted with participants who used the program, and similar results were found. The program was acceptable across all education levels. Acceptability by age group showed that 84% of those over 45 years found working with the computer "very acceptable" and 71% of people under the age of 45 found working with the program "very acceptable".
Conclusions: For the majority of patients, a guided computerized health screening and assessment program in a primary care setting is an acceptable method to identify and evaluate substance use. Future studies should continue to look at feasibility of computerized screenings and acceptability to patients.
Financial Support: NIDA award R01DA026091

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INTERNET USE AMONG OPIOID-DEPENDENT INDIVIDUALS SEEKING PRIMARY-CARE-BASED BUPRENORPHINE/NALOXONE TREATMENT.

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Aims: U.S. census estimates of internet use is 70% among adults 18-64 (CPS, 2007). However, little is known about prevalence of internet use among opioid-dependent individuals seeking buprenorphine/naloxone treatment. We expected prevalence to be lower than national estimates. We sought to determine the demographic and clinical characteristics associated with internet use, and whether internet use was associated with treatment initiation or completion.
Methods: As part of screening for several trials of buprenorphine/naloxone treatment, opioid-dependent individuals answered questions about technology, including internet use, and demographic and substance use items. 236 consecutive screenings from 12-2007 to 11-2009 were collected. Correlates of internet use were evaluated by chi-square and t-tests. Logistic regression was used to evaluate treatment initiation and completion controlling for demographics.
Results: 64% of treatment seekers reported using the internet in the past 30 days, and internet users reported a mean of 16.2 days (10.8) of the past 30. Internet use did not differ by gender (p=.88) or primary opioid use (heroin or prescription opioids, p=.11). However, internet use was more common among white (p=.03), younger (p<.001), and more educated (p=.002) treatment seekers. Although internet use was not associated with treatment initiation (p=.37), of those who entered treatment, it was associated with treatment completion (controlling for age, race, and education, p=.02).
Conclusions: Though lower than national estimates, prevalence of internet use among treatment seekers was high. Correlates of internet use showed a similar pattern to national estimates where internet use is more common among white, younger, and more educated populations. Findings suggest that internet-based interventions may be well-received and warrant exploration among individuals seeking buprenorphine treatment.
Financial Support: NIDA K01DA022398, RO1DA019511, R01DA020576, & The Robert Wood Johnson Foundation

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MOTIVES ASSOCIATED WITH RESILIENCE OF TOBACCO USE AMONG SCHOOL STUDENTS IN SPAIN. DIFFERENCES BY GENDER.

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Aims: To determine the most common motives and those significantly associated with the no consumption of tobacco in school students in Spain, analyzing differences by gender.
Methods: Sample: A total of 706 students from 21 schools in Valencia city that had never smoke tobacco, 49.3% (n=348) males. Instrument: "Pre-Chat Survey on Drug Addiction; during 2007-2008", elaborated by the professionals of the Plan Municipal de Drogodependencias (PMD) of the Ayuntamiento de Valencia. Data analysis: Chi square tests were used for comparison between gender groups.
Results: Reasons for not consuming mentioned most often are: not consumed because it impairs physical and mental health (78.8%), feeling well and do not need to consume (69.7%), because he/she knows how to have a good time without consuming drugs (68.7%). The reasons responded significantly in more proportion by male are: "for personal convictions" (34.5% male vs. 19.3% female; X2=20.67, p<.001), "because they are expensive" (13.3% male vs. 3.9% female; X2=19.7, p<.001). The motive "because I know how to have a good time without consuming drugs" was pointed out significantly in more proportion by females (74.6% female vs. 62.5% male; X2=11.75, p<.005).
Conclusions: Reasons associated with avoiding damage at personal level -physical and mental-, perception of well being, and knowledge of recreation activities that do not include consumption, are common reasons for not consuming tobacco in young population. In prevention programs for tobacco use is important the promotion of entertainment not associated with the consumption of substances, besides teaching the adverse effects related with the consumption.
Financial Support: Funding for this study was provided by the collaboration agreement between the Plan Municipal de Drogodependencias (PMD), Ayuntamiento de Valencia and Univetsitat de València.

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DISRUPTION OF PREPULSE INHIBITION BY APOMORPHINE ACROSS MODALITIES.

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Aims: Sensorimotor gating, the process by which organisms filter extraneous sensory stimuli, is commonly assessed with manipulations of prepulse inhibition (PPI). Alterations in gating are observed in individuals with schizophrenia, HIV-1 dementia and other neuropsychiatric disorders. Dopaminergic pathways play a putative role in sensorimotor gating. It is well-established that apomorphine, a dopamine agonist, disrupts PPI of the auditory startle response at low prepulse intensities (75 dB) at an interstimulus interval (ISI, time between the prepulse and the startle stimulus) of 100msec. In the present study, it was hypothesized that disruption of PPI by apomorphine would also occur with a visual prepulse stimulus, and further, that a range of ISIs would provide a more precise index of any such disruption. It was also hypothesized that PPI of the auditory startle response would be disrupted by apomorphine with a prepulse of a higher intensity (85 dB), when assessed with a range of ISIs.
Methods: Accordingly, sensorimotor gating was measured with visual and auditory prepulse stimuli in the PPI paradigm (ISIs of 0, 8, 40, 80, 120, 4000 msec, 6 trial blocks, Latin-square design). A within-subjects design was used for each experiment, with 12 adult male Sprague-Dawley rats that were tested 5 minutes after a subcutaneous injection of saline or one of three apomorphine (APO) doses (0.1, 0.25, and 0.5 mg/kg) in an ascending series with 48 hr between assessments.
Results: Auditory PPI with a 75dB prepulse was disrupted by APO at the 100 msec ISI, but was not disrupted by APO with an 85dB prepulse, as found previously. The use of a range of ISIs revealed disruption of PPI by APO with the 85dB prepulse; in particular, there was a flattening of the ISI function with an increase in APO dose. The ISI function for visual PPI was also flattened with an increase in APO dose.
Conclusions: These results indicate the generality of PPI disruption by apomorphine across prepulse stimulus modalities and the importance of manipulating the temporal dimension of PPI instead of using a single ISI.
Financial Support: DA13137, HD043680

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EFFECTS OF MORPHINE ON THERMAL SENSITIVITY IN AGED RATS.

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Aims: As the population ages, the prevalence of non-malignant pain increases along with the clinical use of opioids as an intervention. However, little is known regarding older individuals sensitivity to opioids and the most effective treatment strategy. Here we describe the development of a preference procedure to assess changes to thermal sensitivity in adult vs aged rats in response to morphine administration as a preclinical screening tool.
Methods: Adult (12-16 months; n=10) and aged (27-31 months; n=7) male, F344xBN rats were tested in a thermal preference procedure. Rats were placed in an apparatus containing two compartments equipped with floors that were individually temperature-controlled so that sensitivity to "hot" and "cold" thermal stimulation could be assessed during daily 10-minute sessions. Dose-effect curves for morphine (0.56 to 5.6 mg/kg, i.p.) were determined for 3 temperature comparisons [i.e.hot vs neutral (45 vs 30°C), cold vs neutral (15 vs 30°C), and hot vs cold (45 vs 15°C)] during test sessions.
Results: Aged rats were more sensitive to cold stimulation compared with adults at baseline. With morphine administration, the most consistently observed effect in adult rats was antinociception during the hot thermal stimulation compared to the neutral stimulus; an effect which was present but somewhat attenuated in aged rats. In addition, morphine appeared to increase sensitivity to cold stimulation in aged rats only. These differential effects on thermal sensitivity were not simply an artifact of drug-induced changes in locomotor activity, as morphine consistently resulted in greater increased activity in adult relative to aged rats across all testing conditions.
Conclusions: Together, these data demonstrate age-related differences in baseline thermal sensitivity and responsiveness to opioids. Based on behavioral and physiological requirements of this procedure, it is suggested that thermal sensitivity may provide a particularly relevant animal model for the assessment of pain and antinociception.
Financial Support: These studies were supported by NIH grant DA023022.

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THE GLOBAL INFRASTRUCTURE FOR ADDICTION SCIENCE: A PUBLIC HEALTH PERSPECTIVE.

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Aims: Aims: This poster describes historical trends in the global infrastructure supporting addiction science, and evaluates the growth and nature of that infrastructure from a public health perspective, i.e., in terms of its ability to address substance-related problems in vulnerable populations throughout the world. Five areas of infrastructure are considered: 1) research centers; 2) professional societies; 3) addiction-specialty journals; 4) research funding organizations; and 5) drug, tobacco and alcohol policy institutes.
Methods: Methods: The method consisted of an extensive review of internet sources, published articles, and bibliometric analyses in order to obtain quantitative and qualitative information about the cumulative growth of these various infrastructure elements, as well as their contributions to the evolution of addiction science. The authors created growth curves reflecting changes in the numbers of research centers, institutes/funding agencies, addiction journals, and societies.
Results: Results: The findings indicate that there has been tremendous growth in all areas of addiction science in the past 50 years, resembling a log-normal growth curve that has not yet reached asymptote. The findings also show that the growth of addiction science, while being most developed in countries with severe drug and alcohol problems, has nevertheless been disproportionately concentrated in the English-speaking and Nordic countries, especially the USA.
Conclusions: Conclusions: Both the structure and function of the global addiction infrastructure seems to support basic and clinical science, with relatively little attention to the policy and public health implications of the research.
Financial Support: N/A

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GALANTAMINE AMELIORATES THE IMPAIRMENT OF RECOGNITION MEMORY IN MICE TREATED WITH METHAMPHETAMINE REPEATEDLY.

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Aims: Galantamine, a drug for Alzheimer's disease, is a cholinergic agent. Here, we investigated whether galantamine exerts cognitive-improving effects through the allosteric modulation of nicotinic acetylcholine receptors (nAChRs) in an animal model of methamphetamine (METH) psychosis.
Methods: The mice were treated with METH for 7 days and subjected the novel object recognition test. Extracellular dopamine (DA) level and extracellular signal-regulated kinase 1/2 (ERK1/2) phosphorylation were determined by in vivo microdialysis and western blotting, respectively.
Results: Galantamine significantly ameliorated the impairment of recognition memory and increased the extracellular DA release in the prefrontal cortex (PFC) in METH-treated mice. The nAChR antagonist, mecamylamine, and DA-D1 receptor antagonist, SCH 23390, blocked the ameliorating effect of galantamine on METH-induced memory impairment, whereas the muscarinic AChR antagonist, scopolamine, had no effect. The effects of galantamine on the extracellular DA release were also antagonized by mecamylamine. Galantamine attenuated the defect of the novelty-induced activation of ERK1/2. The ameliorating effect of galantamine on recognition memory in METH-treated mice was negated by microinjection of ERK inhibitor, PD98059, into the PFC.
Conclusions: These results suggest that the ameliorating effect of galantamine on METH-induced memory impairment is associated with indirect activation of DA-D1 receptor-ERK1/2 following augmentation with dopaminergic neurotransmission in the PFC through the allosteric activation of nAChRs.
Financial Support: Regulatory Science of MHLW, Academic Frontier Project, KAKEN-HI(20390073,21390045,19659017), SRF

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SMOKER'S DELAY DISCOUNTING INDIFFERENCE POINTS ARE ASSOCIATED WITH CHANGES IN OPPORTUNITY-COST-INFORMED PRICE.

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Aims: Commonly used Delay discounting assessment procedures (DDAP) present numerous series of binary choices for several delay values and empirically determine a single indifference point, or a point of preference reversal, for each delay value. A new unit price equation, opportunity-cost-informed price (OCIP), is especially relevant to binary choice situations because it takes into account the cost of an unchosen alternative, and it can provide a point of preference reversal. The reward amounts and delay values used in DDAP are respectively interpreted as economic benefits and costs, which are the variables in the OCIP equation. We assess the relationship between the indifference points provided by DDAP and OCIP in discounting data collected from a sample of smokers. The assumption that an immediate reward has no cost results in undefined values in OCIP, and is therefore eschewed here. Alternative values for this cost parameter are explored.
Methods: 26 participants completed DDAP tasks for hypothetical future gains of $50 and $1000 and while in 2 states (nicotine deprived and satiated). Each DDAP administration produced 7 empirical indifference points. Theoretical indifference points were also determined by the OCIP equation, with such determinations being made for 6 different immediate reward cost values. Rank correlations of the theoretical and empirical indifference points were computed.
Results: Within each immediate reward cost, there was no evidence that the correlations depended on the amount, state, or their interaction (all p>. 07). Averaging over these combinations, the correlations differed among the 6 immediate reward costs (p<.001); however, the correlations ranged very little: 0.626 to 0.656.
Conclusions: These data support the efficacy of interpreting DDAP results through the OCIP concept. The OCIP concept extends the ability of behavioral economics to integrate under a coherent conceptual framework the data regarding drug-effects collected via diverse approaches and study methodologies.
Financial Support: This work was funded by NIDA grant 5R01 DA022386

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PREDICTING AND EXPLAINING MULTIPLE AND SIMULTANEOUS INTIMATE RELATIONSHIPS AMONG AFRICAN AMERICANS IN DISTRESSED HOUSEHOLDS IN NEW YORK CITY.

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Aims: This mixed method research study seeks to explore the factors contributing to the engagement in multiple and simultaneous relationships over the course of a lifetime among low income, substance abusing African Americans in New York City.
Methods: A total of 103 individuals were interviewed to develop a retrospective relationship timeline which displayed information about all significant relationships that participants engaged in during their lifetime as part of a longitudinal qualitative study. SPSS software was used to conduct a GEE analysis of 508 relationships described by participants. It was hypothesized that age would be a significant contributor in an individual's engagement in simultaneous relationships, when gender, duration/ nature of the relationship (sexual or not), and parental engagement in multiple and simultaneous relationships were controlled for. A case study was used to illustrate quantitative findings and to examine the factors impacting participants' decisions to engage in multiple relationships as they aged.
Results: All participants were African American and reported abusing illegal drugs at some time in their lives. Only two predictors had a significant impact on engagement in multiple and simultaneous relationships: whether the relationships were sexual and participant's age. Specifically, when participants engaged in sexual relationships they were significantly more likely to initiate other simultaneous relationships (OR= 1.475, p=.000). Participants were significantly more likely to engage in multiple and simultaneous relationships as they aged (OR= 1.001, p=.001). Results from the qualitative analysis and implications for HIV prevention and substance abuse will be discussed in the presentation.
Conclusions: Findings suggest factors contributing to engagement in risky health behaviors among low income African Americans.
Financial Support: Supposted by the National Institute on Drug Abuse

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IS DOPAMINERGIC NEURON PROJECTING FROM THE VENTRAL TEGMENTAL AREA TO THE CINGULATE CORTEX CRITICAL FOR THE MORPHINE-INDUCED REWARDING EFFECT?

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Aims: The cingulate cortex (CG) that is a major subregion of the prefrontal cortex is considered to play an important role in the expression of the emotionality and reward. Here we investigated the role of the neurons projecting from the ventral tegmental area (VTA) to the CG in opioid reward.
Methods: Conditioned place preference test, rat *in vivo* microdialysis study to quantify released dopamine, RT-PCR and immunohistochemical approach were performed in the present study.
Results: Microinjection of the retrograde tracer fluoro-gold (FG) into the CG revealed a number of retrogradely-labeled cells in the VTA. Some of FG-positive reactions were noted in tyrosine hydroxylase (TH)-positive VTA neurons. The levels of dopamine and its major metabolites in the CG were markedly increased by the microinjection of the selective mu-opioid receptor (MOR) agonist, [D-Ala2,N-MePhe4,Gly-ol5]enkephalin (DAMGO), into the VTA. The MOR-like immunoreactivity was partially seen in TH-positive VTA neurons projecting to the CG. Under these conditions, the place preference induced by intra-VTA injection of DAMGO was significantly suppressed by a depletion of dopamine in the CG. Next, we investigated whether epigenetic modification in the CG occurs in rats conditioned by morphine. We found that mRNA levels of a H3K9 demethylase, JMJD2b decreased 24 hr and 2 weeks after the last morphine treatment. Moreover, the mRNA levels of a DNA methyltranferase, DNMT3a decreased 2 weeks after the last morphine treatment.
Conclusions: These findings provide novel evidence that VTA-CG transmission can be facilitated by activation of MOR located on both dopaminergic and non-dopaminergic VTA neurons, and this pathway accompanied by epigenetic modification may play a crucial role in the consolidation, as well as the induction by opioid reward.
Financial Support: Grants from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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GRAY MATTER DECLINE WITH DEPRESSION SCORES IN METHAMPHETAMINE USERS AND CONTROL SUBJECTS.

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Aims: Depression is associated with smaller gray matter volumes. Methamphetamine (METH) is also associated with smaller gray matter volumes as well as depression. However, whether gray matter of METH-users with higher depression scores is synergistically more affected is unknown and was evaluated in this study.
Methods: 61 subjects (33 METH users and 28 non-METH using controls) were evaluated with high-resolution structural MRI. METH-users were included if they were abstinent (up to 5 years) or were current METH users. All subjects were required to be healthy, HIV negative, without a history of other drug-dependence, and without significant illness. MRI was performed on a 3T Siemens scanner. We acquired a 3D high-resolution axial T1W scans (MP-RAGE). FSL software was used.
Results: The two groups were well matched. However, METH users had lower education (p <0.0001), lower estimated verbal IQ (p<0.0001) and higher Center for Epidemiologic Study- Depression (CES-D) scores (p= 0.002). Using the cranium volume-adjusted MRI volumes, the CES-D scores were inversely associated with gray matter volumes in the parietal (p=0.005, R=-0.37), limbic (p=0.0025, R=-0.39), frontal (p=0.003, R=-0.38), occipital (p=0.002, R=-0.41), and temporal lobes (p=0.02, R=-0.31). No interactions were observed between drug status and CES-D for the volumes of the main lobes.
Conclusions: Although CES-D was higher in METH-users, CES-D was inversely associated with gray matter volumes of the main lobes of both METH-users and control subjects, regardless of METH usage. This consistent reduction in gray matter volumes across multiple brain regions suggests that depressive symptoms causes gray matter volume shrinkage due to its known neurotoxic effects, regardless of METH status. Therefore, the combination of METH use and higher depression scores had an additive negative effect on gray matter volumes.
Financial Support: NIH (1R01-DA12734; HHSN271200688514C; K24-DA16170; K02-DA16991; 5P20-RR11091; G12-RR003061; 1U54NS56883) and the ONDCP.

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CONCORDANCE BETWEEN SELF-REPORT AND URINE DRUG SCREEN DATA IN ADOLESCENT OPIOID-DEPENDENT CLINICAL TRIAL PARTICIPANTS.

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Aims: To determine the relationships between urine drug screen and self-reported substance use outcomes among adolescents and young adults with opioid dependence participating in a clinical trial of buprenorphine.
Methods: 154 subjects seeking treatment for opioid dependence were randomized to 2 week detoxification with buprenorphine/naloxone (DETOX) or 12 weeks buprenorphine/naloxone (BUP), each with weekly individual and group drug counseling. Urine drug screens and self reported frequency of drug use were obtained weekly, and more extensive assessments were completed at 4, 8, and 12 weeks. For analyses of concordance, self report data were dichotomized (positive vs. negative), and the drug screen was treated as the gold standard. For each major class of drug of abuse, we computed the kappa statistic and the sensitivity, specificity, positive predictive value, and negative predictive value of self report in relation to the drug screen data.
Results: Strong relationships were seen between self report and urine drug screens for most substances. For opioids, kappa = .731. For marijuana, kappa = .791. For benzodiazepines, kappa = .641. For amphetamines/methamphetamine, kappa = .706. The association was weaker for cocaine, kappa = .239. This appeared to be due to a high rate of negative urines among those self-reporting cocaine use (positive predictive value = .29). With respect to opioid use, participants in the BUP group had concordance rates similar to participants in the DETOX group (kappa = .721 versus kappa = .701, respectively), but self report was less sensitive and more specific in the BUP group.
Conclusions: In general these findings support the validity of self report under the conditions of this study. The high rate of "false positive" self-reports of cocaine use may be related to the frequently sporadic pattern of cocaine use and the greater time window for self-report (1 week) than the drug screen (2-3 days) in this study, which could make the self-report more sensitive to infrequent cocaine use.
Financial Support: NIDA Clinical Trials Network.

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NONMEDICAL USE OF PRESCRIPTION STIMULANTS AMONG ADOLESCENTS: RURAL VS. URBAN.

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Aims: Nonmedical use of prescription drugs among adolescents grew rapidly from 1992 (Ford, 2009) but declined from 2002(SAMHSA, 2009). Rural youth, whose protective factors include greater family cohesion (Martino, 2008), may also have higher risk factors including greater poverty compared to urban youth (Bouffard, 2006).Data were analyzed from NMAPSS (National Monitoring of Adolescent Prescription Stimulants Study) to determine whether the prevalence of non-medical stimulant use would differ by urban/rural status.
Methods: N-MAPSS (Cottler, LB PI; Washington University's Epidemiology & Prevention Research Group) is sampling adolescents 10-18 year old from ten US cities and their contiguous suburban and rural areas. In wave 1 in 2008, adolescents in multiple venues filled out a brief survey. We dichotomized the youth into rural (n=390; 24%) vs. urban (n=1252, 76%) youth, and restricted the sample to those who used any of five common prescription stimulants (n=114). We used number of meals per week with their family and living with both parents as measures of family cohesion, and amount of money they carry as a measure of income.
Results: Bivariate analysis showed that among users of prescription stimulants, 52% of the rural youth versus 43% of the urban youth endorsed nonmedical use. Although suggestive, this difference was not statistically significant. Rural youth were more likely to live with two parents than urban youth (65% vs. 53%, p<.0001). There was no difference between rural and urban youth in the number of meals per week with their family or in their income.
Conclusions: Our findings indicate that rural adolescents are no more or less likely to use prescription stimulants nonmedically than urban youth. Some uniqueness was found in risk and protective factors. Research needs to consider the unique risk and protective factors of rural youth in prevention efforts.
Financial Support: N-MAPSS is implemented by Washington University in St. Louis under contract from Pinney Associates, Inc., with funding provided by Shire Pharmaceuticals.

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REINFORCING EFFECTS OF NICOTINE AND COCAINE COMBINATIONS IN RHESUS MONKEYS.

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Aims: The concurrent use of cocaine and nicotine is well documented in clinical literature. However, little is known about the behavioral pharmacology of cocaine and nicotine interactions, and there have been few attempts to characterize this form of polydrug abuse in animal models. Some studies in rodents suggest that nicotine may increase the stimulus effects of cocaine. The purpose of the present study was to examine the reinforcing effects of nicotine and cocaine combinations in rhesus monkeys. We hypothesized that nicotine-cocaine combinations would maintain higher levels of self-administration than either drug alone.
Methods: Four adult male rhesus monkeys (Macaca mulatta) were trained to self-administer cocaine and banana-flavored food pellets during alternating periods under a second-order schedule of reinforcement seven days per week. After characterizing the cocaine dose-response relationship in each monkey, several doses of nicotine were combined with cocaine doses on the ascending limb of the cocaine dose-effect curve.
Results: Addition of nicotine to low doses of cocaine led to an increase in the numbers of self-administered injections. The nicotine-cocaine dose combinations maintained greater responding than either dose of nicotine or cocaine alone.
Conclusions: Combinations of cocaine and nicotine serve as reinforcing stimuli. These data suggest that nicotine may enhance the reinforcing effects of low doses of cocaine. These findings may be significant for understanding the pharmacology of comorbid nicotine and stimulant dependence, as well as informing development of new treatment strategies.
Financial Support: This research was supported by R01DA026892-01 (NKM) from the National Institute on Drug Abuse, NIH.

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PERSONALITY DISTURBANCES AND HIV RISK BEHAVIORS IN HIV+ INDIVIDUALS.

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Aims: Some HIV+ individuals engage in high risk behaviors. To tailor risk reduction interventions, factors associated with ongoing risk behavior must be identified. Our aim was to study the relationship between Axis II pathology and risk behavior.
Methods: We assessed Axis II pathology in 179 HIV clinic patients using the Millon Clinical Multiaxial Inventory (MCMI-III). Patients were categorized as subclinical (BR<75) or as having traits/disorders (BR>75). Risk behaviors assessed included number of sex partners (0, 1, or multiple), any sex without a condom, lifetime and recent IDU and sharing injection equipment.
Results: Participants were middle aged (35.9), African-American (63%) males (79%). Antisocial patients were more likely to have multiple sex partners ($\chi2$=9.75, p=0.008). Borderline patients were less likely to be celibate ($\chi2$=11.57, p=0.003) and to regularly use condoms ($\chi2$=4.10, p=0.043). Self-defeating patients also evidenced irregular condom use ($\chi2$=4.14, p=0.042). Paranoid patients were more likely to be monogamous ($\chi2$=7.93, p=0.019). Patients with antisocial traits/disorders demonstrated increased drug risk, including both lifetime ($\chi2$=8.04, p=0.005) and recent IDU ($\chi2$=15.80, p<0.001) and the sharing of injection equipment ($\chi2$=11.49, p=0.001).
Conclusions: Transmission risk behavior was associated with clinically elevated scores on personality disorder scales of the MCMI-III. Antisocial patients had more sexual partners and engaged in more drug risk behavior than other patients. A higher percentage of borderline patients was sexually active, but used condoms only irregularly. Self-defeating patients also were having unprotected sex, although the reasons for this likely are different. Patients with risk-taking tendencies (ASP, BPD) or who have a reduced capacity to decline unprotected sex or otherwise engage in good self-care (BPD, self-defeating) may require modifications to standard risk reduction interventions to address feelings of power and invincibility or, conversely, powerlessness.
Financial Support: Supported by Substance Abuse Mental Health Services Administration (SAMHSA) Grant #UD5SM51689

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INHIBITING GLYCINE TRANSPORTER-1: EFFECTS ON EXTINCTION AND REACQUISITION OF COCAINE SELF-ADMINISTRATION.

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Aims: D-cycloserine, a partial agonist at the glycine site of NMDA receptors, augments extinction learning that delays reacquisition of cocaine self-administration (SA) in rats and monkeys (Nic Dhonnchadha et al 2009). This study investigated if a similar combination of extinction training with the selective glycine transporter-1 inhibitor Ro4543338 results in comparable effects in rats.
Methods: Rats were trained to self-administer cocaine (0.3 mg/kg) paired with a 2-sec light cue under a second-order schedule. Ro4543338 (30 and 45 mg/kg) or vehicle was administered 30 min prior to three 1-hr extinction sessions spaced 1 wk apart (n=5-7/treatment). Responses were extinguished by substituting saline for cocaine while maintaining response-contingent cue presentations. Cocaine SA reacquisition began 7 days after the last extinction session under conditions identical to SA training.
Results: Following vehicle, extinction learning was evident by extinction session 3; responding declined to ~ 45% of the cocaine SA baseline rate. Ro4543338 enhanced extinction learning; responding declined well-below 45% of the baseline rate during the first and all subsequent extinction sessions. During extinction sessions 1 and 2, responses were lower after 30 (p<0.05) and 45 (p<0.01) mg/kg Ro4543338 relative to vehicle. The accelerated extinction in Ro4543338-treated rats was specific as neither dose of Ro4543338 altered responding maintained by active cocaine SA. Over reacquisition sessions 1-5, vehicle-treated rats emitted responses above baseline rates (128%) while Ro4543338-treated rats emitted responses below baseline rates (82% after 30 mg/kg and 67% after 45 mg/kg), indicating that reacquisition of cocaine SA was delayed as a result of Ro4543338 combined with cocaine cue extinction training.
Conclusions: GlyT-1 inhibitors may be useful adjuncts to extinction therapy targeting drug-related cues in addicts.
Financial Support: DA024315 and Roche

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DIFFERENCES BETWEEN TREATMENT-SEEKING PRESCRIPTION OPIOID AND HEROIN USERS IN AUSTRALIA.

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Aims: Pharmaceutical opioid misuse is an emerging problem globally. In Australia treatment for opioid dependence was established to meet the needs of heroin users. Few studies have examined characteristics and treatment needs of prescription opioid users. The aim of this study was to compare prescription opioid users with heroin users presenting for treatment in Australian treatment services.
Methods: A convenience sample of 192 opioid dependent recent treatment entrants who reported unsanctioned pharmaceutical use were recruited from alcohol and drug treatment services across four Australian jurisdictions. A semi-structured interview collected data on demographic characteristics, pharmaceutical use, illicit drug use, mental and physical health (using the K10 and the SF12), crime (OTI crime scale) and harms resulting from drug use. Multivariate analyses were used to identify characteristics that differed between those seeking treatment for heroin use and those seeking treatment for problems with pharmaceutical opioids.
Results: The two groups differed on some variables. Prescription opioid users were less likely to report recent stimulant use (B = -.431; 95%CI = -.841, -.022) or an overdose history (B = -0.062; 95%CI = -0.124, -0.00) and more likely to initiate opioid use for pain (B = .593; 95%CI = .037, 1.15). Most participants in both groups reported a history of heroin use and intravenous opioid use.
Conclusions: While some differences appear to exist between prescription and illicit opioid users, the opioid users attracted into treatment did not differ on many fundamental characteristics. This may related to the treatment system being oriented to the needs of heroin users. These findings support anecdotal reports that prescription opioid users without a history of illicit drug use may not be attracted into existing treatment services.
Financial Support: This study was funded by the Ministerial Council for Drug Strategy and the Victorian Department of Health

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EPIGENETIC EFFECTS OF COCAINE ON WHITE MATTER.

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Aims: In humans, cocaine addiction is associated with alteration of white matter in the corpus callosum as revealed by diffusion tensor imaging and with a reduction in myelin proteolipid protein (*PLP1*) expression. We hypothesized that chronic cocaine treatment of rats will cause hypermethylation of specific CpG sites in the (*Plp1*) gene promoter region. Hypermethylation may decrease gene expression and altered PLP1 expression can cause neurodegeneration.
Methods: Male Sprague-Dawley rats were trained to self-administer cocaine (0.75 mg/kg/0.1 ml for 3 hrs/day) until administration stabilized. Thereafter, rats self-administered cocaine for 14 days, after which the rats underwent abstinence for either one (N = 6) or 30 days (N = 6). For each group, there were sham animals (N = 7; vein exposed at time of surgery, no catheter implanted, no drug administered). Corpus callosum was dissected from the animals and DNA methylation analysis of the *Plp1* promoter region was performed by direct sequencing of bisulfite-treated DNA.
Results: A single CpG site in the *Plp1* promoter region was found to be hypomethylated in the cocaine treated rats (1 day abstinence). Specifically, the +64 CpG site in *Plp1* was hypomethylated in DNA from the corpus callosum of cocaine animals (64.9% sham versus 45.4% 30 day cocaine-1 day abstinence, p = 0.008 uncorrected). Methylation levels were not significantly different than that of sham animals following 30 days abstinence (55.5%, +64 CpG site).
Conclusions: Hypomethylation of a specific CpG site in the *Plp1* promoter region in the corpus callosum in response to cocaine treatment could increase the expression of *Plp1* and may contribute to damaged white matter in cocaine dependence. This study provides a model system to explore the mechanisms whereby cocaine alters DNA methylation and, perhaps, white matter structure.
Financial Support: R01 DA06511 (KAC), K05 DA020087 (KAC), P50 DA009262 (FGM), K02 DA00403 (FGM), P50 DA18197 (DAN)

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BDNF IN THE PREFRONTAL CORTEX: INVOLVEMENT IN PSYCHOSTIMULANT- AND SOCIAL DEFEAT STRESS-INDUCED BEHAVIORAL SENSITIZATION.

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Aims: Brain-derived neurotrophic factor (BDNF) is involved in synaptic plasticity induced by psychostimulants. The output of prefrontal cortex (PFC) regulates cellular activity in mesolimbic system which mediates reward and reinforcing effects of abused drugs. Previously we have shown that repeated social defeat stress induced cross-sensitization to amphetamine which was accompanied by prolonged BDNF expression in the ventral tegmental area. However, the role of endogenous BDNF in the PFC, which underlies drug-induced sensitization and cross-sensitization after intermittent social stress, is unknown.
Methods: Two types of sensitization protocols have been used. One group of male rats received intermittent social defeat stress, consisting of brief confrontations between the experimental rat and an aggressive rat. Another group received 5 daily injections of amphetamine. Control rats were handled according to the same schedule. Immunohistochemistry for BDNF, Fos or FosB/deltaFosB was performed in the PFC at the time corresponding to the expression of behavioral sensitization to psychostimulants.
Results: BDNF expression in PFC and number of BDNF-labeled cells expressing FosB/deltaFosB was significantly greater in stressed rats than in handled control. In amphetamine-treated animals, a subsequent amphetamine challenge increased BDNF expression in the PFC, and more Fos-BDNF double-labeled cells were observed in sensitized rats compared to drug-naïve rats receiving amphetamine.
Conclusions: BDNF expression in the PFC that accumulates after repeated amphetamine administration or social defeat stress may trigger behavioral sensitization. Repeated amphetamine exposure enhances PFC BDNF expression in a sensitized manner. DeltaFosB expression in BDNF-containing neurons of the PFC could be an important part of the neuroadaptive changes that induce vulnerability to psychostimulants after social defeat stress.
Financial Support: USPHS awards DA024817, DA026451, and MH066954

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IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES AND ENRICHED MOLECULAR PATHWAYS BY TOPIRAMATE FOR TREATMENT OF METHAMPHETAMINE DEPENDENCE USING GENOME-WIDE EXPRESSION MICROARRAYS.

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Aims: Although topiramate is promising for treating patients with methamphetamine dependence, the molecular mechanism underlying its effect is not well understood. The primary goal of this study was to identify differentially expressed genes and enriched pathways that correlate with the response to topiramate treatment.
Methods: According to a latent class analysis of six secondary efficacy outcome measures for Weeks 1-12, among 69 individuals with RNA samples available at Weeks 8 or 12, 28 and 41 individuals were classified as responders and non-responders to their respective treatments.
Results: By using both the conventional Student's t-test and the more innovative empirical Bayes approach, we identified 1,052, 450, 935, and 676 differentially expressed genes (P<0.05) in Week 8 topiramate, Week 8 placebo, Week 12 topiramate, and Week 12 placebo groups, respectively. Of them, 58 were up-regulated and 59 were down-regulated at a fold-change of more than 20% for both Weeks 8 and 12 topiramate groups. Subsequently, we performed pathway analysis on 206 genes detected exclusively in topiramate-treated groups and found 18 enriched pathways specific for the topiramate response, which could be classified into three categories: neuronal plasticity, cancer signaling, and metabolism and immune function.
Conclusions: In sum, we conclude that genome-wide transcriptional profiling of peripheral leukocytes represents a powerful approach to identifying significantly modulated genes and pathways associated with treatment response.
Financial Support: NIDA, NIH

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ATTENUATION OF COCAINE SELF-ADMINISTRATION BY NOVEL DOPAMINE D3 RECEPTOR LIGANDS.

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Aims: The dopamine D3 receptor (D3R) subtype has received increasing attention for its potential role in addiction. Some obstacles to studying D3Rs are that most drugs have limited selectivity for D3Rs relative to D2Rs or can not pass the blood-brain barrier. This study examined 3 novel D3R ligands on cocaine self-administration (WC-10, antagonist, 43-fold selectivity for D3R vs. D2R; WC-44, agonist, 23-fold selectivity for D3Rs;WC-26, partial agonist, 51-fold selectivity for D3Rs). All of these compounds cross the blood brain barrier (log P > 3.5).
Methods: Rats were trained with alternating variable-interval (VI) 60 sec schedules of sucrose (45 mg pellets) or cocaine (0.375 mg/kg/0.1 ml, IV). Rats received daily 2-h sessions with 15 min periods of alternating access to each reinforcer. Once responding stabilized, rats were pretreated with WC-10, WC-44, or WC-26 (0.0, 1.0, 3.0, 5.6, 10.0 mg/kg, IP) on separate test sessions. Separate cohorts of rats trained to self-administer cocaine (0.75 mg/kg/0.1 ml, IV) on a VI60 schedule of reinforcement were tested with various doses of cocaine (0.000, 0.094, 0.188, 0.375, 0.75, and 1.5 mg/kg, IV) following pretreatment with WC-10 (5.6 or 10.0 mg/kg, IP) or WC-44 (10.0 mg/kg, IP).
Results: All 3 compounds decreased cocaine and sucrose intake at the 10.0 mg/kg dose; however, there was a significantly greater decrease in cocaine vs. sucrose intake at the dose of 5.6 mg/kg for WC-10, the 3.0 and 5.6 dose for WC-26, and at the 10.0 dose for WC-44. WC-10 and WC-44 also flattened the cocaine dose-effect function resulting in similar reinforcement rates across all doses of cocaine in contrast to the normal inverted U-shaped function.
Conclusions: These findings are consistent with previous reports of dopamine D3 ligands inhibiting cocaine reinforcement. They suggest that the D3R is a useful target for medications aimed at treating cocaine dependence.
Financial Support: Supported by NIDA grant DA023957.

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ALCOHOL AND OTHER DRUGS RELATED VIOLENCE REPORTED AT SPECIAL POLICE STATIONS FOR WOMEN.

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Aims: To quantify and describe the preliminary findings of alcohol and other drugs related family violence reported in all nine Police-Stations specific for women in São Paulo city.
Methods: A sample was composed by 1025 women who pressed charges of family violence at the nine special Police-Stations. We used standardized interviews based on a questionnaire developed for a multi-country study (WHO).
Results: In 40.8% of the charges, offenders had ingested alcohol prior to the violent behavior; 12.2% had used cocaine. Most of the offenders were male (95%), aged 20-39 years (62 %) and intimate partner of the victim (44.1%). Concerning the victims, most were aged 20-39 years (64%) and only 4.4% had ingested alcohol.
As regards the characteristics of the violent episode reported, the victim's household was the most frequent place (66.6%), where the violence took place on Sundays (20,7%) after 6 pm (57.1%). The children's (< 18 years) presence was reported in 46.6% of the cases. Most of the charges portrayed more than one type of aggression, such as: insults, intimidation, slaps, pushes and throwing of objects. 65.4% of the women were looking for help at the Special Police for the first time and only 9.3% chose to actually sue the offender (optional in the Brazilian law).
Conclusions: The high frequency of alcohol and other drugs related family violence charges associated to few lawsuits points to the need for complementary interventions, such as follow-up of the cases and integration with health services.
Financial Support: FAPESP (Fundação de Amparo a Pesquisa do Estado de São Paulo)
CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior)

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A POPULATION-BASED INVESTIGATION OF THE CO-OCCURRENCE OF NON-MEDICAL PRESCRIPTION STIMULANT USE AND CIGARETTE SMOKING AMONG US YOUTH (AGE 12-21).

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Aims: A growing body of clinical and laboratory literature has shown high rates of co-occurrence between cigarette smoking and the non-medical use of prescription psychostimulants. Few studies, however, have sought to understand how various dimensions of nicotine dependence are uniquely related to levels of psychostimulant use as a plausible pathway linking these phenomena.
Methods: Using a diverse community-based sample of smokers, we draw on data from the 2005-2008 National Survey on Drug Use and Health (NSDUH) to compare past-month levels of psychostimulant use to patterns of nicotine dependence among young adults (aged 12-21) in the United States. Nicotine dependence was measured by 19 items from Nicotine Dependence Syndrome Scale which measures symptoms along 5 key dimensions (smoking drive, tolerance, continuous smoking, behavioral priority, stereotypy). Adjustments were made to account for the multi-stage probability sample and aggregation of multiple years of NSDUH data.
Results: Of the 16,602 past month users of cigarettes or prescription psychostimulants, 95.1% used cigarettes only, 1.1% used stimulants only, and 3.8% used both. Among cigarette users, total NDSS score was positively related to past month use of prescription ($p<.05$) psychostimulants, and the number of days in which stimulants were used non-medically. Moreover, tolerance and drive were also significantly related to both psychostimulant outcomes (any use, number of days used), whereas little effect was observed for continuous smoking, priority, or stereotypy. This effect persisted when controlling for the co-occurring use of other non-prescription psycho-stimulants (e.g., cocaine, methamphetamine/crank).
Conclusions: The results highlight the importance of understanding nicotine dependence as a multidimensional construct. Future studies should consider how different phenotypes of nicotine dependence are uniquely related to specific neurological reward structures, while also considering differences in exposure to poly-drug use.
Financial Support: R01DA020902 and R01DA023377

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THE RELATIVE ROLE OF PERCEIVED PARTNER RISKS IN CONDOM USE IN A THREE-CITY SAMPLE OF LOW-INCOME WOMEN.

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Aims: To examine the effect of women's perceptions of partners' health risks on condom use.
Methods: Women from three U.S. cities (n=1,967) were recruited through respondent-driven sampling (RDS) to provide data on HIV risk behaviors with sexual partners. Multilevel random effects models controlled for reporting on multiple partners.
Results: In univariate models, respondents' being unaware of partner HIV status, bisexuality, and/or injection drug use, and perceiving that partners had concurrent (i.e.,overlapping) partners, each were associated with increased odds of condom use. Odds changed when contextual factors were included in a multivariate model. Perceptions of partner bisexuality were associated with 84% lower odds of condom use when the respondent exchanged sex for money or drugs, and perceptions of a partner having concurrent partners were associated with 48% lower odds of condom use when the respondent was HIV positive. Other factors associated with decreased odds of condom use were sex main partners (AOR 0.13, 95% CI 0.10 - 0.18), alcohol use (AOR 0.66, 95% CI 0.46 - 0.93), and crack use (AOR 0.62, 95% CI 0.43 – 0.89).
Conclusions: Awareness of partner risk factors may not be sufficient for increasing condom use. Interventions should address risks associated with unprotected sex with bisexual partners, partners with concurrent partners, and main partners, and the effects of alcohol and crack on condom use.
Financial Support: Study: NIDA grants U01DA017373, U01DA017377, U01DA017378, U01DA017387, and U01DA017394. Analysis: UCLA AIDS Institute.

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THE CLINICALLY VALIDATED MGLUR5 RECEPTOR ANTAGONIST FENOBAM DECREASES METHAMPHETAMINE SELF-ADMINISTRATION FOLLOWING ESCALATION OF INTAKE.

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Aims: Numerous preclinical studies have shown that blockade of the type 5 metabotropic glutamate receptor (mGluR5) attenuates the self-administration of various drugs of abuse when animals are allowed to self-administer the drug under limited access conditions (i.e., 1-2 hr/day). However, no studies to date have examined the effects of mGluR5 blockade on drug intake under extended access conditions (i.e., 6+ hr/day), which has been shown produce a gradual escalation in total drug intake and the rate of drug intake that more closely resembles patterns of drug self-administration in human addicts. The purpose of the present study was to determine if mGluR5 antagonism decreases methamphetamine self-administration following escalation of drug intake.
Methods: Male Sprague-Dawley rats (n=12) were implanted with jugular vein catheters and trained to self-administer methamphetamine at a dose of 0.05 mg/kg/infusion in 1 hr daily sessions under an FR1 schedule of reinforcement. Following 7 days of methamphetamine self-administration under these limited access conditions, rats were then allowed to self-administer methamphetamine under extended access conditions (6 hr/day) for 12 days.
Results: Rats demonstrated a gradual increase in total methamphetamine intake (mg/kg/session) and the rate of methamphetamine intake (mg/kg/1st hour) over the course of the 12 days of extended access. Patterns of self-administration then stabilized following the escalation phase, and fenobam (3, 10 or 30 mg/kg i.p.) or vehicle (0.3% Tween 80) was subsequently administered prior to 6 hr sessions in a randomized crossover design. The 10 mg/kg dose of fenobam reduced methamphetamine intake during the first hr of the session, whereas the 30 mg/kg dose reduced methamphetamine intake throughout the 6 hr session.
Conclusions: These data suggest that fenobam, which is currently being tested in clinical trials for the treatment of Fragile X syndrome, may be of potential use to aid in the reduction of methamphetamine intake in addicted individuals.
Financial Support: Supported by NIH grant DA025606.

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EFFECTS OF CYCLOSERINE AND GABAPENTIN IN METHADONE-MAINTAINED HUMANS UNDER A NALOXONE NOVEL-RESPONSE DISCRIMINATION PROCEDURE.

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Aims: Previously, we showed that the partial glycine agonist d-cycloserine at a dose up to 500 mg somewhat attenuated the discriminative stimulus effects of naloxone. The present study examined further the efficacy of d-cycloserine (CYC) as well as the N-type calcium channel blocker gabapentin (GBP) in attenuating the behavioral effects of NX in opioid-dependent humans responding under a NX discrimination procedure.
Methods: Methadone-maintained subjects were trained to distinguish between a low dose of NX (0.15 mg/70 kg, i.m.; i.e., Drug A) and placebo (i.e., Drug B) under an instructed novel-response drug discrimination procedure, in which subjects identify the drug condition as "A", "B", or "N" (neither A nor B - 'novel'). Once the discrimination was acquired, doses of CYC (0, 500, 625, 750 mg) and GBP (0, 100, 200, 400 mg) each alone and in combination with the training dose of NX were tested.
Results: Thus far, 3 participants have completed the GBP-NX dose sequence and 1 participant completed the CYC-NX test dose. Because of symptoms associated with the higher CYC doses, the 750 mg dose was discontinued. CYC alone produced predominantly placebo-appropriate responding. When administered with NX, CYC produced 100% NX-appropriate responding at the 500 (n=4) and 625 (N=1) mg doses. GBP alone produced only placebo-appropriate responding. When administered with NX, GBP produced 66.7, 75, and 33.3% NX-appropriate responding with 0% novel-appropriate responding at all doses tested.
Conclusions: These preliminary results suggest that GBP is more effective than CYC in attenuating the discriminative stimulus effects of NX.
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EARLY VS. LATE ONSET CRACK USE: A CASE-CONTROL STUDY.

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Aims: Data are sparse with respect to correlates of late onset drug use. We explored the relation between late onset (≥age 40) crack use, marijuana onset and trauma exposure. We hypothesized two possible relationships: compared to those with early (<age 40) crack onset (1) late onset users also initiate marijuana later but have a similar length of time between marijuana and crack onset or (2) late onset users have a similar age of marijuana onset but a longer time between marijuana and crack onset. We also hypothesized that late onset users would be more likely to experience trauma in the year prior to crack initiation (proximal) and have experienced multiple trauma types in their lifetime (cumulative).
Methods: A community-based sample of current and former drug users aged ≥18 were recruited New York City from 2005-2009. Demographics, drug use, and trauma exposure were assessed through cross-sectional interviewer-administered surveys. Cases were those with crack onset at ≥age 40 (n=64). Age-matched (±2 years) controls were those with crack onset at <age 40 (case:control ratio~1:5, n=313).
Results: The sample was 66.1% male, 70.8% black, 18.3% Hispanic; 30.5% were recently (last 6 months) homeless. Mean age was 51.4. Mean age at marijuana and crack onset were 16.4 and 32.1, respectively. In bivariate analysis, cases were more likely to be Hispanic (28.1% vs. 16.3%, p<0.001) and less likely to be employed (6.3% vs. 18.9%, p=0.01) and homeless (21.9% vs. 32.3%, p=0.10). Cases were slightly older at marijuana onset (17.1 vs. 16.3 yrs, p=0.10). Cases had a significantly longer time between marijuana and crack onset (27.3 vs. 13.2 yrs, p<0.001). There were no significant differences with respect to proximal and cumulative trauma.
Conclusions: These results support the hypothesis that late onset crack users have a similar age of marijuana onset but a longer time between marijuana and crack onset as compared to early onset users. Proximal and cumulative trauma does not appear to be associated with late crack onset. Further research is needed to explore reasons for late onset of crack use.
Financial Support: This study was funded by NIDA and NIMH.

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PRELIMINARY EVALUATION OF TWO HIGH-REACH INTERVENTIONS FOR SMOKING DURING PREGNANCY: COMPUTER-DELIVERED 5AS AND LOW-INTENSITY CONTINGENCY MANAGEMENT.

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Aims: Despite the availability of efficacious interventions for smoking during pregnancy, multiple obstacles have limited their implementation in primary care settings. We therefore developed two highly replicable interventions for smoking during pregnancy, based on evidence-based approaches: (a) computer-delivered 5As-based brief intervention; and (b) computer-assisted, simplified and low-intensity Contingency Management (CM).
Methods: In this preliminary study, pregnant women (N = 110) reporting any smoking in the past week were randomly assigned to single-session computer-based 5As, CM, 5As plus CM, or treatment as usual conditions. Notably, testing for CM took place only if initiated by participants at a prenatal care appointment. At present, a total of 74 participants have completed an 8-week follow-up at which smoking was measured by self-report, cotinine, and breath CO.
Results: Participants in this study were overwhelmingly African-American (85%) and low SES. Approximately 90% of participants gave the software the highest rating possible for acceptability, ease of use, and helpfulness; ratings of state motivation and self-efficacy increased significantly following the intervention. There were no significant group differences at follow-up, although variation in abstinence was modest (e.g., 40% abstinence in the brief intervention alone group vs. 19% for control). Using intent to treat analysis, abstinence in the CM conditions was similar to control; abstinence rates appeared higher for CM only than for CM plus 5As.
Conclusions: Results suggest that both the computer-delivered brief intervention for smoking and the modified low-intensity CM were feasible and well-accepted. Confirmatory trials should seek to confirm the potential efficacy of the computer-delivered brief intervention, and should also evaluate whether low intensity CM, as predicted by Self-Determination Theory, might inhibit internalization of abstinence goals.
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THE BRAZILIAN SMOKER: A CROSS-SECTIONAL SURVEY IN BRAZIL.

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Aims: To describe characteristics of smokers compared to non-smokers and the patterns of use of tobacco in Brazil

Methods: A household survey was carried out in the 108 most populous Brazilian cities in 2005. A probabilistic sample stratified by clusters units was performed in 3 stages: census tracts, households, and 12 to 65-years-old respondents. The instrument to collect the data was based in SAMHSA, with questions on sociodemographics and drug abuse, including tobacco. Data was initially analyzed with the Chi square test followed by a logistic regression

Results: Among 7,939 respondents, 44% reported a lifetime use of tobacco and 16.4% (n=1,302) daily use, which were classified as smokers. The patterns of smoke habits showed that women begin to smoke later than men, smoke less quantity and delayed more time to light the first cigarette of the day. The final logistic regression model identified a positive association with smoke and being adult, having low education and low socioeconomic profile. The first time use of tobacco after 15 years old decreased in 27% the chance to use cigarettes daily (p=0.001). A pattern of drinking behavior was found among smokers, like binge drinking (OR=1.27; p=0.022), frequent or heavy use of alcohol (OR=1.79; p<0.001) while alcohol dependence itself has had a borderline significance (OR=1.24; p=0.050). Another factor associated with daily smoke was a greater chance of lifetime use of other drugs (OR=1.30; p=0.010)

Conclusions: This study shows the main characteristics associated with the Brazilian smoker: adults, lower income and education, exposed to tobacco before 15 years old and abuse of alcohol. Besides, it found differences between gender and age of first use, the intensity of symptoms of dependence and the quantity of cigarettes used daily. These kind of studies are important to improve information for preventive and treatment policies that reduce the prevalence of smoking in Brazil

Financial Support: SENAD and AFIP

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CHOLINERGIC TRANSMISSION IN THE NUCLEUS ACCUMBENS IS LOWER IN ADOLESCENT VS ADULT RATS EXPERIENCING NICOTINE WITHDRAWAL.

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Aims: AIM: Previous work has shown that adolescent rats are less sensitive to the behavioral effects of nicotine withdrawal relative to adults. However, the neurochemical mechanisms that mediate these developmental differences are unknown. The goal of this study was to compare acetylcholine (ACh) levels in the NAcc of adolescent and adult rats experiencing withdrawal.

Methods: METHOD: Male Wistar adolescent (PND 28-30) and adult (PND 60-70) rats were prepared with subcutaneous pumps that delivered an equivalent nicotine dose in these age groups (4.7 mg/kg/day for adolescents and 3.2 mg/kg/day for adults). Following 13 days of nicotine exposure, rats were implanted with microdialysis probes in the NAcc. The next day, dialysate samples were collected following systemic administration of the nicotinic-receptor antagonist mecamylamine (1.5 mg/kg or 3.0 mg/kg) to precipitate withdrawal. ACh levels were also compared in these groups following systemic administration of the ACh-esterase inhibitor, methanesulfonyl fluoride (MSF; 2.0 mg/kg). This was done to examine whether our results were due to age-dependent differences in the metabolism of ACh. Dialysate levels of ACh were quantified using HPLC-EC methods.

Results: RESULTS: Adult rats experiencing withdrawal displayed a dose-dependent increase in ACh levels (128% and 149%) relative to baseline, consistent with other laboratories. However, adolescent rats displayed less of an increase in ACh levels (112% and 130%) as compared to adults. Both age groups displayed a similar change in ACh levels following MSF administration.

Conclusions: CONCLUSION: These results suggest that cholinergic systems play a role in mediating developmental differences to nicotine withdrawal. Our results further suggest that adolescent rats maybe less sensitive to the modulatory effects of nicotinic receptors in mediating withdrawal as compared to adults.

Financial Support: Supported by NIDA Grant R01DA021274 and a diversity supplement fellowship to this award.

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INTIMATE PARTNER CHARACTERISTICS AND SEXUAL BEHAVIORS AS CORRELATES OF SEXUALLY TRANSMITTED INFECTIONS AMONG AFRICAN-AMERICAN FEMALE DRUG USERS.

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Aims: While drug use is similar across racial groups in the US, African Americans are disproportionately more likely to experience severe health consequences, such as sexually transmitted infections (STIs), as a result of drug use. This study examines the relationship between characteristics of African American female drug user's intimate partners as well as sexual behaviors and STI status.

Methods: Baseline data were collected from 201 African American female drug users as part of the Black Women in the Study of Epidemics project (B-WISE). Significant variables at the bivariate level were entered into a multivariate logistic regression model to identify the significant correlates of a positive STI diagnosis by a healthcare professional over the lifetime.

Results: The majority of participants were single (89%) and heterosexual (76%), with a mean age of 35 years. Almost three-fourths of the sample (73%) had been diagnosed with a STI in their lifetime. Regarding characteristics of intimate partners, 72% dated outside of their race, 54% dated a married man, 68% dated someone at least 10 years older, 11% dated a man who has had sex with another man, 78% dated someone who was unfaithful, and 87% have dated someone who has been incarcerated. In the multivariate model, having dated a married or older man, as well as having ever traded sex were not associated with ever having a STI; however, having dated an unfaithful partner and having dated an incarcerated male increased the odds of having a STI by 2.9 and 4.7 respectively (p<.05). In addition, each additional male sex partner regardless of their characteristics significantly increased the likelihood of having a STI by 9% (p<.05).

Conclusions: Findings suggest that the number and characteristics of sexual partners are associated with having a STI and have implications for increasing knowledge surrounding safer sex practices for African American female drug users.

Financial Support: This research was supported by the National Institute on Drug Abuse (R01-DA022967; K01-DA021309, PI: Carrie Oser).

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SUBSTANCE USE AND HETEROSEXUAL ANAL SEX AT THE MOST RECENT SEXUAL ENCOUNTER.

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Aims: To investigate whether drug use influences the likelihood of heterosexual anal sex.

Methods: Data came from the Chicago site of NIDA SATHCAP. Respondent-driven sampling was used to recruit drug users, MSM, and their sex partners. Analyses were restricted to 1,937 men and 1,256 women who reported on sex and substance use with 1-6 opposite sex partners in the past 6 months. Mixed effects regression was used, including random intercepts for subjects to adjust for clustering effects. The effects of each drug were tested in separate models, then multivariate models were tested including all drugs significant in the separate models and including an indicator of bisexual activity as a covariate.

Results: The sample is 70% Black and 14% Latino, poor, and has a median age of 43 years. For the most recent sexual encounters, 15% of women and 21% of men reported anal sex with a least 1 partner. Drug use prevalence at an encounter was high for men and women: crack or heroin, 41-47%; speedball, about 25%; alcohol (>4 drinks), about 20%; marijuana, >15%. Only 2% reported ecstasy use. Condom use during anal sex was low, about 25%, regardless of drug use. For women, crack use was associated with greater odds of anal sex (OR 1.62, 95% CI 1.07-2.45), as was the use by a male sex partner of marijuana (OR 1.70, 95% CI 1.01-2.86), speedball (OR 1.93, 95% CI 1.24-3.02) and ecstasy (OR 4.29, 95% CI 1.36-13.53). For men, the use of marijuana (OR 2.60, 95% CI 1.79-3.78) and speedball (OR 1.75, 95% CI 1.25-2.45) were associated with greater odds of anal sex, as were a female partner's heavy use of alcohol (OR 2.41, 95% CI 1.68-3.47) and use of ecstasy (OR 1.75, 95% CI 1.25-2.45).

Conclusions: Anal sex was fairly common, condom use infrequent, and some drugs increased the odds of having anal sex. Though ecstasy use was uncommon, the large effect of men's ecstasy use on anal sex reported by women, and men's reports indicating women's use of ecstasy is a potential contributing factor, suggests this deserves further investigation and should be addressed in HIV prevention interventions.

Financial Support: National Institute on Drug Abuse, U01DA017378

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ASSOCIATIONS BETWEEN HEROIN-DEPENDENT PATIENT SATISFACTION WITH METHADONE MAINTENANCE TREATMENT CENTERS AND CYP3A4, CYP2B6, CYP2D6, OPRM1, AND DRD2 GENETIC POLYMORPHISMS.

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Aims: Background: Heroin-dependent patients who are CYP2D6 ultrarapid metabolizers according to genotyping present deficient satisfaction with methadone maintenance treatment centers (Pérez de los Cobos et al., 2007; Drug Alcohol Depend. 89:190-4). This finding justifies the evaluation of other associations between heroin-dependent patient satisfaction and methadone pharmacogenetics. The genes involved in methadone pharmacogenetics are mainly CYP3A4, CYP2B6, and CYP2D6 from the pharmacokinetic angle, and OPRM1 and DRD2 from the pharmacodynamic angle.
Aims: To assess the relationship between heroin-dependent patient satisfaction with methadone treatment centers and the polymorphisms of following genes (susceptibility variations shown in brackets): CYP3A4 (rs2740574), CYP2B6 (rs2279343, rs3211371, rs3745274), OPRM1 (rs1799971), and DRD2 (rs1800497).
Methods: Methods: The DNA samples of the 205 patients who participated in the above referenced study were genotyped in order to analyse the polymorphisms of genes CYP3A4, CYP2B6, OPRM1, and DRD2. The phenotype was assessed using the Verona Service Satisfaction Scale for Methadone Treatment. Multiple linear regression was used in order to analyse potential associations. Previous data about CYP2D6 polymorphisms were included in the multivariate model.
Results: Results: New associations were not found.
Conclusions: Conclusions: Only CYP2D6 polymorphisms are associated to heroin-dependent patient satisfaction with methadone treatment centers.
Financial Support: Supported by FIS 060531 and 0901072, Spanish Network of Addictive Disorders (RTA), and Catalonia Government.

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RE-ENTRY PROGRAMMING FOR OFFENDERS WITH CO-OCCURRING DISORDERS: PROCESS AND OUTCOME FINDINGS FROM A PILOT STUDY.

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Aims: The aim of this project was to evaluate the process and outcomes of implementing a structured and inter-agency program focusing on treatment, re-entry planning, criminal recidivism, community service engagement, and clinical profiles of offenders with co-occurring disorders.
Methods: Process evaluation activities sought to monitor and understand the manner and the quality with which the program was implemented. Outcome evaluation utilized a randomized assignment design (total of 190 subjects) to evaluate program impacts upon the criminal recidivism of male offenders. A one-group, repeated measures design was used to assess changes in the clinical profile of those offenders receiving enhanced re-entry services as assessed by three standardized assessments: BPRS, ASI, and SOCRATES, occurring at the time of the offenders' entry to the prison-based treatment program, exit from prison, and 6-months following their re-entry to the community.
Results: Statistically significant clinical improvements were seen in the treatment group from program intake to program exit, as measured by the ASI and BPRS. A slightly lower proportion of the program participants had been re-arrested within 6 months of their prison release, relative to their control participants, although results were not statistically significant. Approximately one quarter of the control and treatment groups violated parole within 6 months of their release from prison, with no significant differences across groups.
Conclusions: Clinical assessments revealed that participants in the treatment group showed great improvements in mental health symptomology, as well as substance use and related areas.
No significant differences were found across groups for either parole violations or new charges.
Financial Support: This study was supported in part, by a grant from the Substance Abuse and Mental Health Services Administration.

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ANALYSIS OF CONTENT AND IN VITRO DISSOLUTION OF MORPHINE IN MORPHINE IMPLANT PELLETS FOR RELEASE AND STABILITY.

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Aims: The NIDA Drug Supply Program requires a constant supply of dosage forms of various drugs including morphine for basic research programs. RTI supplies morphine implant pellets (tablets) of consistent quality by testing the content and dissolution of morphine and the stability of these dosage forms over time.
Methods: RTI has been supplying morphine implant tablets (placebo, 8 mg, 25 mg and 75 mg morphine per pellet) to NIDA investigators since 1985. RTI performs the analytical testing on these dosage forms for initial release after manufacturing, and for subsequent on-going monitoring of the quality and stability. Analytical methods for purity, assay, and in vitro dissolution of morphine dosage forms were developed. The method for assay and purity analyzes morphine in bulk drug and in drug product. It involves HPLC analysis using a reverse phase C18 column, gradient elution using an acetonitrile/1% ammonium acetate mobile phase and a photodiode array (PDA) detector. The assay for strength and purity is determined at 280 nm and the PDA data is also used for peak purity assessment. The method is validated for precision, linearity, accuracy, and specificity. Dissolution of morphine from pellets is performed using USP<711> Apparatus 1 (basket) method in 0.1N hydrochloric acid sampled at periodic intervals up to 45 minutes. The samples are analyzed by HPLC with UV detection at 280 nm. Stability of morphine tablets is monitored at room temperature by analyzing the content annually and dissolution periodically.
Results: Validation of the HPLC method for assay and purity met the criteria for precision, linearity, accuracy, and specificity. At least 80% of morphine is dissolved in 30 minutes from the implant pellets and stays consistent over time.
Conclusions: Morphine implant tablets have sufficient stability (5 to 8 years) based on analysis for morphine content and in vitro dissolution to ensure consistent quality for NIDA Drug Supply Program.
Financial Support: NIDA, NIH

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SEXUAL RISK PREDICTED BY MOTIVATION TO CHANGE RISK BEHAVIOR, TEMPTATIONS FOR AND DECISIONS AROUND UNSAFE SEX IN YMSM.

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Aims: Young men who have sex with men (YMSM) and use drugs are at high risk for contracting HIV due to co-occurrence of these behaviors. We examined baseline data from YMSM in a randomized controlled trial testing the efficacy of a brief Motivational Interviewing intervention to reduce substance use and sexual risk. We hypothesized that higher temptations for and more endorsements of benefits of unsafe sex would predict more frequent unsafe sex under the influence of alcohol/drugs, while higher motivation to change risky behavior would attenuate these relationships.
Methods: These HIV negative YMSM (N=231) had ≥ 5 days of drug use and ≥ 1 incident of unsafe anal sex with a high risk partner in the last 90 days. Average age was 29.6 (7.4), 60% were non-White. Our predictors were Motivation to Change Sexual Risk Behavior, Temptations for Unsafe Sex and Decisional Balance for Unsafe Sex. The percentage of total sex acts that were high risk (%SAHR) and percentage of high risk sex acts under the influence of alcohol/drugs (%HRSAUI) constituted our outcomes. We employed mediational analyses, as outlined by Baron and Kenny (1986), and tested the significance of indirect paths in cases of partial mediation (Sobel, 1982).
Results: Temptations for unsafe sex predicted %SAHR and %HRSAUI, with motivation to change risky sexual behavior partially mediating these relationships. One's endorsement of pros of unsafe sex predicted %SAHR and motivation to change risky sexual behavior partially mediated this relationship. All indirect mediation paths were significant.
Conclusions: High risk sexual behavior under the influence of drugs/alcohol was predicted by temptations for and endorsement of pros of unsafe sex. Motivation to change risky sexual behavior played a role in these relationships, therefore increasing YMSM's readiness to reduce high risk sex should be a consideration in HIV prevention intervention.
Financial Support: Research supported by NIDA grant R01DA20366.

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EFFECT OF LONG-TERM Δ9-THC EXPOSURE ON RAT COGNITIVE PERFORMANCE.

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Aims: The purpose of this study was to characterize neurocognitive function in rats given long-term intermittent exposure to Δ9-THC doses that produce clinically relevant plasma Δ9-THC levels.
Methods: Dosing: Δ9-THC was administered in repeating 14d cycles comprised of 6d drug treatment (VEH, 0.3, 3.0 mg/kg; 2x/day) and 8 drug-free days for behavioral testing.
Behavioral Testing: Separate groups of Wistar rats were tested in four tasks: (1) 5-CSRTT (n = 20/grp); (2) Delay Discount (n = 7/grp); (3) DRL-30 (n = 7/grp); (4) Novel Object Exploration (n = 8/grp).
Dependence Measures (precipitated withdrawal): Δ9-THC dependence was evaluated by administering 0.3 mg/kg SR141716A and scoring somatic signs of withdrawal.
Results: All tests were conducted over the course of at least 10 cycles of Δ9-THC treatment.
5-CSRTT: There was no significant effect of Δ9-THC on performance in standard tests. However, a dose-dependent Δ9-THC effect was evident in decreased accuracy at short ITIs ($p < 0.05$) and increased impulsive responding at long ITIs ($p < 0.05$).
Delay Discount: There was no significant effect of Δ9-THC on DRL performance.
DRL-30: Enhanced performance (rewards/total responses) was evident in the 3 mg/kg group following 4 cycles of Δ9-THC treatment.
Object Exploration: Δ9-THC treated animals displayed increased exploration latency (index of anxiety-like behavior) and decreased novel object recognition in substitution tests (index of recognition memory).
Conclusions: Despite evidence of dependence, increased anxiety-like behavior and deficits in recognition memory, Δ9-THC treated rats displayed no alterations in attention, impulsive behavior or inhibitory control when tested under well-established, familiar conditions. However, 5-CSRTT trials with increased task difficulty revealed significant increases impulsive behavior and decreases accuracy that correlated with the Δ9-THC treatment dose. These findings suggest that long-term Δ9-THC exposure results in diminished behavioral performance under conditions of increased cognitive load.
Financial Support: Supported by NIDA P20 DA024194

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SMOKING PREVALENCE IN ADDICTION TREATMENT: A LITERATURE REVIEW.

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Aims: Epidemiologic studies show that tobacco dependence is highly comorbid among persons with any alcohol use disorder (34% tobacco dependent) and persons with any drug use disorder (45% tobacco dependent). However, surveys among persons enrolled in addiction treatment often report higher smoking prevalence.
Methods: A systematic literature review was performed using electronic databases to identify reports of smoking rates among addiction treatment clients. Search limits included articles published in English between 1987 and 2009.
Results: Seventy-three papers met inclusion criteria. Of these, 38 reported original findings from U.S. adult samples and were included in analysis. Other papers (n=29) reported original findings from countries outside the U.S. and were not included. Average client smoking prevalence across all studies was 69.5% among outpatient clients (12 studies), 74.1% among inpatient clients (16 studies), and 89.4% among methadone clients (5 studies). Smoking prevalence by primary drug treated was 75.7% for those in alcohol treatment (67 studies), 71.5% for alcohol or drug treatment (16 studies), 74.8% for cocaine/crack (8 studies) and 79.9% for opiate/narcotics (7 studies). U.S. smoking prevalence decreased from 28.8% in 1987 to 19.8% in 2008. We aggregated studies into five time groups (1987-90, 1991-95, 1996-00, 2001-05, 2006-08). Average smoking prevalence in these groups of studies were, respectively, 76.7%, 73.6%, 74.2%, 68.8%, and 79.1%.
Conclusions: Smoking prevalence among persons enrolled in addiction treatment is higher than epidemiologic estimates based on co-occurring disorders. In these treatment settings smoking rates are highest for persons in methadone treatment, followed by those in residential and outpatient settings. There is little evidence of decreasing prevalence, over time, among persons entering addiction treatment. Addiction treatment systems should aggressively address tobacco dependence, and also offer a compelling arena for tobacco control intervention.
Financial Support: NIDA R01 DA020705, U10 DA015815, P50 DA009253

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EFFICACY OF AN HIV/HEPATITIS EDUCATIONAL INTERVENTION DURING BUPRENORPHINE DETOXIFICATION IN PRESCRIPTION OPIOID ABUSERS.

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Aims: Prevalence of HIV and hepatitis among opioid abusers presents a serious public health problem. Efforts to enhance HIV/hepatitis knowledge in this population are important. We have an ongoing NIDA-funded, 12-week trial aimed at treating prescription opioid (PO) abuse using outpatient buprenorphine detoxification. While the primary focus is on opioid abstinence, the trial also provides an opportunity to examine HIV/hepatitis knowledge in this sample and whether an educational intervention, administered early in treatment, may improve knowledge.
Methods: Our intervention begins with a baseline assessment of knowledge and risk behavior. Subjects then meet individually with a therapist to review, correct and discuss the assessments. They watch an HIV/AIDS educational video, followed by discussion of the video, review of additional HIV/hepatitis materials and provision of information on HIV testing centers and an offer to assist with pursuing testing. The knowledge assessments are administered again following the intervention, as well as at Study weeks 6, 8, and 12.
Results: Thus far, 51 subjects have completed the intervention (27 yrs old, 30% female). Preliminary analyses suggest 70% and 45% accuracy on HIV-and hepatitis-related items, respectively. The educational intervention significantly improves HIV/hepatitis knowledge, with accuracy scores increasing by 20% and 38% ($p < .05$) from pre- to post-intervention on total HIV and hepatitis scales, respectively. Of particular interest is that these knowledge improvements persist throughout the 12-week assessment period.
Conclusions: Our brief educational HIV/hepatitis intervention appears to improve both HIV and hepatitis knowledge in a sample of PO-dependent adults. Data from the completed trial (N=105) will be presented and will include examination of overall HIV/hepatitis scores, individual items, and measures of HIV/hepatitis risk behavior. These data will offer important clinical and scientific information on HIV/hepatitis knowledge and risk behaviors in the emerging population of PO abusers.
Financial Support: R01 DA019989 & T32 DA007242

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COMPARISON OF ACQUISITION OF NICOTINE VS. COCAINE SELF-ADMINISTRATION WITHOUT FOOD RESTRICTION OR PRIOR TRAINING.

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Aims: This study compared acquisition of self-administration of nicotine versus cocaine without any prior training, light or tone cues, or food restriction in adolescent male rats using a limited access model.
Methods: During 20 daily training sessions, responses on one lever had no scheduled consequences (inactive lever) while responses on another lever (active lever) resulted in simultaneous retraction of both levers for a 20-sec time out and drug delivery of an assigned dose of nicotine (0.015, 0.03, 0.06 mg/kg, IV), cocaine (0.75 mg/kg IV), or saline. Reinforcers obtained across sessions were analyzed by curve fitting and acquisition was defined as a better fit to a sigmoid over a linear function. For animals that met this criterion, the day at which the midpoint between initial baseline and asymptote of responses rates was used to estimate rate of acquisition. Extinction was examined by response-contingent lever retraction without drug.
Results: For both drugs, active lever responses began to increase after 7-13 days. Unexpectedly, nicotine, but not cocaine, produced a similar increase in inactive lever responses. A greater percentage of animals acquired cocaine self-administration at a higher asymptote relative to nicotine self-administration; however, rate of acquisition across days appeared comparable. During extinction, nicotine-trained animals exhibited low initial response rates that persisted without decrement across 21 sessions, whereas cocaine-trained animals had high initial responses rates that declined across sessions.
Conclusions: The main differences across drugs were the higher reinforcement and extinction response rates with cocaine and the higher inactive lever response rates with nicotine. The reason for nicotine-induced inactive lever responses is not clear, but a possible explanation is that the act of lever pressing acquires nicotine-conditioned reinforcing effects.
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DRUNK AND DRUGGED DRIVING ON BRAZILIAN HIGHWAYS.

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Aims: To obtain the prevalence of alcohol and drugs in a sample of private and professional drivers of highways that cross the 27 state capitals.
Methods: randomly selected drivers were interviewed from 12pm to 12am (Fridays and Saturdays). After each interview, 3,398 drivers (94.3% male, 79.9% cars+motorcycles, 20.1% buses+trucks) were breathalized, and had their saliva tested for drugs.
Results: 309 (9.1%) drivers reported drinking on the day of the interview. The overall BAC+ rate was 4.8% (4.9% for cars, 1.2% for buses, 4.5% for trucks, and 5.8% for motorcycles (p=0.006). BAC+ findings were more frequent after 8pm (6.8% vs 3.7%, p<0.001). Overall, the drug prevalence was low (2.1% cocaine, 1.5% marijuana, 1.0% benzodiazepines). Truck drivers had higher levels of amphetamines compared to others (3.8%, vs. 0.4% for cars and 0.2% for motorcycles - bus drivers had no amphetamine detected p<0.001). However, amphepramone and femproporex were not included in analysis. Reported DUI was more frequent among car (18.6%) and motorcycle (17.4%) drivers, and less frequent among truck (7.4%) and bus (4.4%) drivers (p<0.001). Drinking 4x or more/week was reported by 3.6% of motorcycle, 3.2% for car and bus and 2.4% of truck drivers (p=0.01). Binging in last year was evenly distributed among cars, motorcycles and trucks (72.6%, 71.9% and 71.2%) but lower for buses (61.1%, p<0.001). On average, 60% reported ever being a passenger of a drunk driver. A preliminary survival curve of the temporal effects of the law divided by three groups shows an increase in the cumulative probability of drinking and driving from almost 0 in month 1 to 0.3 after 15 months.
Conclusions: Frequent/binge drinking were common, but professional drivers seem to be more conservative. Although BAC levels were low, there is an increasing trend,potentially due to lack of enforcement. Amphetamine levels may be artificially lowered, since specific types were not analyzed.
Financial Support: SENAD, Brazil

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TRAUMATIC EVENT RE-EXPOSURE INCREASES TREATMENT-SEEKING IN SYRINGE EXCHANGE PARTICIPANTS.

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Aims: Approximately one-third of injecting drug users not in treatment are re-exposed to a traumatic event each month (Peirce et al., 2006). The present study was designed to determine whether this alarmingly high rate of re-exposure is associated with changes in treatment-seeking or drug use patterns.
Methods: Syringe exchange participants (N=160) were followed for 12 months (111 men and 49 women). Monthly assessments included the following dichotomous variables: re-exposure to any traumatic event; stated interest in substance abuse treatment; having called to obtain treatment; entering treatment; any use of syringe exchange; any use of other community resources; any cocaine use; and daily heroin use. Generalized estimating equations (Zeger & Liang, 1986) were used to model the relationship between traumatic event re-exposure and the outcome variables across months and participants. Results are presented as odds ratios with 95% confidence intervals.
Results: Traumatic event re-exposure increased participants' interest in treatment [OR=1.30 (1.06-1.60)] and calls to obtain treatment [OR=1.39 (1.07-1.81)]. Participants who were re-exposed also were more likely to use syringe exchange services [OR=1.32 (1.04-1.68)] as well as other community resources, such as housing shelters, medical or psychiatric clinics, and support groups [OR=1.36 (1.06-1.75)]. However, participants with traumatic event re-exposures were no more likely to enter substance abuse treatment [OR=.95 (.77-1.17)]. There was also no change to their pattern of cocaine use [OR=1.23 (.97-1.56)] or heroin use [OR=.98 (.76-1.27)].
Conclusions: Results indicate that re-exposure to traumatic events increases treatment- and help-seeking in substance users not in treatment, although does not necessarily change their drug use. Efforts to make the most of this increased motivation for treatment could translate to higher rates of treatment entry for these individuals with chronic and severe substance dependence disorders.
Financial Support: This research supported by NIH-NIDA grants K23DA015739 and R01DA012347.

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DURATION TO ACHIEVE "TAKE HOME" PRIVILEGE IN METHADONE MAINTENANCE TREATMENT AS OUTCOME PREDICTOR: RETENTION AND SURVIVAL.

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Aims: Take-home methadone dose is a privilege that can be achieved based on at least 3 months drug abstinence and normative behavior. We studied whether timing to first methadone take-home dose privilege reflect long term retention and survival of MMT patients.
Methods: All 657 former heroin addicts admitted to MMT clinic between June/25/1993 and June/24/2008 were followed up until October/2008. Duration to first take home dose and its relation to retention in treatment and survival were analyzed using Kaplan Meir survival analyses.
Results: Of the 657 patients, 435(66.2%) ever achieved take-home dose. Mean retention was longest among 110 patients with first take-home after 3-6 months 10y (95%Confidence Interval (CI) 8.8-11.2), followed by 9y (95%CI 7.7-10.3) among 98 with take home ≥ 6 and <1y, and 8.3y (95%CI 7.2-9.4) among 127 with take-home after >1y. Retention was lower among patients who got take-home before 3 months: 30 for medical reason 5.1y (95%CI 3.4-7.8), 14 admitted directly from other MMT 9y (95%CI 6.7-11.3) and 53 did not adherent guidelines 6.3y (95%CI 5-7.6). The shortest retention was among 222 who have not achieved any take home doses 2.2y (95%CI 1.8-2.7) (p<0.0005). Survival since admission was longest among patients who ever vs. never got take-home doses: 13.2y (95% CI 12.8-13.6) vs. 12.3y (95% CI 11.5-13.1) respectively, (p=0.04), and was longest among those who achieved take home dose after 3-6 months 14.1y(95% CI 13.4-14.7.
Conclusions: Short time to achieve first "take home" dose reflects patient's best outcome, (longest retention and survival). More studies are needed to characterize this subgroup of patients that are getting better faster and for longer period.
Financial Support: The Adelson Family Foundation

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EXTENDED-RELEASE INJECTABLE NALTREXONE ATTENUATES BOLD SIGNAL ACTIVATION TO OLFACTORY AND VISUAL CUES IN DETOXIFIED ALCOHOL-DEPENDENT VOLUNTEERS.

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Aims: Oral naltrexone reduces heavy drinking via diminished reward and craving, but is less consistent as an abstinence promoter, whereas once-monthly XR-NTX appears to help maintain abstinence as well. Because enhanced reactivity to conditioned cues is thought to play an important role in relapse, the present study was conducted to determine if cue reactivity is attenuated by XR-NTX.
Methods: Twenty-eight detoxified alcohol-dependent adult (48.36 ± 7.43 yrs) men and women participated in a structured cue reactivity paradigm during BOLD fMRI. They were randomized to receive a single i.m. injection of either XR-NTX or placebo under double-blind conditions; the fMRI/cue reactivity procedure was repeated two weeks later. Both visual (neutral and alcohol) and odor (rose water or preferred alcoholic beverage) cues were presented in an interleaved manner for 28 minutes. Participants responded to queries "want to drink alcohol" and "want to avoid drinking alcohol" every 2 minutes while in the scanner via a 9-point Likert scale.
Results: Alcohol-related visual and olfactory cues elicited significant increases in multiple brain regions including orbital and cingulate gyri, inferior frontal gyrus and middle frontal gyrus. Compared to baseline, BOLD signal activation in these regions during the second scan was significantly attenuated in XR-NTX-treated individuals compared with the placebo-treated group. Mean craving scores decreased 1.1 ± 0.52 with XR-NTX vs. 0.47 ± 0.54 with placebo (p=NS).
Conclusions: As the affected brain regions in this study are associated with the integration of emotion, cognition, reward, punishment and learning/memory, these findings suggest that XR-NTX may attenuate the salience of cues that have been associated with alcohol. Such an effect on brain function may interrupt the processes associated with "slips" and relapse and thus may contribute to XR-NTX's ability to maintain abstinence.
Financial Support: Sponsored by Alkermes, Inc and NIDA Grant DA000343 (SEL)

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PSYCHOSOCIAL CORRELATES OF SEX TRADE AMONG FEMALE DRUG USERS IN BALTIMORE, MARYLAND.

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Aims: To examine psychosocial correlates of sex trade among women who use illicit drugs in order to inform interventions for HIV and other infectious diseases, including those that are sexually transmitted.

Methods: Two hundred and ninety-two women (63.9% African-American, 36.1% White) who had used drugs in the past 6-months were recruited from Baltimore, Maryland to participate in the NEURO-HIV Epidemiologic Study. Participants completed a baseline assessment including the HIV Risk Behavior Interview and a demographic questionnaire. Participants also gave blood to test for their HIV, HBV, and HCV serostatus. Simple and multiple logistic regressions were used to identify univariate and multivariate psychosocial correlates of sex trade. Significant simple correlates at p<.10 were included in the multiple regression analysis.

Results: Thirty nine percent of women reported a lifetime history of sex trade for either drugs or money. Thirteen psychosocial correlates were significantly associated with sex trade in the simple regression analyses and eight remained significant in the multiple regression analysis. The multivariate model accounted for 55% of the variance in lifetime sex trade. Drug use variables associated with lifetime sex trade in the multivariate model included ever used cocaine and family history of drug use. Drug-using women who had ever used cocaine (AOR = 5.23, 95% CI = 1.23-21.22), and or who had a family history of father using drugs (AOR = 2.56, 95% CI = 1.13-5.76), were significanty more likely to have traded sex during their lifetime compared to drug using women who had never used cocaine and/or had no family history of father's drug use.

Conclusions: These results identify a number of psychosocial correlates of sex trade that may inform future HIV and infectious disease prevention interventions.

Financial Support: This research was supported by grants 2T32DA007292 and R01DA014498 from the National Institute on Drug Abuse (PI: William Latimer, Ph.D., M.P.H) as well as grant R03DA024981 from the National Institute on Drug Abuse (PI: Leah J. Floyd, Ph.D.)

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ELEVATED EXPRESSION OF 5-HT1B RECEPTORS IN THE MESOLIMBIC PATHWAY ENHANCES THE REINFORCING EFFECTS OF COCAINE USING THE SELF-ADMINISTRATION MODEL IN RATS.

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Aims: The mesolimbic pathway originating in the nucleus accumbens (NAc) and projecting to the ventral tegmental area (VTA) is densely populated with serotonin-1B receptors (5-HT1BRs), which have been shown to modulate drug experience-dependent behavioral plasticity including cocaine-induced hyperactivity and conditioned place preference.

Methods: To further elucidate the role of these receptors in cocaine reinforcement, this study utilized viral mediated gene transfer to transiently increase the expression of 5-HT1BRs in the mesolimbic pathway. After establishing a stable within session cocaine dose-response function, rats received a viral vector containing either hemagglutinin-tagged 5-HT1B and green fluorescent protein (5-HT1B–GFP) cassettes or a green fluorescent protein cassette alone (GFP-only) injected into the medial NAc shell, which sends projections to the VTA.

Results: 5-HT1B–GFP injections shifted the dose–response curve for cocaine self-administration upward and to the left and increased break points on a progressive ratio schedule, indicating increased reinforcing effects of cocaine.

Conclusions: These results demonstrate that 5-HT1BRs within the NAcsh and VTA modulate the reinforcing effects of cocaine and further suggest that 5-HT1BRs may be a novel target for developing medications for cocaine dependence.

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A COMPARISON OF COMMUNITY CORRECTION PARTICIPANTS ENROLLED IN METHADONE MAINTENANCE TREATMENT.

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Aims: Research on community corrections participants enrolled in Methadone Maintenance Treatment (MMT) is scarce. This study examines the characteristics of opioid dependent persons in Treatment Alternatives for Safer Communities (TASC) in Alabama who enrolled in MMT compared to opioid dependent participants in TASC who were not in MMT.

Methods: Data from 24,365 participants who were enrolled in TASC from 2002 to 2007 were analyzed; 3,027 (12.4%) of whom met criteria for opioid dependence. The sample of participants with opioid dependence were young (M = 31.19 years), Caucasian (79.6%), males (65.4%), not married (79.8%), with at least a high school education or GED (60.5%). Forty-six percent reported being employed; however, 73.4% of the sample did not have insurance.

Results: Approximately 9% of opioid dependent participants (N=268) were enrolled in MMT. Analyses comparing MMT to non-MMT participants found MMT participants were more likely to be white (10.7% vs. 2.1%; p<0.001), older (Median age = 32 years vs. 29 years; p<0.001), have insurance (12.4% vs. 7.7%; p<0.001), and be married (14.2% vs. 6.4%; p<0.001). Participant who did not participate in MMT were more likely to be dependent on other substances (i.e., alcohol, cocaine, amphetamines, or marijuana (p < .001) or hallucinogens, (p < .05). Gender, education, having children, or a history of violence did not impact MMT participation. Participation in MMT was also associated with successful completion of TASC (44.2% vs. 30.5%; p<0.001).

Conclusions: These findings suggest that individuals who participated in MMT may have fewer barriers to accessing treatment (e.g., have insurance and fewer substance use problems). Further, being able to access MMT was related to a positive TASC outcome. Targeting MMT to underserved opioid dependent users (e.g., young, uninsured, African Americans) may improve community corrections outcomes.

Financial Support: This study was supported by UAB Department of Psychiatry internal funding.

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FROM CONCEPT TO PRACTICE: A STRATEGIC APPROACH IN DISSEMINATING MOTIVATIONAL INTERVIEWING IN A RURAL AND FRONTIER STATE.

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Aims: Learning to communicate utilizing motivational interviewing (MI) with fidelity is challenging for most counselors, especially if they have been used to a more confrontational style of doing counseling. Counselors often find that MI is intuitively easy, but in reality find implementation difficult. Furthermore, clinical supervision is crucial in maintaining fidelity. The goals for this poster are to present a model for implementation of MI in a rural/frontier state: 1) Intro MI training, 2) Advanced MI training, and 3) clinical supervision training enhanced through the use of MIA-STEP. In addition, results from the pre and post survey among the counselors will be presented, including their subjective level of comfort with implementation of MI.

Methods: Subjects: 210 counselors and 42 clinical supervisors were recruited from 8 public health service centers across the State of North Dakota.

Results: The results from the pre and post survey indicated that the counselors are very satisfied with the model of training, and also with the clinical supervision they received. Furthermore, they felt they were able to implement MI in their clinical practice.

Conclusions: This project was very resource intensive, and only survey data so far were available, the level of implementation on MI with fidelity is not possible to be certain about until tape-reviews are completed.

Financial Support: This project is supported by the Center for Substance Abuse Treatment (CSAT) and Substance Abuse and Mental Health Services Administration (SAMHSA) and the North Dakota Department of Human Services Division of Mental Health & Substance Abuse Services.

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DAILY LIFE HOUR-BY-HOUR, WITH AND WITHOUT COCAINE: AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY.

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Aims: To compare hour-by-hour daily activities in cocaine-dependent outpatients during urine-verified periods of use and abstinence.
Methods: In a cohort design, a volunteer sample of 112 methadone-maintained cocaine- and heroin-abusing outpatients provided ecological momentary assessment (EMA) data on handheld computers. EMA responses to questions about current companions, location, activities, and moods were compared across periods of use and abstinence using SAS Proc Glimmix (binary outcomes) and Proc Mixed (continuous outcomes).
Results: A total of 112 participants contributed 10,781 person-days. Participants' mean age was 40.7 (SD 8.1) years, 61% were African-American, 38% were unemployed, and 45% lived with their parents or other family member. Participants reported using cocaine a mean of 20 out of the last 30 days (SD 9.2) and the primary route of cocaine administration was smoking (48%). During cocaine-using weeks, participants were more likely to be alone (OR 1.32 [1.18-1.47], p<0.0001) or with coworkers (OR 1.01 [1.00-1.02], p<0.02); more likely to be at work (OR 1.54 [1.20-1.96], p<0.002), at another's house (OR 1.54 [1.27-1.85], p<0.0001), or waiting for a bus, ride, etc. (OR 1.15 [1.01-1.30], p<0.04); and more likely to be watching TV/DVDs/Video (OR 1.35 [1.16-1.56], p=0.0002), working (OR 1.43 [1.16-1.75], p<0.002), or walking (OR 1.52 [1.28-1.82], p<0.0001). They were also more likely to report feeling bored (F[1,33]=7.22, p<0.02) or tired (F[1,33]=4.15, p<0.05) and less likely to report feeling relaxed (F[1,33]=11.09, p<0.003). Many of these reports showed complex hour-by-hour patterns.
Conclusions: Weeks of cocaine use and abstinence in outpatients are associated with distinct patterns of behavior and mood; the detailed hourly data reported here should help inform treatment interventions aimed at changing daily activities.
Financial Support: This study was supported by the Intramural Research Program (IRP) of the National Institute on Drug Abuse (NIDA), National Institutes of Health.

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DEVELOPMENT OF A RISK REDUCTION INTERVENTION FOR INJECTION DRUG USERS TO REDUCE BACTERIAL AND VIRAL INFECTIONS.

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Aims: Aims: Risk reduction interventions to reduce disease for injection drug users (IDUs) have focused primarily on reducing viral infections (e.g., HIV). Although bacterial infections (e.g., skin infections, endocarditis) are high amongst IDUs and create significant morbidity and mortality, little focus has been placed on ways to reduce these infections. We utilized the Stage Model of Behavioral Therapies to develop a risk reduction intervention that addresses bacterial and viral infections among IDUs within the framework of the Information-Motivation-Behavioral Skills Model. Focus group data were used to guide the development of a two-session intervention.
Methods: Methods: Four gender-specific focus groups (N = 32) were conducted with active IDUs in Denver. Four major themes (Experiences with Bacterial Infections, Perceived Factors Contributing to Bacterial Infections, Barriers to Practicing Risk Reduction, and Intervention Format Preferences) were examined in a qualitative content analysis to inform intervention development.
Results: Results: IDUs named skin abscesses as the major type of bacterial infection experienced in Denver. The most commonly mentioned contributing factors included: the cut of the drug and how it is transported, reusing needles, injecting intramuscularly or subcutaneously, missing one's vein, injecting black tar heroin or cocaine, and failing to clean one's skin before injecting. Participants reported that access to needles and other injection supplies was the most significant barrier to risk reduction, followed by withdrawal symptoms. Participants were divided about whether a risk reduction intervention should be a group or individual format.
Conclusions: Conclusions: Focus group participants discussed perceptions of bacterial infection risks that have aided in the development of the two-session intervention manual, which will be presented and discussed.
Financial Support: Support: Supported by NIDA 1 R21 DA026773-01

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PSYCHOSOCIAL AND SUBSTANCE USE SEVERITY IN UNEMPLOYED PATIENTS ENROLLED IN METHADONE MAINTENANCE AND PSYCHOSOCIAL ABSTINENCE-BASED PROGRAMS.

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Aims: Employment is a potent predictor of positive treatment outcomes (Kidorf et al, 2004). Efforts to improve rates of employment in persons with substance use disorders (SUDs) have generally been disappointing. The present study examined psychosocial and medical co-morbidities in unemployed patients, separately in methadone maintenance and psychosocial abstinence-focused programs participating in a multi-site clinical trial through the NIDA Clinical Trials Network (CTN).
Methods: Participants were recruited from 6 drug free (DF)(N = 327), and 5 methadone maintenance (MM) (N = 301) community treatment programs participating in the RCT of the Job Seekers' Workshop (JSW) through the CTN. Eligible participants were ≥ 18 years old, met DSM-IV criteria for lifetime SUD, reported unemployment or underemployment (<20 hrs/week in month before study enrollment) and completed at least 30 days of SUD treatment. Participants completed a standardized interview at baseline, including demographic information and the Addiction Severity Index-Lite. Analyses compared MM and DF program patients on a variety of measures using chi-square for categorical variables and student's t-test for continuous variables.
Results: Demographic comparisons: MM participants were more likely to be older (44 years and 39 years, respectively (p<.05), female (60% vs 46%), unemployed (87% vs 80%), have a disability (23% vs 9%), and less likely to be Caucasian (26% vs 55%) than participants enrolled in DF treatment (p<.05 for all analyses). Psychosocial characteristics: MM participants spent significantly less time enrolled in psychiatric treatment than DF participants (56% vs 73%, p<.001) but were more likely to experience chronic medical problems (66% vs 51%).
Conclusions: Future research will examine how psychosocial characteristics related to employment outcomes with JSW intervention and control group conditions. Study findings have implications for future drug abuse treatment programming and linkages with programs that provide job training and employment support.
Financial Support: NIDA 2U10DA013034

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TOXIN DELIVERY AFTER BLACK & MILD LITTLE CIGAR SMOKING.

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Aims: There has been an increasing use of little cigars among urban, African American youth with a popular brand choice being the Black & Mild (B&M). Some users "freak" or "hype" the B&M by removing the inner paper liner and then repacking the tobacco in the belief that the liner causes cancer and addiction. Carbon monoxide (CO), nicotine boost, and heart rate change were compared to determine if there are differences in exposure.
Methods: We recruited volunteers who ordinarily smoke both cigarettes and B&M. In two sessions they smoked ad lib B&M with and without (amended) the paper liner; in another session they smoked their usual brand of cigarette ad lib. Twelve participants (all African American; 10 men) completed the study. Their average age was 43.7 yr (range 29-55). Three participants reported usually smoking the entire B&M tobacco rod at one time; the others reported smoking between 1/3 – 5/6 of the rod and saving the remainder for later consumption. In the lab, they smoked that portion of the B&M that they ordinarily smoked.
Results: CO boost averaged: cigarette smoking, 7.2 ppm; B&M, 26.9; B&M (amended), 13.5. Heart rate increased with each smoking condition as follows: cigarette, 4.9 bpm; B&M, 7.9; B&M (amended), 6.4. Plasma nicotine increased after each condition: cigarette, 25.1 ng/ml; B&M, 10.5; B&M (amended, 11.8. Time to smoke averaged: cigarette, 6 min; B&M, 13; B&M (amended), 11.
Conclusions: Unlike typical cigar smoking where the product is puffed, 11 participants reported inhaling the smoke of the B&M. This was verified by the substantial CO boost. B&M smoking is associated with significant toxin exposure (nicotine and CO) and changes in resting heart rate. Contrary to popular belief, it does not appear that removing the paper liner of the B&M cigar reduces toxin exposure. An unintended consequence of tobacco regulation may be consumption of alternative tobacco products such as little cigars that could lead to significant toxin exposure.
Financial Support: This research was supported by grants from National Heart Lung and Blood (1R21HL086514-02) and the National Cancer Institute (1RO1CA138973-01).

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EXERCISE AND FITNESS LEVELS AMONG TREATMENT-SEEKING SUBSTANCE-DEPENDENT INDIVIDUALS.

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Aims: Participation in sports and exercise has been shown to help prevent the development of substance use and abuse among adolescents. The protective mechanisms may involve mood, self-efficacy or simply the incompatibility between peak athletic performance and acute intoxication. In addition, prior research has found that aerobic exercise is useful for reducing tension and stress during recovery from substance use disorders (Read & Brown, 2003). However, fitness and exercise levels among substance-dependent individuals have not yet been examined. As such, we chose to characterize baseline exercise and fitness levels for individuals entering outpatient substance abuse treatment in order begin developing exercise-based interventions for outpatient treatment.
Methods: The Physical Activity Rating (PA-R) scale was developed to provide an assessment score of 0-7 on a person's level of regular physical activity (George et al., 1997). The PA-R was administered to 109 consecutively screening treatment seeking individuals with cocaine, alcohol, or combined cocaine and alcohol (CAD) dependence. Additional data on height and weight, gender and race were gathered.
Results: Results indicate that there were no differences in fitness and exercise overall, when all substance dependent groups were aggregated $F(2,106) = 1.58$, $p = .21$ for PA-R. However, when only alcohol dependent individuals were examined, there was a significant difference between Caucasians and African Americans for PA-R only, with Caucasians reporting significantly higher rates of exercise $F(1,72) = 5.54$, $p = .02$. Overall, fitness levels were below average for all subjects, and mean BMI was 29.24, with 43 (39.45%) subjects classified as obese, 44(40.37%) as overweight and only 22 (20.18%) as normal weight.
Conclusions: Taken together, findings indicate that there is substantial room for improving fitness and exercise among treatment-seeking substance-dependent subjects. As such, exercise may be a viable adjunctive or stand-alone treatment for substance abuse.
Financial Support: Supported by NIH grants P50DA012756, P60DA005186 and K01DA025073.

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BLOCKADE OF 5-HT2A RECEPTORS IN THE MEDIAL PREFRONTAL CORTEX ATTENUATES CUE-ELICITED REINSTATEMENT OF COCAINE-SEEKING BEHAVIOR IN RATS.

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Aims: Blockade of serotonin 5-HT2A receptors with the selective antagonist M100907 attenuates both cue-elicited and cocaine-primed reinstatement of cocaine-seeking behavior when administered systemically. 5-HT2A receptors are densely clustered in the medial prefrontal cortex (mPFC), an area that has been implicated in the inhibition of cocaine-seeking behavior during extinction. This study examined the hypothesis that 5-HT2A receptors in the mPFC modulate incentive motivational effects of cocaine priming and cues.
Methods: Male Sprague-Dawley rats were trained to self-administer cocaine (0.75 mg/kg, IV) paired with light and tone cues. Once behavior stabilized, animals were tested for the effects of microinfusions of M100907 (0, 0.01, 0.03, 0.1, or 1.5 μg) into the mPFC on cocaine self-administration. Animals then underwent daily extinction sessions, during which responding had no consequences. After responding diminished, rats were tested for reinstatement of responding by either response-contingent presentations of the cocaine-paired light/tone cues or by cocaine priming injections (10 mg/kg, IP).
Results: Intra-mPFC M100907 microinfusions produced a small, nonspecific decrease in cocaine self-administration and cocaine-primed reinstatement that was not dose-dependent. In contrast, M100907 decreased cue-elicited reinstatement at the two highest doses (1.0 and 1.5 μg). M100907 administered without either cocaine-associated cues or a cocaine priming injection did not alter responding.
Conclusions: Overall, the results suggest that the blockade of 5-HT2A receptors in the mPFC attenuates the incentive motivational effects of cocaine-paired cues, but does not alter cocaine priming or reinforcing effects.
Financial Support: This research was supported by DA11064.

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THE SAFETY AND EFFICACY OF VARENICLINE IN COCAINE-USING SMOKERS MAINTAINED ON METHADONE: A PILOT STUDY.

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Aims: In this 12-week double-blind, placebo-controlled study we evaluated the following aims: 1) that varenicline is safe to administer in a cocaine and opiate dependent sample, and 2) that subjects assigned to the varenicline treatment condition would show lower levels of cocaine use over time.
Methods: In this double-blind, placebo-controlled trial, we compared varenicline (2 mg) to placebo treatment for cocaine dependence in 31 methadone-maintained subjects over 12 weeks. Subjects received urine screens three times per week, as well as CO levels once weekly. Weekly counseling was also provided during the 12-week study participation.
Results: Our results indicate that varenicline is safe to give to this subject population, as there were no adverse events related to medication during this study. Varenicline was no more effective than placebo for abstinence from cocaine. Treatment with varenicline was associated with a reduced number of cigarettes smoked per day, even though subjects received only a brief education for smoking cessation. The self-report reduction in smoking was corroborated by CO levels and the Fagerstrom Test of Nicotine Dependence.
Conclusions: These preliminary findings provide evidence that varenicline is safe to administer in a cocaine and opiate dependent sample. In addition, these results may point to potential therapeutic value of varenicline for smoking cessation in cocaine users maintained on methadone. While we did not find evidence that varenicline reduced cocaine use, the sample size of our pilot study may to too modest to detect any results.
Financial Support: This study was supported by the New England Veterans Administration MIRECC, NIDA grants R01DA021264, R01DA014537 and R01DA014537.

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INFLUENCE OF METHYLPHENIDATE ON THE REINFORCING EFFECTS OF CIGARETTE SMOKING.

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Aims: Stimulants increase cigarette smoking in humans in the naturalistic environment and laboratory. This study further examined stimulant-induced increases in smoking in order to elucidate the underlying behavioral mechanism(s).
Methods: This study examined the influence of methylphenidate on a discreet cigarette versus money ($0.25) choice task. Six moderate cigarette smokers (i.e., 10-20 cigarettes/day) age 18-50 completed the study, one is currently enrolled, and one to three additional participants will be recruited. Volunteers participated in six sessions (one practice and five experimental). Four doses of methylphenidate (0, 10, 20, and 40 mg) were administered, with placebo administered twice. One hour following medication administration and at 30-minute intervals thereafter, participants chose between smoking a cigarette or $0.25. The primary behavioral measure was number of cigarette choices. Data were analyzed using repeated-measures ANOVA and planned comparisons.
Results: The high dose of methylphenidate (40 mg) increased the number of cigarette choices significantly above placebo levels.
Conclusions: Results of this study suggest that methylphenidate, like d-amphetamine, increases the reinforcing effects of cigarette smoking. Future studies should examine the influence of methylphenidate on the reinforcing effects of cigarette smoking using alternative reinforcers that vary in terms of magnitude.
Financial Support: Supported by NIDA DA012665, University of Kentucky Department of Psychiatry Professorship Funds, and NCI CA124881

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THE IMPACT OF AGE OF DRUG USE DEBUT ON SUBSEQUENT HIV RISK BEHAVIOR AMONG INJECTION DRUG USERS.

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Aims: Our team of investigators is currently conducting a randomized controlled trial of the Community-friendly Health Recovery Program (CHRP) among patients entering an inner-city methadone maintenance program in New Haven, CT. In this analysis, we compare participants who met study criteria due to recent drug- or sex-related HIV risk behavior (High HIV Risk Group) vs. those who did not meet criteria (Low HIV Risk Group). The study screening form from which data were taken required a brief self-reported history of drug use including: heroin, oxycodone, cocaine, marijuana, and speedball. We compared HIV risk groups in terms of their debut using each of these drugs.
Conclusions: Our analyses demonstrated that age of first drug use was younger among members of the High HIV Risk Group vs. the Low HIV Risk Group, suggesting that age of first drug use may predict subsequent HIV risk behavior. Studies have found that those who engage in drug use at an early age tend to subsequently engage in more risky behavior. Research has shown that "early injectors" - those who report initiating injection drug use by age 15 – report overall drug use debut as early as age 12. The vast majority of HIV prevention interventions target older populations of IDUs, whereas our findings suggest that it may be worthwhile to also intervene with younger populations, with an aim toward disrupting the progression from early drug use to subsequent HIV risk behavior. Implications for the optimal timing and tailoring of behavioral HIV prevention interventions among drug users are discussed.
Financial Support: NIH/NIDA R01 DA022122 (Copenhaver, PI), Testing a Community-Friendly Risk Reduction Intervention for Drug Users.

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WHICH PAROLEES BENEFIT FROM CASE MANAGEMENT SERVICES? AN APPLICATION OF CLASSIFICATION AND REGRESSION TREE ANALYSIS.

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Aims: Using a sample of parolees who had participated in a test of case management to increase parolees' participation in community drug treatment and to improve drug use and crime outcomes. we sought to determine characteristics associated with admission to community treatment and with arrest.
Methods: Characteristics predictive of outcomes were identified using Classification and Regression Tree (C&RT) analysis, a non-parametric method that identified mutually exclusive sets of characteristics predictive of a desired outcome. Covariates were age, race, gender, employment, education, marital status, social support, primary drug, drug severity, treatment motivation, prior treatment, self-help participation, Brief Symptom Inventory, criminal thinking scales, and prior arrests. C&RT analysis was applied to all study participants (N=812), and then the treatment and control groups were compared on the resulting sets of characteristics.
Results: For treatment admission, parolees with high motivation were more likely to enter treatment. Among those with high motivation, those who scored low on Personal Irresponsibility were more likely to enter treatment. Among those with low motivation, older parolees were more likely to enter treatment.
For arrest, parolees scoring high on Power Orientation had a higher likelihood of being arrested. Among those with high Power Orientation, arrests were higher among those whose primary drug was either cocaine or one of the less commonly used drugs.
The two study groups did not differ on any of the sets of characteristics.
Conclusions: To increase treatment participation, correctional systems might target case management services to older parolees with high motivation and low Personal Irresponsibility. To reduce arrest, case management services would seem important for parolees who use cocaine and who have high Power Orientation. C&RT Analysis offers an alternative approach to developing clinical decision rules about how to provide services that will increase clients' likelihood of success.
Financial Support: NIDA U01DA16211

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IMPAIRED ANTERIOR CINGULATE CORTEX GLUTAMATERGIC NEUROTRANSMISSION IN ADOLESCENT MARIJUANA USERS.

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Aims: Converging evidence from neuroimaging and neuropsychological studies indicates that heavy marijuana use is associated with cingulate dysfunction. However, there has been limited human data on *in vivo* biochemical brain changes after chronic marijuana exposure. The present study used ^{1}H MRS to determine whether reductions in glutamate (Glu) or other proton metabolite concentrations would be found in the anterior cingulate cortex (ACC) of adolescent marijuana users compared with non-using controls.
Methods: Adolescent marijuana (MJ) users (N = 17; average age 17.7 years) and age-matched healthy control (HC) subjects (N = 22; average age 17.5 years) were scanned using a Siemens 3T Trio MRI system. A PRESS sequence (TE = 30 ms) was used to acquire metabolite and unsuppressed water ^{1}H MRS data from a 22.5 mL voxel within the ACC. Spectra were fitted using LCModel and all metabolite integrals were normalized to the unsuppressed water integral (scaled; x 10^{-10}). Two-tailed t-tests were performed for Glu, creatine (Cre), myo-inositol (Ins), N-acetyl aspartate (NAA) and choline (Cho).
Results: Within-voxel tissue-type segmentation did not reveal any significant differences in gray/white matter or CSF content between the two groups. The MJ cohort showed significantly decreased ACC Glu (MJ/HC = 2.35 ± 0.23/2.61 ± 0.45, P = 0.034) and Cre (MJ/HC = 2.06 ± 0.23/2.22 ± 0.19, P = 0.016) levels with a trend towards significance observed for reduced Ins (MJ/HC = 1.66 ± 0.22/1.80 ± 0.22, P = 0.063). No significant differences were detected for ACC NAA or Cho levels.
Conclusions: The reduced Glu levels in the MJ cohort is consistent with precedent rat electrophysiological and human ^{1}H MRS data, and likely reflects an impairment of ACC glutamatergic neurotransmission within these individuals. The reduced Cre and Ins levels observed in the MJ subjects might infer altered ACC energetic status and glial metabolism, respectively. These results expand on previous fMRI data reporting altered cingulate function in individuals with marijuana-abuse.
Financial Support: Supported by NIH R01 DA020269.

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RESOLVING DIAGNOSTIC COMPARABILITY OF OPIATE ADDICTION USING TWO DATASETS COLLECTED 30 YEARS APART.

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Aims: Historical changes in diagnostic criteria for drug addiction make it near impossible to compare rates of "addiction" using one diagnostic system to another. Some scholars considered the diagnostic criteria used in Robins et al.'s classic Vietnam veteran study (1975) insufficient to arrive at an accurate rate of opiate addiction comparable to the present day DSM-IV rate. Re-estimating the dependence and abuse rates that would have the same interpretation as the contemporary literature is a worthwhile effort because this study influenced drug policies at that time. Furthermore, re-estimate methods can be used for other studies of historical significance because diagnostic criteria continue to evolve today as in the case of the upcoming DSM-V release. The main objective of this paper is to re-estimate the one-year prevalence rates of opiate addiction and abuse among this Vietnam veteran cohort using limited DSM-IV criteria.
Methods: Two datasets were reanalyzed. (1) Vietnam Era Study (VES): The original Vietnam veteran cohort included 898 service members who were interviewed within 12 months post-deployment in 1972. (2) National Epidemiologic Survey on Alcohol and Related Conditions (NESARC): The Wave 1 dataset included a general-population sample (n=43,093). Opiate addiction criteria, withdrawal symptoms, other related questions and a duration requirement in the 1972 VES were mapped onto the DSM-IV dependence or abuse symptoms and duration criteria in NESARC.
Results: Preliminary results show that the weighted one-year (in-Vietnam) opiate dependence prevalence was 18.9% based on the available DSM-IV withdrawal symptom criteria, while Robins reported 18.9% from their published addiction criteria. The addiction rate would have been lower if the DSM-IV duration criteria had been applied.
Conclusions: A rapid pace of dependence to opiates is possible in certain situations. Appropriateness of the current 12-month duration criteria for opiate dependence is undetermined from the current study.
Financial Support: R01DA09281, R01MH60691

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IMPACT OF D-CYCLOSERINE ON COCAINE CUE EXTINCTION.

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Aims: Aims: Considerable evidence suggests that the glutamate system plays a role in associative learning and memory consolidation as well as in the maintenance of and relapse to cocaine use. The aim of the present study was to evaluate the effect of the partial glutamate NMDA-receptor agonist, D-cycloserine (DCS), on cocaine cue reactivity and extinction learning in cocaine-dependent individuals.

Methods: Methods: Subjects were outpatients aged 18-65 who met DSM-IV criteria for cocaine dependence; a negative UDS was required before each extinction session. Multi-modal cocaine cues were presented 3 times over 1 hour during 3 separate extinction sessions (Mon, Wed, and Fri). Subjects were randomly assigned to receive 50mg DCS or placebo (PBO) 5 min prior to each session on 1 of 3 schedules: PBO/PBO/PBO; DCS/PBO/DCS; DCS/DCS/DCS). Subjective craving ratings during baseline and after each cue sequence were evaluated. A linear mixed model was used to test for group and time effects.

Results: Results: 29 participants completed study procedures (group Ns=9-11). There were no group differences in demographic characteristics or in baseline craving ($p=0.97$). Although all groups exhibited significant extinction [$F(1,489)=123.64$, $p<0.0001$), a significant group x time interaction [$F(4,489)=5.57$, $p=0.004$] indicated that extinction of craving was greatest in the placebo-treated group.

Conclusions: Conclusions: Under the current drug administration parameters, DCS did not facilitate extinction of cue-induced craving. While extinction-based learning may have therapeutic potential for cocaine dependence, the critical role of glutamate in the reinforcing properties of cocaine may give glutamatergic agents a unique profile in cocaine-dependent individuals and the parameters of DCS administration must be carefully explored.

Financial Support: Supported by: NIDA grant R01DA023188 (Brady).

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ARE ADOLESCENTS GAMBLING WITH CANNABIS USE? A LONGITUDINAL STUDY OF OBSERVED AND REPORTED IMPULSIVITY MEASURES IN RELATION TO ADOLESCENT SUBSTANCE USE. THE TRAILS STUDY.

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Aims: To examine what role impulsive behaviors play in lifetime and repeated cannabis use, as compared to tobacco use during adolescence. This study examined (1) the predictive value of observed versus reported measures of impulsivity on the onset of cannabis use, and if lifetime tobacco and cannabis users can be differentiated by their level of impulsivity, and (2) the predictive value of observed versus reported measures of impulsivity on repeated cannabis use, and to determine if repeated tobacco and cannabis users can be differentiated by their level of impulsivity.

Methods: The present study involves data from 667 male and female adolescents, from two time points of the TRacking Adolescents' Individual Lives Survey (TRAILS) study, who participated in the Groningen Behavioral Experiment Bangor Gambling Task and completed self-report surveys assessing cannabis use behavior (mean age 16.11 years) and personality characteristics (mean age 13.56 years)

Results: Higher levels of BAS functioning increased the likelihood that adolescents would ever use substances such as tobacco or cannabis during their lifetime. In contrast, low BIS functioning increased the likelihood of repeated cannabis use. Repeated tobacco users did not significantly differ from lifetime users or repeated cannabis users by their BIS functioning. The BGT measures were not significant in relation to lifetime or repeated use of cannabis or tobacco.

Conclusions: High BAS seems to be more important for experimental substance use whereas low BIS seems to be more important for progression into regular cannabis use.

Financial Support: In part by the Netherlands Organization for Scientific Research (NWO) – Vidi scheme, Netherlands (452-06-004 to ACH and APvL).

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GENETIC STUDIES OF THE PROOPIOMELANOCORTIN GENE WITH HEROIN ADDICTION IN ETHNICALLY DIVERSE POPULATION.

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Aims: Our group has found that variant -184G>A of the promoter of the ACTH receptor (melanocortin receptor type 2, MC2R) gene is associated with the protective effect from heroin addiction in Hispanics. Clinical data from another group showed that -179A>G, located in proximity to -184G>A, influences the outcome of the ACTH stimulation test in Europeans. Proopiomelanocortin (POMC) is a source of a peptide, ACTH, which plays a key role in regulation of the HPA axis that controls stress. In this study we genotyped the POMC gene and evaluated a number of known variants for association with heroin addiction.

Methods: To search for novel variants, we performed Sanger sequencing of the exons 1, 2, and 3 and 500 bp promoter region of the POMC gene (NM_000939) using 205 DNA samples. The variants rs28930368 (282C>T), rs35254395 (288-289ins AGCAGCGGC), rs2071345 (585C>T) and rs1042571 (867C>T) were found in high frequency (>2%) in one or more ethnicities studied. Known variants rs1042571 (exon 3), rs934778 (intron 1), rs6545975 and rs6713532 (both in intron 2) were genotyped using TaqMan in a larger number of samples (633 total). Because of technical issues which precluded use of TaqMan for genotyping of rs28930368, rs35254395 and rs2071345, these variants were genotyped in 633 samples by Sanger method.

Results: We found that 282C>T and 585C>T were in complete linkage disequilibrium. No new variants were identified. We did not find an association of any variants with heroin addiction in any ethnicities.

Conclusions: We did not find an association of the variants of the POMC gene with heroin addiction. However, previous evidence suggests involvement of disregulation of HPA axis in the initiation and perpetuation of drug addiction. Testing of other variants of POMC and other genes involved in stress responsivity is needed.

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TRYING TIMES: REAL-TIME REPORTS OF COCAINE-USE OCCASIONS WHEN EFFORTS AT ABSTINENCE WERE LOW OR HIGH.

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Aims: To examine the amount and context of cocaine use when patients express high versus low intention to be abstinent.

Methods: In a cohort design, a volunteer sample of 70 methadone-maintained outpatients provided ecological momentary assessment (EMA) data of cocaine use on handheld computers. Each time participants reported cocaine use, they were asked: "Had you been trying not to use?" They also reported their companions, location, and activities when the use episode started. Results were examined using contingency tables of observed and expected values.

Results: Participants reported trying not to use in most (600 of 661) cocaine use events. Although the amount of cocaine used did not differ between the low and high intention events, the context of use did differ. Use when trying to abstain was especially likely: at another's home; in the presence of other family members (i.e. not spouse or children); and while eating, listening to music, talking on the phone, or walking. Use when not trying to abstain was especially likely: at home and at work; in the presence of spouse or coworkers; and while resting, working, copping, or hustling for money.

Conclusions: Most cocaine use occurs when patients report actively trying to abstain. Reports of high or low effort to abstain may represent two different types of risk: situations associated with low efforts to abstain are those in which individuals let down their guard; situations associated with high efforts to abstain are those in which circumstances overcame those efforts.

Financial Support: This study was supported by the Intramural Research Program (IRP) of the National Institute on Drug Abuse (NIDA), National Institutes of Health.

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PRELIMINARY NIATX 200 RESULTS: WAITING TIME REDUCTION FROM FIRST REQUEST TO ASSESSMENT.

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Aims: This study presents preliminary findings from the 201 treatment agencies participating in the NIATx 200 research initiative. Over the 18-month intervention period, providers were encouraged to adopt a number of business practices aimed at improving treatment access, such as walk-in intake appointments and paperwork reduction. The primary research question was: Did providers reduce waiting time from first request to assessment?
Methods: Using a standard client profile (self-referral, self-pay from the community) we randomly called the intake department of each participating agency on a monthly basis, beginning two months prior to the start of the intervention and throughout the 18-month intervention period. We recorded the date of each phone inquiry and asked the agency for the date of the first available assessment opportunity. We calculated the mean monthly waiting time across the 201 agencies and tested for trends within each site using polynomial regression models with autocorrelated errors associated with repeated observations for each agency.
Results: We obtained monthly data from an average of 195 of the 201 randomized participants over the analysis period. Waiting time from first request to assessment was reduced from 7.6 days at baseline to 5.7 days at the end of the intervention period. The quadratic time effect was found to be statistically insignificant while the linear trend was estimated to be a reduction of 0.1 waiting days per month with a p-value of 0.003. Consecutive agency model errors were autocorrelated at 49 percent.
Conclusions: These results indicate that NIATx 200 providers were successful in reducing the waiting time from first request to assessment, an important but often ignored dimension of the client's treatment experience.
Financial Support: This project was supported by the National Institute on Drug Abuse (R01 DA020832)

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COCAINE INDUCES SEX DIFFERENCES IN PKA PHOSPHORYLATION SUBSTRATES, BUT NOT ERK PHOSPHORYLATION.

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Aims: Sex differences in intracellular dopamine pathways may contribute to the known sex differences in psychomotor responses to cocaine and differential development of dependence. This study aimed to determine whether there are sex differences in the activation of the extracellular signal-regulated kinases (ERK1/2, or p44/p42 MAPK) and PKA phosphorylation-dependent substrates in the nucleus accumbens (NAcc) of male and female rats.
Methods: Total locomotor responses and protein levels of ERK1/2 and phosphorylated PKA substrates in the nucleus accumbens (NAc) and caudate-putamen (CPu) were measured in male and female rats at baseline or after acute cocaine administration (one 30-mg/kg intraperitoneal injection).
Results: Similar to our previous findings, total locomotor activities were higher in female rats after this single cocaine administration. Females had higher levels of phosphorylated PKA substrates after cocaine administration, and this change lasted longer and had a greater magnitude than in cocaine treated male rats. Furthermore, although cocaine administration increased the phosphorylation of ERK proteins, there were no sex differences in p-ERK protein levels either at baseline or after acute cocaine administration.
Conclusions: Taken together, these findings suggest that sex differences in basal and cocaine-induced alterations in PKA signaling activity in the NAcc may contribute to sex differences in psychomotor responses to cocaine. However, not all the components of the DA-intracellular signaling pathway maybe heightened in female rats as ERK phosphorylation patterns did not differ between the sexes.
Financial Support: This work was supported by SCORE 506-GM60654, MIDARP DA12136, and RCMI RR-03037.

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CUMULATIVE OCCURRENCE OF ILLEGAL DRUG USE CLINICAL FEATURES IN 16 WORLD MENTAL HEALTH SURVEYS COUNTRIES.

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Aims: Studying community samples of adult users of internationally regulated drugs (IRD) across 16 countries, we sought to estimate the cumulative occurrence of 13 clinical features associated with IRD use.
Methods: Data are from community surveys conducted in 16 countries for the World Mental Health Surveys Initiative (WMHSI). All assessments used the WMH CIDI structured interview, with coverage of basic demographics and IRD use clinical features such as social problems and tolerance. The cumulative occurrence of individual clinical features was estimated for adults who had used any illegal drug at least once, accounting for a complex sample design and appropriate weights. Subsequently we used meta-analysis for estimation of a summary value.
Results: Cumulative occurrence of clinical features reflecting socially maladaptive behavior ranged from 2% for recurrent legal problems (95% CI: 0.02, 0.03) to 10% for hazard laden use (e.g., operating machinery; 95% CI: 0.09, 0.11). "Difficulties cutting down on drug use" were at a lower level (3%; 95% CI: 0.03, 0.04) and "using more than intended" was in a higher level of cumulative occurrence (10%; 95% CI: 0.09, 0.11). Heterogeneity was observed more in analyses concerning lifetime history of use, less in analyses focused upon recent users.
Conclusions: Individual experiences after onset of illegal drug use vary across different clinical features. Observed heterogeneity between sites may prompt caution when considering whether public health or treatment interventions are adapted from one site to another (e.g., U.S.A. to overseas).
Financial Support: R01DA016558, K05DA015799, and see WMHSI web site (http://www.hcp.med.harvard.edu/wmh/index.php).

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TREATMENT ACCEPTABILITY OF INTERNET-BASED CONTINGENCY MANAGEMENT FOR CIGARETTE SMOKING.

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Aims: Contingency management (CM) increases smoking abstinence by making consequences, such as money, contingent on negative carbon monoxide (CO) levels. To broaden the reach of CM, we developed an Internet-based CM intervention. The current study assessed user acceptability of the treatment.
Methods: Smokers were randomly assigned to receive vouchers contingently (n =30) or noncontingently (n = 27) on smoking abstinence, verified by web-camera recorded CO samples submitted over a website. At the end of the 7-week treatment, participants rated the program using a 100mm visual analog scale (higher scores were more favorable).
Results: Participants in the contingent group were abstinent for more consecutive days than participants in the noncontingent group (mean = 4.3, 8.3; $t(55) = 2.25$ $P < 0.05$). All participants rated the intervention on ease of use and convenience (mean = 91, 89), earning vouchers, monitoring CO, seeing progress on a graph (mean = 82, 83, 86), and how helpful and effective it was (mean = 72, 73). A subset of participants (n=24) who had tried quitting via cold turkey and nicotine replacement therapy (NRT) ranked Internet-based CM as more effective, helpful, and enjoyable than the other interventions ($X2[2] = 15.25, 25.58, 25.39$ $P < 0.05$); however, cold turkey was ranked more convenient and easy to use than the other treatments($X2[2] = 13.57, 8.58$ $P < 0.05$). Seventy-three percent of participants in the contingent group said they would use the intervention again if they needed help quitting, compared to 63% of those in the noncontingent group.
Conclusions: Participants rated the program favorably on a number of dimensions. Internet-based CM was ranked more helpful, enjoyable, and effective than other interventions. Although Internet-based CM was ranked less convenient than cold turkey, the majority of users reported that they would use it again. The current study suggests that Internet-based CM is not only effective at increasing smoking abstinence, but that it is also an acceptable form of treatment to potential users.
Financial Support: NIDA grant DA019580

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CONCURRENT NICOTINE AND METHAMPHETAMINE DEPENDENCE – WHY USE BOTH?

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Aims: The goal of this project is to define the relationship between concurrent methamphetamine and nicotine use in methamphetamine (METH)-dependent individuals who are current cigarette smokers.
Methods: Participants answered questionnaires, including the Fagerstrom Test for Nicotine Dependence (FTND), Tiffany's Craving Questionnaire (TCQ), and a Multiple Drug Use Questionnaire (MDUQ).
Results: Participants (N=60, to date) are primarily Caucasian males who are 36.5±8.8 years of age, who reported using METH for 11.5±8.3 years and have used METH 14.8±10.4 days out of the last 30 days. They had also been using nicotine for 17.3±9.7 years and smoked cigarettes 25.4±9.3 days out of the last 30 days. The mean FTND score was 4.9±2.3. The two questions on the MDUQ scale (-5: reduces, 0: no change, +5: increases) included "Does nicotine affect the high that you experience from METH?" and "Does nicotine affect your desire for METH?" The scores were 0.37±2.1 and 0.46±2.0, respectively. TCQ evaluated interactive effects of nicotine and METH on a scale of 0 (not at all) to 100 (most ever). In response to "When using [METH], smoking a cigarette would give me something to do"; "When using, I smoke out of habit"; and "When using, I smoke the entire cigarette", participants rated these as 65.8±35.8, 74.5±29.1 and 69.8±32.4, respectively. Other statements include "When using, smoking a cigarette would make me feel better physically" and "When using, smoking a cigarette would make my high more intense", participants rated these as 34.1±33.0 and 31.3±30.0, respectively.
Conclusions: The results indicate a positive correlation between years of nicotine use and years of METH use. In general, participants self-report that nicotine use does not appear to accentuate the high or desire produced by METH, but appear to use nicotine due to habit and boredom. In addition, the concentration boost that participants feel as a result of concurrent nicotine and METH use appears to decrease as years of nicotine use increases. Data acquisition is continuing and a larger sample size will be presented at the conference.
Financial Support: DA023964

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ADOLESCENT ACCESS TO SUBSTANCE ABUSE TREATMENT IN THE UNITED STATES.

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Aims: Geographic proximity is a fundamental component of access to health care that can impact the likelihood that young people will attend treatment, stay in treatment, or that their families will participate in treatment. In this study, we estimate the proportion of adolescents in the United States that live more than 30 minutes driving distance to specialty substance abuse treatment and the association between geographic factors and access after accounting for state-level block grant funding.
Methods: We link data on substance abuse treatment facilities from the 2006 National Survey of Substance Abuse Treatment Services (N-SSATS) to community characteristics from the CY2000 decennial census and to state-level data on SAMHSA block grant funding levels and HMO penetration. Using Geographic Information Systems (GIS), we identified census tracts in which the nearest adolescent treatment facility was more than 30-minutes driving distance away.
Results: 37% of adolescents in the US live more than 30-minutes away from a specialty substance abuse treatment facility (range across states: 6% to 89%). As expected based on the funding formula, states receiving more federal funding were those in which youth had to travel longer distances to access care. Even after adjustment for state-level funding, rural census tracts and those with more people living under the poverty level had more limited access to care, whereas tracts with a larger proportion of non-white residents had greater access.
Conclusions: Over one-third of adolescents in the US live beyond a reasonable driving distance from substance abuse treatment. Funding is going to states with less access, though poor and rural areas continue to have fewer treatment options.
Financial Support: 5R01DA017507-05

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TWELVE MONTHS OF NIGHTLY ZOLPIDEM DOES NOT ENHANCE THE LIKELIHOOD OF REBOUND INSOMNIA: A PROSPECTIVE PLACEBO CONTROLLED STUDY.

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Aims: Chronic use of hypnotics may enhance the risk of rebound insomnia, a worsening of sleep following drug discontinuation. Short-term studies show rebound at supra-therapeutic doses, but duration of use does not increase its risk. This study is the first to repeatedly test for rebound insomnia during 12 months of nightly use of a therapeutic dose of zolpidem (10mg).
Methods: Primary insomniacs (N=29) ages 32-64, meeting DSM-IV criteria and a baseline sleep efficiency (sleep time/bed time) of <85% with no other primary sleep disorders on a 8-hr sleep recording, without psychiatric diseases or drug dependency and in good general health were recruited. Participants received 10mg zolpidem or placebo, double-blind, nightly for 12 months. On two laboratory nights in Months 1, 4, and 12 placebo was administered in both groups. Eight-hour sleep recordings were collected and rebound was assessed by comparing change in sleep efficiency from baseline.
Results: Baseline sleep efficiency for the placebo group was 72.7+/-10.1% and for the zolpidem group 75.6+/-8.6%. Rebound, a worsening of sleep efficiency relative to baseline, did not occur at any time point. Change scores (positive scores reflect better sleep) did not differ between placebo and zolpidem groups on the first night in month 1 (7.1% vs. 2.5%); month 4 (6.4% vs. 5.4%); and month 12 (5.6% vs. 0.6%; overall p=0.492). Percent of subjects whose sleep was worse than baseline also did not differ between placebo and zolpidem groups at any time point (month 1: 31% vs 33%; month 4: 25% vs 31%; month 12; 31% vs 40% p=0.85). Analyses of sleep latency and wake after sleep onset and the night 2 recordings showed no rebound.
Conclusions: At therapeutic doses zolpidem 10 mg was not associated with rebound insomnia and its likelihood did not increase as a function of chronic nightly administration for 12 months.
Financial Support: NIDA, grant#: R01DA17355 awarded to Dr. Roehrs

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A PERFORMANCE-BASED PILOT PROJECT IN ALCOHOL AND OTHER DRUG TREATMENT.

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Aims: The aim of the Los Angeles County Performance-Based Pilot Project (PBPP) was to assess the performance areas that impact LA County alcohol and other drug (AOD) treatment programs. The project sought to determine procedures to improve areas of performance and to develop the contract language, data systems, and reports that would facilitate the implementation and use of a performance-based management system.
Methods: PBPP participants included 14 participating agencies: 11 outpatient counseling programs (OC) and three narcotic treatment programs (NTP). ADPA and UCLA modified the existing web-based data collection system. Each agency submitted "encounter data" including dates of assessment, case management, dosing (for NTPs), drug tests, group counseling sessions, individual counseling sessions and treatment planning.
Results: Correlations indicate that as the number of individual counseling sessions increase, so does length of stay (LOS) and social support. In addition, total amount of sessions correlate with reductions in primary and secondary substance use. Overall, OC clients received more counseling services than NTP clients. Results examining data collected from OCs indicated: Less than one third of clients enrolled during the pilot project left treatment after 30 days or less of care, approximately 51% remained in treatment at 60 days and an additional 33% were in treatment at 90 days. For all clients, those who received more services in the first 30 days, were more likely to remain in treatment at 60 and 90 days. More group sessions predicted greater reductions in primary substance use. For NTPs dosing predicted retention in treatment above and beyond all other variables.
Conclusions: It is difficult to know definitively why some clients were successful with regards to achieving the longer lengths of stay. Whatever the reason, client motivation to stick with treatment during the intensive first 30 days must be addressed by future research.
Financial Support: This research was supported by the Los Angeles County Alcohol and Drug Program Administration.

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SEX DIFFERENCE IN KAPPA OPIOID RECEPTOR MODULATION OF ACUTE COCAINE-INDUCED HYPERACTIVITY IN THE GUINEA PIG.

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Aims: Clinical and preclinical studies have demonstrated that females are more sensitive than males to the effects of psychostimulants. In a few studies sex differences in kappa opioid receptor (KOPR) modulation of cocaine-induced locomotor activity have been examined but only in mice and rats. Here, we used guinea pigs to examine whether sex differences in KOPR modulation of cocaine-induced locomotor activity was present in this species. Guinea pigs are of interest, since unlike mice or rats, distribution and abundance of KOPR in the brain more closely resembles those of humans.
Methods: Age-matched adult female (600-800 g; n=8) and male (700-1100 g; n=8) guinea pigs were used in this study. Locomotor activity was measured using a Digiscan D Micro System (Accuscan, Columbus, OH).
Results: Females showed greater responses to acute cocaine (20 mg/kg, i.p.)-induced increase in total and ambulatory activities, compared to males. However, although a trend was observed (p=0.06), there was no significant sex difference in cocaine-induced stereotypy. In females, but not males, U50,488H (1 mg/kg, s.c.) 30 min prior to cocaine greatly reduced cocaine-induced increase in total and ambulatory activities but did not significantly affect cocaine-induced stereotypy. Notably, U50,488H alone did not produce significant effects on locomotor activity.
Conclusions: This study supports previous findings reporting that females are more sensitive to psychostimulants than males. Furthermore, in females, but not males, a single exposure of U50,488H reduced cocaine-induced increase in activity, suggesting that KOPR-modulation of cocaine-induced hyperactivity is sex-dependent. Future studies will examine whether sex differences in brain distribution of KOPR exist in guinea pigs using [3H]U69,593 receptor binding and autoradiography.
Financial Support: T32 DA 07237-19 (Ellen M Unterwald);DA 17302 (Lee-Yuan Liu-Chen)

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THE EFFECTS OF ORAL D-AMPHETAMINE ON IMPULSIVITY, MOOD AND PERFORMANCE IN SMOKED COCAINE USERS.

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Aims: Impulsivity, as measured by a GoStop task, has been shown to be greater in cocaine users than controls. Further, amphetamine increased impulsivity in cocaine users and decreased impulsivity in controls. However, it is unclear if 1) cocaine users are more impulsive than controls on various behavioral measures of impulsivity and 2) acute doses of d-amphetamine alter various measures of impulsivity differently in cocaine users and controls.
Methods: To date, 11 non-treatment seeking smoked cocaine users (average of $402 of smoked cocaine/week) and 11 normal controls were administered placebo or oral d-amphetamine (10 or 20 mg) during three outpatient sessions. Each session participants completed a range of tasks including subjective measures of abuse liability, cognitive performance tasks, and behavioral measures of impulsivity and risk-taking. These measures were assessed at baseline and several times after drug administration.
Results: Amphetamine produced dose-dependent increases in ratings of Drug Liking and Stimulation in normal controls but not in cocaine users. Although normal controls performed better on a motor coordination task and the Digit Symbol Substitution Task than cocaine users, amphetamine did not improve performance in either group. Based on the self-report Barratt Impulsivity Scale, there were no differences between normal controls and cocaine users. Three behavioral tasks were used to measure different components of impulsivity: the Immediate and Delayed Memory Task (IMT/DMT), a GoStop task and a Delayed Discounting Task (DDT). Cocaine users were more impulsive than normal controls on the IMT, DMT and the DDT, but not on the GoStop task. However, amphetamine did not alter these impulsivity tasks in either group. Also, there was no difference in risk-taking between the groups or in response to amphetamine on the Balloon Analog Risk Task.
Conclusions: Overall, various aspects of impulsivity were greater in smoked cocaine users than normal controls, but oral d-amphetamine had little effect on impulsivity in either group.
Financial Support: Supported by NIDA grants DA 022282 (SCR) and DA 009114 (SME).

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A PLACEBO-CONTROLLED TRIAL OF VARENICLINE TREATMENT ON THE ACUTE EFFECTS OF CIGARETTE SMOKING FOLLOWED BY A ONE-WEEK QUIT ATTEMPT.

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Aims: Previous phase III clinical trials indicate that varenicline reduces cigarette craving and attenuates the rewarding properties of a relapse cigarette among smokers attempting to quit. The current study examined these effects in a placebo-controlled, double-blind trial of varenicline treatment (2 week duration, titrated up to 1.0 mg BID by Day 6).
Methods: Nicotine withdrawal and cigarette craving were assessed on Day 8, following a verified overnight (12-15 hr) smoking abstinence period. Immediately thereafter, the acute psychological and physiological effects of a smoked cigarette were evaluated in a clinical lab testing paradigm. Further assessments of nicotine withdrawal and cigarette craving were completed on Days 9, 11 and 14, during a 1 week quit attempt. Treatment seeking participants (N=48) were tested.
Results: Preliminary analyses indicate that varenicline did not reduce symptoms of nicotine withdrawal or cigarette craving, either on Day 8 following the overnight withdrawal period or on Days 9, 11, and 14 during the 1 week quit attempt. Rather, varenicline was associated with a minor increase in nausea, and decrease in diastolic blood pressure, on Day 8. Data from the laboratory smoking tests indicate that varenicline did not reduce the rewarding or reinforcing effects of a smoked cigarette. Rather, varenicline was associated with a minor increase in smoking-induced nausea and decrease in smoking-induced diastolic blood pressure. Data from subjects that relapsed during the quit week were consistent with this, and indicated that the overall effects of the smoked cigarette may have been enhanced.
Conclusions: These results failed to support the hypothesis that varenicline reduces nicotine withdrawal and cigarette craving. Moreover, varenicline may enhance the overall somatic experience of a smoked cigarette. Further data including plasma nicotine levels and dopaminergic genotyping will be presented.
Financial Support: Support: Pfizer IIR No. GA30513U

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DRUG USE AND HELP-SEEKING BEHAVIORS AMONG MALE AND FEMALE VICTIMS OF INTIMATE PARTNER VIOLENCE.

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Aims: Research indicates that when one or both partners are involved in substance use, the risk of intimate partner violence is higher. Prior research has not examined whether drug use impacts the disclosure of intimate partner violence. The purpose of this study is to examine whether characteristics of the violence and male and female victims' drug use are associated with disclosing victimization.
Methods: Data were drawn from wave four of the Fragile Families and Child Well-being Study. Analysis is limited to men (N=198) and women (N=389) reporting current intimate partner violence. Physical violence questions were drawn from the Conflict Tactics Scale, while measures of drug and alcohol use were drawn from the Composite International Diagnostic Interview short-form. Separate bivariate and logistic regression models were conducted for the male and female samples to examine correlates of victimization disclosure.
Results: 29 men (15%) and 81 women (21%) reported disclosing victimization to a friend, family member, social worker or police officer. Both men and women were significantly more likely to disclose abuse when it occurred in front of their child/children ($p = .02$ and $p < .001$ respectively). Although drug use was not a significant predictor of disclosure of victimization for the men, women who reported any drug use were significantly less likely to disclose victimization ($p = 0.4$).
Conclusions: Results support previous research indicating that many victims of intimate partner violence do not disclose abuse and provide particular insight on how women's drug use may impact women's help-seeking behaviors for intimate partner violence. These results are important both in understanding the help seeking behaviors and coping strategies of abuse victims.
Financial Support: Wayne State University

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SUBSTANCE USE DISORDERS IN SIBLINGS.

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Aims: Substance use disorders (SUD) are common among siblings. But what about siblings in which one develops SUD yet the other does not? We prospectively examined sibling pairs in whom one has developed a DSM-IV diagnosis of SUD by age 19 while the other has no disorder. The aim of this study was to examine environmental, psychological and behavioral characteristics which distinguished the siblings at age 10-12 and predict future SUD. We hypothesized that the siblings would differ in psychological and behavioral but not environmental characteristics.
Methods: Subjects were 40 sibling pairs (80 subjects) participating in the Center for Education and Drug Abuse Research (CEDAR) prospective, longitudinal study of SUD in families. Subjects entered the study at age 10-12 and were followed to age 30. Siblings in this analysis were both males and females aged 19 or older. Subjects and parents were administered a battery of instruments assessing the child's behavioral, psychological, family and social environment characteristics. Paired samples t-tests and McNemar tests were used to conduct preliminary bivariate analyses. Variables which differentiated the SUD and non-SUD siblings were included in a conditional logistic regression analysis which considers dependency between sibs in predicting SUD by age 19.
Results: Significant predictors included General Activity, as measured on the CBCL self-report (Z=52.76, p<.001; 95%CI: .095 -.102), and two measures of peer relationships. The first that it is alright for kids to have friends of whom their parents disapprove (Z=12.27, p<.001; 95% CI: .733 -1.012), and the other that most of their friends are good students (Z=-1.94, p=.052; 95% CI: -1.101 -.0054). Thus the siblings who developed SUD were more active and had friends of whom their parents disapprove, while the siblings who did not develop SUD had friends who were good students.
Conclusions: While more variables need to be examined, our hypothesis was not proven as we conclude that a child's environment (peers) as well as the child's behavior (general activity) at age 10-12 influence the risk for future SUD.
Financial Support: Supported by NIH grant 3P50DA005605

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THE SOCIAL NETWORKS OF DRUG-USING PROBATIONERS IN A RANDOMIZED TRIAL IN MARYLAND.

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Aims: This study uses data from a randomized trial of probationers, to examine the characteristics of the social networks of those who have substance use issues and are involved in the criminal justice system. Differences by gender,race, and age are examined, as well as by primary drug of choice (alcohol vs. polydrug users).
Methods: A total of 250 subjects were used in the analysis. Data from the Orientation of Social Support (OSS) and the Community Assessment Inventory (CAI) forms was used to determine the characteristics of the networks including size, percent of family members, importance, frequency, and perceived general support.
Results: The average number of persons that subjects reported having contact with was 5.7 (range 1 to 14), with their drug networks averaging 4.6 persons and their crime networks averaging 3.6 persons. Men had more people in their crime networks (3.8 vs. 2.7, p=.001) than women, and those who had alcohol as their primary substance issue reported less persons they had contact with on a daily basis (5.6 vs. 6.3, p=.040) than those who were polydrug users. Those who had a high risk for criminal justice involvement had a lower number of persons in their network who accepted them as they were (4.8 vs. 5.8, p=.006) than those with a lower recidivism risk. The number of drug users in one's network was associated with age, with those under 35 more likely to have 4 or more drug using peers (OR=2.04, 95% CI: 1.21, 3.44).
Conclusions: The social network characteristics of this group of probationers demonstrate that both crime and drug use are influenced by a person's daily contacts and that these contacts vary by demographic traits. Changing the composition of a person's social network can increase pro-social behaviors and decrease drug use and recidivism over time.
Financial Support: This study was funded by the National Institute on Drug Abuse (R01 DA018279), Effects of Manualized Treatment on a Seamless System of Care.

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STRATEGIES DEVELOPED BY CRACK USERS TO DEAL WITH THE RISKS RESULTING FROM THE CONSUMPTION.

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Aims: The objective of this study was to identify, from the perspective of crack users and ex-users, the risks resulting from crack consumption and the strategies they use to minimize or prevent them.
Methods: We chose the qualitative research method, developed through in-depth semi-structured interviews. We interviewed an intentional sample selected by criteria composed by 30 crack users and ex-users of both genders aged between 20 and 47 years. They were recruited by means of the snowball technique, comprising 8 different chains, which assured the diversity of the profiles investigated as well as the theoretical saturation. The interviews were transcribed literally, fed into and analyzed by the software NVivo 8, with the data exploration following the techniques of discourse and content analysis.
Results: The sample presented diversity as regards gender, social-economical level and schooling. The interviewees believe that the higher risks resulting from the use of crack are those related to the psychic effects of the drug – craving, temporary paranoid symptoms and depressive symptoms, as well as those that result from the illegality of the drug, such as the police and issues regarding trafficking. Organic risks associated with the use, on the other hand, were hardly ever mentioned. Their strategies are focused on the control of the psychic effects, mainly through the association of alcohol and marijuana. As regards a better relation with the illegal aspects of the drug, they reported concern about where and with whom they use the drug, as well as the attitude they adopt in relation to the dealer and the police.
Conclusions: The strategies developed to curb the main risks they believe they are exposed to focus on an attempt to self-protection, be it from violence or from unpleasant symptoms. The strategies were sometimes contradictory among users, which can aggravate the symptoms and, in some cases, add other dependences, such as alcohol.
Financial Support: FAPESP, CNPq and AFIP.

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DEVELOPMENTAL MOMENTUM AND RISK FOR SUBSTANCE USE DISORDER: NATURAL HISTORIES OF RISK FACTORS IN YOUTH EXPERIENCING CHRONIC STRESS.

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Aims: Explicating the association between age and risk for substance use (SU) is important partly because earlier initiation of SU corresponds to greater risk for substance use disorder (SUD) and other harmful outcomes of SU. However, a paucity of research exists to elucidate the natural history of antecedents to youth SU. Such data are needed to inform etiology, SU/SUD prevention and early treatment. This study prospectively investigated the natural histories of 24 well-established SU predictors in a sample of 951 8-to-16 year olds at high risk for problematic SU because of chronic stress.
Methods: Mixed model analyses were used to elucidate growth curves, age-related variability and within-person variability not accounted for by individual differences or age-related factors. The sample was 50.0% male, 71.5% Caucasian, 55.4% received free school lunches and had a mean age of 11.3 years (SD=1.87).
Results: Age-related change for half the SU predictors is linear, whereas for the other SU predictors age-related change is curvilinear and accelerates or decelerates beginning between ages 10 and 12. Growth curves for 21 SU predictors represent increasing risk from ages 8 to 16. The majority of variance in all but three predictors is attributable to within-person change. The largest proportion of within-person variance that can be attributed to age-related factors alone was 27.1%. Thus, factors other than normative age-related change account for 2/3 or more of within-person change in these SU predictors.
Conclusions: Results suggest that potentially large opportunities exist for prevention to reduce SU/SUD liability. However, individual epigenetic trajectories were characterized by complex ontogeny. Accordingly, in high-risk individuals multiple risk factors ought to be targeted and combinations of intervention strategies are needed which are based on the recipient's risk profiles.
Financial Support: This investigation was funded by grants from the National Institute on Drug Abuse (K01-00434, P50-005606).

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A MULTI-SITE TRIAL OF OROS-MPH WITH CBT FOR ADOLESCENTS WITH ADHD AND SUBSTANCE USE DISORDERS.

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Aims: To evaluate the safety and efficacy of Osmotic-Release Methylphenidate (OROS-MPH) with cognitive behavioral therapy (CBT) in adolescents with co-occurring attention deficit hyperactivity disorder (ADHD) and substance use disorders (SUD).
Methods: 303 adolescents (13-18) with DSM IV ADHD and SUD were randomly assigned to 16 weeks of OROS-MPH or placebo. All participants concurrently received weekly individual CBT targeting substance abuse.
Results: There was a clinically and statistically significant decrease in ADHD symptoms in both treatment groups (45%, $p<0.0001$) but no difference between groups based on adolescent DSM IV ADHD symptom checklist scores. Parent ratings of ADHD symptoms and severity were lower in adolescents treated with OROS-MPH compared to placebo at 8 ($p<0.0025$) and 16 weeks ($p< 0.0015$). Significant improvement in problem solving ability ($p<0.0023$) and focused coping skills ($p<0.003$) were reported by adolescents treated with OROS-MPH + CBT but not placebo + CBT. Past 28 day drug use decreased significantly in the OROS-MPH + CBT (-6.1 days; 43%) and placebo + CBT (-4.9 days; 33%) treatment groups but was not statistically different between groups. However, subjects treated with OROS-MPH had more negative urine drug screens (3.8) compared to placebo + CBT (2.8; $p=0.045$).
Conclusions: OROS-MPH was safe and well-tolerated despite non-abstinence in most subjects. Results support some "added value" of OROS-MPH over placebo for ADHD. However, greater than expected decrease in ADHD symptoms in both groups suggests that CBT may have contributed to both ADHD and substance outcomes.
Financial Support: National Institute on Drug Abuse (NIDA) U10 DA013732)

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RELATIONSHIP OF CRIMINAL THINKING TO PERSONALITY AND CRIMINAL BEHAVIOR AMONG FEMALE OFFENDERS.

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Aims: Investigated the relationship of criminal thinking styles and personality with criminal behavior among female offenders.
Methods: Measures: Psychological Inventory of Criminal Thinking Styles (PICTS), NEO Personality Inventory, Structured Clinical Interview for DSM-IV (SCIDII) Anti Social Personality Disorder (ASPD), Borderline Personality Disorder (BPD) and Conduct Disorder (CD) Modules, Global Appraisal of Individual Need's (GAIN) Crime and Violence Scale (CVS), the Lifetime Criminal Screening Form (LCSF) and indicators of criminal justice system involvement.
Results: The sample (N=899 females) was predominantly African-American (82.5%) with 34.4% on furlough. Average age was 37.5 years (range 18-63). Nearly half (46.2%) reported opioids as their primary drug, followed by cocaine (25.2%), marijuana (15.4%), and alcohol (10.1%). The CVS was significantly related to the PICTS's four factor scores: Self-Assertion/Deception (r=.34), Denial of Harm (.29), Problem Avoidance (.28), and Interpersonal Hostility (.22) and was associated with the NEO- Agreeableness (-.29) and SCID measures of ASPD (.32), BPD (.32) and CD (.32). The LCSF was significantly related in a similar range to the same measures, as well as NEO-Conscientiousness (-.22). Measures of lifetime justice system involvement were mostly related to Self-assertion/deception (.11 to .25) and Problem Avoidance (.08 to .17). Lifetime range of arrest charges was also related to PICTS factor scores (.12 to .14), ASPD (.26) and CD (.24).
Conclusions: While the findings are generally consistent with previous studies of male offenders, they require further exploration in terms of their impact on criminal behavior and justice system involvement.
Financial Support: National Institute on Drug Abuse (5R01DA021174-03)

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FALSE POWER: QUALITATIVE RESEARCH WITH WOMEN WHO USE METHAMPHETAMINE.

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Aims: This paper reports on the results of in-depth interviews and focus groups to examine power issues among non-injecting methamphetamine (MA)-using women in Denver, Colorado. Outcomes included structural power, cultural/gender power, interpersonal power, and individual power.
Methods: Convenience sampling and street outreach were used to recruit participants for 15 in-depth interviews and two focus groups (N=9). Interviews were digitally recorded, transcribed and coded in Atlas.ti. Half of the participants were under 30 years old, over half were White (71%), and 8% reported Hispanic/Latina ethnicity. All participants had used MA in the past month as verified by UA; 83% reported smoking MA and 58% had been using MA for 10 or more years. Almost half (46%) were homeless. On average, participants reported 5 sex partners and 63% reported never using condoms with recent sex partners.
Results: Several themes emerged related to different aspects of power. The most frequently endorsed attribute relating to power was money. Most women described chaotic and unstable childhoods, as well as past and current abuse. Social prestige, as defined as being trusted and respected among friends, was identified as giving someone power. However, many of the women described a lack of female friends and indicated that MA-using women were competitive and distrustful. Several women described being the one holding their families together, making money and taking care of children, but allowed men to think they were the ones in control. On a dyadic level, women talked about relationships being equal but this was often contradicted in other parts of the interview. Participants also talked about how MA gave them power but in the end caused them to lose everything.
Conclusions: This study used qualitative methods to understand how meth-using women define power. Structural level power constructs were identified as important constructs in this study.
Financial Support: This study was supported by the National Institute on Drug Abuse DA024574-01A2.

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EXPOSURE TO NICOTINE DURING PERIADOLESCENCE IMPACTS THE REINFORCING EFFECTS OF ALCOHOL IN ADULTHOOD.

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Aims: Since the aversive effects of drugs of abuse are thought to limit intake (and abuse potential) and it has recently been shown that nicotine exposure during adolescence attenuates the aversive effects of alcohol (EtOH) in adulthood, the present study examined whether nicotine's ability to reduce the aversive effects of EtOH impact its reinforcing effects, measured by oral EtOH self-administration.
Methods: Male Sprague Dawley rats were given daily injections of saline (n=21) or nicotine (n=21; 0.4 mg/kg–base, IP) from postnatal day (PD) 34-43 (periadolescence). At PD75 (adulthood), the reinforcing effects of EtOH were examined using a modified saccharin-fading procedure. Animals were first habituated to a restricted fluid access schedule, i.e., animals received 2 h of fluid access 2.5 h into their dark cycle (1330-1530 h) and then 2 h later were given access to tap water for 1 h (1730-1830 h). Animals were habituated for 1 week to water, then given access to saccharin during the 2-h access period. Half of the subjects preexposed to nicotine and half preexposed to saline were maintained on saccharin during the 2-h access period for the remainder of the study, the remaining half of animals preexposed to nicotine or saline were given access to saccharin + EtOH in increasing concentrations (1, 2, 3, 4 & 5%; 1 week minimum at each concentration).
Results: Fluid consumption (ml) was converted into ml/kg (g/kg for EtOH), and the last 3 days of consumption at each concentration were analyzed using a 2 (Preexposure) x 3 (Days) repeated measures ANOVA. There was no effect of preexposure on saccharin consumption among subjects given saccharin only. Among animals given access to saccharin + EtOH, ANOVAs revealed a significant main effect of preexposure on EtOH consumption at 2, 3 & 4% EtOH (p<0.05), with nicotine-preexposed subjects consuming more EtOH than those preexposed to saline.
Conclusions: Thus, nicotine exposure during adolescence increases the reinforcing effects of EtOH, as evidenced by increased EtOH intake later in life, and therefore may increase its risk for abuse.
Financial Support: Supported by grants from the Mellon Foundation to ALR.

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ROBUST OPTIMAL DECISION POLICIES FOR ADAPTIVE, TIME-VARYING INTERVENTIONS USING MODEL PREDICTIVE CONTROL.

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Aims: To design optimal decision policies for adaptive interventions that are robust (i.e., meet desired levels of effectiveness) for all members of a prevention or treatment population, without demanding excessive effort in their design and implementation.
Methods: The approach taken relies on an understanding of the relationship between adaptive interventions and feedback control systems. We rely on Model Predictive Control (MPC), a control system technology from engineering, as the basis for robust optimal decision policies that can be meaningfully used in prevention and treatment settings. The MPC approach is shown to possess a number of advantages, among them the ability to robustly assign dosages in multicomponent interventions, to recognize delays and lagged effects, and to enforce constraints that reflect clinical guidelines, for example, avoiding rapid changes in intervention dosages during the course of the intervention.
Results: The usefulness of the proposed approach is shown through simulation. As a representative case study of a time-varying adaptive behavioral intervention we examine a hypothetical scenario based on an adaptive component of the Fast Track program (CPPRG, 1992) involving assigning frequency of at-home counselor visits to families with at-risk children. Simulation results confirm that the proposed scheme can efficiently assign intervention dosages and reduce outcome variability to participant families that display differing levels of response, while reducing waste of intervention resources.
Conclusions: Model Predictive Control represents an effective means for decision-making in adaptive behavioral interventions. Sensible tuning and prudent dynamic modeling are important considerations in making the best use of this methodology.
Financial Support: Support for this research has been provided by NIH-OBSSR and NIDA through grants K25DA021173, R21DA024266 and P50DA010075.

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THE EVOLUTION OF COMBINED ECONOMIC, SOCIAL NETWORK AND GEOGRAPHIC RESEARCH WITH MARGINALIZED POPULATIONS.

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Aims: This research program combines quantitative economic and qualitative ethnographic interviews, diaries, and social network analysis/mapping to understand the daily lives of marginalized Detroiters (heroin users, sex workers, those in recovery, and ex-offenders), using a dynamic model of behavior change. Specific Aims: 1.Use multiple measures to describe the social and economic contexts of marginalized populations at distinct time periods. 2.Examine and compare the results to produce measures of change during the institutional process. 3.Code and calculate measures that correlate with successful treatment and recovery outcomes to develop proxies for pre- and post-test analysis. 4.Train a subset in social geography. 5.Augment the daily living maps with GIS data.
Methods: We apply economic interview and ethnographic/social network instruments in tandem. A subsample of participants wears GPS watches for select periods. Participants are trained to upload data and create maps of their daily routines and activities that link to their economic and social network diaries as well as GIS datasets. Surveillance technologies used by law enforcement are inverted to place the individual as the mapping subject rather than the mapped object. In the spirit of community based participatory research we engage participants in learning a new skill and empower them with knowledge of how geography plays a role in their experience.
Conclusions: Most social science research engages in "backward mapping", examining correlations between structural or demographic characteristics and measureable outcomes and then theorizing about mechanisms that produce these outcomes. Our design captures characteristics of individuals and their social contexts, both objectively and subjectively, to uncover internal and external factors that produce change, either in the direction of social integration or toward the underground economy and substance misuse.
Financial Support: Supported by NIH R01 DA015462, R21 DA027145 and Joe Young, Sr. Funds (State of Michigan).

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MARIJUANA USE PATTERNS, BUT NOT DEPRESSIVE SYMPTOMS, ARE ASSOCIATED WITH VERBAL LEARNING AND MEMORY FUNCTION IN MARIJUANA-DEPENDENT INDIVIDUALS IN TREATMENT.

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Aims: The purpose of this study was to assess the influence of depression on verbal learning function in marijuana smokers.
Methods: The California Verbal Learning Test – Second Edition (CVLT-II) was administered to 174 near-daily marijuana smokers who were beginning treatment for marijuana dependence. In addition to marijuana dependence, a subset of these participants (n=64) met DSM-IV criteria for current major depression or dysthymia. The depressed (MJ+D) and non-depressed (MJ) participants were similar in demographic characteristics and marijuana use patterns.
Results: Overall, the sample exhibited signs of mild performance impairment on CVLT-II measures of auditory attention (Trials 1 and B), recall (Long Delay Free Recall) and recognition (False Positives), when compared to published normative data. Contrary to expectations, however, no differences between the MJ and MJ+D subgroups were found on these or other CVLT-II indices ($p>0.05$). Further, no significant correlations were found between measures of depressive severity (HAM-D; BDI-II) and CVLT-II performance ($p>0.05$). However, correlations were found between objective and self-reported marijuana use indicators and CVLT-II performance on numerous indices (r's ranging from -0.16 to -0.26; $p<0.05$), indicating that greater frequency and amount of marijuana use was associated with decreased verbal learning and memory function.
Conclusions: Consistent with prior findings, these results suggested that verbal learning and memory performance is mildly impaired in near-daily marijuana smokers. Further, marijuana use frequency and amount may be mildly associated with the degree of impairment, while depressive symptoms may be unrelated to verbal learning and memory functioning in this population.
Financial Support: This research was supported by NIDA grants 15451, 00465, and 09236.

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TWELVE MONTHS OF NIGHTLY ZOLPIDEM DOES NOT LEAD TO DOSE ESCALATION: A PROSPECTIVE PLACEBO-CONTROLLED STUDY.

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Aims: Long-term management of insomnia with hypnotics is thought to increase the risk of abuse. Some studies suggest that nightly chronic hypnotic use is associated with tolerance development which increases drug self-administration. This prospective study in insomniacs evaluated the abuse liability associated with 12 months of nightly use of zolpidem.
Methods: Primary insomniacs (N=27), ages 32-64 yrs, meeting DSM-IV criteria and a polysomnographic sleep efficiency of <85% with no other primary sleep disorders, without psychiatric diseases or drug dependency and in good health were recruited. Participants received 10mg zolpidem or placebo, double-blind, nightly for 12 consecutive months. In months 1, 4 and 12, self-administration assessments occurred in the laboratory. The zolpidem group had a color-coded zolpidem (10mg) or a placebo capsule on sampling nights 1 and 2 in counter balanced order. The following five nights, participants chose either 1, 2, or 3 zolpidem (5mg each) or placebo capsules. The placebo group self administrated color-coded placebo capsules. All medications were taken 30 min before bedtime.
Results: Overall, the zolpidem group selected zolpidem (80.3%) more often than placebo ($chi2=5.37$; $p=0.020$). The percentage of insomniacs in the zolpidem group choosing zolpidem over the 5 nights did not differ significantly from month 1 to month 4 (69% vs.89%; $chi2=0.841$; $p=0.359$), month 4 to month 12 (89% vs.83%; $chi2=0.063$; $p=0.802$), month 1 to month 12 (69% vs.83%; $chi2=0.477$; $p=0.490$). Percentage of zolpidem capsules self-administered nightly (3 per night available) did not differ from placebo self-administration on months 1 (46% vs 53%; $chi2=0.817$; $p=0.366$), 4 (43% vs 45%; $chi2=0.021$; $p=0.885$), and 12 (55% vs 60%; $chi2=0.279$; $p=0.597$). On average, the zolpidem group self-administered a 7.9mg nightly dose in month 12 and 7.5 mg on month 1.
Conclusions: Nightly 10 mg zolpidem use by insomniacs for 12 months was not associated with increased dose or frequency of use.
Financial Support: NIDA, grant#: R01DA17355 awarded to Dr. Roehrs

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EXAMINING THE IMPACT OF AN FASD CURRICULUM INFUSION ON NURSING AND SOCIAL WORK STUDENTS' ATTITUDES RELATED TO FASDS AND ALCOHOL USE AMONG WOMEN OF CHILD-BEARING AGE.

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Aims: To examine social work and nursing students' attitudes related to FASDs/alcohol use among women of childbearing age; To evaluate the impact of infusing a 2-hour research-based FASD curriculum infusion package (CIP) into existing upper-division social work and nursing courses on those attitudes.
Methods: A 2-hour FASD-CIP was developed based on the CDC's FASD Competency-Based Curriculum Development Guide (2009). The pre/post-test attitude measure consisted of four scenarios depicting women in various alcohol-related situations, using a 5-point Likert scale response option. University social work and nursing programs in the seven-state Frontier Regional FASD Training Center area were used to test the impact of the CIP on students' attitudes related to FASDs and alcohol use among women of childbearing age.
Results: Nursing and social work students (N=246) received the CIP. The response rate was 80% (n=196) for completed pre/post-infusion measures. Results suggest that 1) attitudes about substance use disorders are significantly more negative towards women who are pregnant vs. non-pregnant; and 2) there was a significant decrease in stigmatizing attitudes between pre-test vs. post-test measures (complete item level analyses will be presented).
Conclusions: Results suggest that using a brief intensive research-based CIP can effectively decrease nursing and social work students' stigmatizing attitudes about FASDs/alcohol use among women of childbearing age. These findings could have long-term implications for preparing social workers and nurses, as attitudes can impact the way in which individuals approach various situations (e.g., working with women of childbearing age who have substance use disorders).
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THE EXPONENTIAL MODEL OF DEMAND: A NOVEL, ROBUST, AND BROADLY APPLICABLE ASSAY FOR TRANSLATIONAL BEHAVIORAL PHARMACOLOGY.

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Aims: Methods for quantifying natural and drug reward in clinical and preclinical research often yield mixed results due to procedural limitations or differences between subject populations or treatments. However, the recently introduced "exponential model of demand" may serve as a unifying behavioral methodology for assessing reward and motivation.
Methods: The model is rooted in behavioral economics and involves a single "price" (fixed-ratio requirement) per unit of reinforcement per session across several sessions of increasing price. Rather than defining reinforcement as response output or absolute consumption at any one point, the "essential value" of the reinforcer is the rate of decrease in consumption across the range of prices. This change in demand elasticity is calculated in the model as a single value for each subject that is informative yet resilient to dose, potency, concentration, and endogenous biological/genetic confounds.
Results: The novel concept of "essential value" is arguably the most sophisticated, comprehensive, and realistic laboratory model of reward and motivation to date. Retrospective and recently collected data support the model's utility.
Conclusions: Its impact could be significant for translational behavioral pharmacology, with applications to drug abuse, medications testing, and elucidating the neural and genetic mechanisms mediating reward using a homologous methodology within and across species.
Financial Support: The data presented herein were collected with support from various sources, including[|#11#|] the National Institutes of Health, the US Department of Defense, and the Mellon[|#11#|] Foundation. The authors have no interests that may be perceived as conflicting with the research.

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EFFECTS OF INFECTIOUS DISEASES, HCV & HIV, AND THEIR TREATMENTS ON THERAPEUTIC MANAGEMENT IN OPIATE-DEPENDENT PATIENTS UNDERGOING A REPLACEMENT THERAPY PROGRAM IN SPAIN:THE PROTEUS STUDY.

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Aims: To describe how HCV&HIV/AIDS and its treatment affect the therapeutic management of opiate-dependent patients undergoing a RTP.
Methods: 624 patients from 74 centers in Spain were included(september 2008-February 2009) in an observational, cross-sectional, multicenter study. Patients were>18 years, had a diagnosis of opiate dependence according to DSM-IV-TR criteria, were currently scheduled in a RTP.
Results: The mean age of patients was 38.89±7.95 y.o.5% were in replacement therapy with buprenorfine/naloxone(BUP/NLX)and 94% were undergoing a Methadone(MTD) Maintenance Program. MTD doses ranged between 40-80mg/day(40%), or under 40mg/day(38%). At least 1 infectious comorbidity was detected in 57% of the patients.(HCV in 82.6%, HIV/AIDS in 36.46%, co-infection in 24.78%).Significant differences were found in the proportion of HIV+(p=0.0024) and HCV+/HIV+ patients (p=0.025) between MTD doses. Patients with HIV+ infection took statiscally significant higher dosis of MTD than HCV+ infected patients. Short rates of retention in PMM were shown in patients with HIV infection(31.7%), in comparison with HIV+/HCV+(25.2%)and HCV+(84.3%)patients. Antiretroviral(ARV) treatment was used in 80% of patients receiving treatment for infectious comorbidities. The proportion of patients taking ARV drugs was significantly higher for patients treated with higher MTD doses(p>0.0001)
Conclusions: Combined treatment of ARV for HIV infection and MTD in MMP force to use higher doses of MTD to achieve the steady stage of therapeutic management in opiate-dependent patients. These higher doses of MTD reflect a high decrease in retention in patients with ARV regiment for HIV. New drugs such as BUP/NLX with better profile of interactions with ARV could avoid poor retention in RTP.
Financial Support: PROTEUS PROYECT was supported by a grant from Schering-ploug.Spain

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PREVALENCE OF HIV AND HEPATITIS SEROLOGY AMONG BLACK DRUG USERS IN SOUTH AFRICA.

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Aims: Hepatitis A, B, and C viruses (HAV, HBV, and HCV) and human immunodeficiency virus (HIV) are all significant public health concerns. The present study investigates the prevalence of HIV, as well as such viruses as HAV, HBV, and HCV in black South African drug users.
Methods: The data for this study was a secondary analysis of a cross-sectional descriptive epidemiologic examination of the neuropsychological social and behavioral risk factors for HIV, HAV, HBV, and HCV with sites in the US, South Africa, and Russia. The present study is focused on the South Africa site. Blood was drawn to ascertain HIV, HAV, HBV, and HCV statuses. Also detailed HIV-risk behavior information was collected from participants. Recent self-reported drug use was assessed and verified via a urine sample.
Results: Of the 382 black South African drugs users, 195 were female and 187 males. Bi-variate chi-square analyses indicated a higher proportion having education (50.0% vs. 44.4%), lower proportion testing positive for cannabinoids (77.4% vs. 94.1%, p <0.001), a higher proportion testing positive for cocaine (41.0% vs. 30.5%, p=0.032), a higher proportion of positive anti-HIV (51.0% vs. 21.4%, p <0.001), higher proportion of positive anti- HBc (45.6% vs. 21.4%, p <0.001), and higher proportion of positive anti-HBs (48.7% vs. 16.0%, p <0.001) among females as compared to males. We did not find any significant differences in age, positive anti-HCV, or opiate positive urine tests among males and females.
Conclusions: What is clear from this study is that there is an exceptionally severe epidemic of HIV/AIDS in South Africa. This epidemic affects all parts of the population, though women are more likely to be infected than men. There is need for improvement of women's knowledge of HIV/AIDS prevention, treatment, and care.
Financial Support: This research was supported by grants 2T32DA007292 and R01DA014498 from the National Institute on Drug Abuse (PI: William Latimer, Ph.D., M.P.H).

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COMPARATIVE FINDINGS ON SUGAR DEPENDENCE BETWEEN OBESE AND SUBSTANCE DEPENDENCE MALE AND FEMALE SUBJECTS.

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Aims: Sugar dependence is a plausible hypothesis, since sugar seems to share pathways with the cerebral reward system.We verified the prevalence of a new construct – sugar dependence – in male and female subjects with and without obesity and substance dependence.
Methods: A convenience sample of 562 individuals (64% female, 35% obese, 10% substance dependents, mean age 37±12 yrs) responded to a questionnaire on sugar dependence based on DSM-IV criteria for substance dependence. Data were collected in two Brazilian state capitals. The Chi-square test was used for comparisons. All subjects gave informed consent and the study was approved by the local ethics committee.
Results: Overall, 44.7% of the sample had a diagnosis of sugar dependence. After bivariate analyses, women had more diagnoses than men (53% vs. 30%; p=0.000), obese were more diagnosed for sugar dependence than non-obese (56% vs. 39%; p=0.000), and substance-dependent individuals had more diagnoses than non-dependents (63% vs. 43%; p=0.007). The criteria more frequently reported for sugar dependence were "using more than intended" (63.5%) and "Eating in spite of knowledge of adverse consequences" (55.7%).
Conclusions: A large number of respondents had diagnoses for sugar dependence, which occurred more frequently in women, obese and substance-dependent subjects. Sweet substances stimulate the endogenous opioid system in humans by inducing a release of β endorphin and by increasing the binding affinity for opioids. This mechanism could be related to difficulties in losing weight in women and obese subjects, associated with the high consumption of sugar in substance-dependent individuals.
Financial Support: CNPq;FAPEMIG

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ADVISOR-TELLER MONEY MANAGER THERAPY FOR SUBSTANCE ABUSE.

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Aims: Patients with concomitant psychiatric and substance use disorders are commonly assigned representative payees or case managers to help manage their funds, but money management has not been conceptualized as a theory-based treatment. This randomized clinical trial was conducted to determine the effect of a money management-based therapy, Advisor-Teller Money Manager (ATM), on substance abuse.
Methods: Ninety patients at a community mental health center with histories of cocaine and/or alcohol abuse were assessed after random assignment to 36-weeks of ATM (n=47) or a control condition in which a financial workbook was reviewed (n=43). Patients assigned to ATM were encouraged to deposit their funds to a third-party account, plan weekly expenditures and negotiate monthly budgets. Substance use calendars and urine toxicology tests were collected every other week for 36 weeks and again 52 weeks after randomization.
Results: Patients assigned to ATM had significantly more negative toxicologies for cocaine metabolite over time than control patients and treating clinicians rated ATM patients as significantly more likely to be abstinent from illicit drugs. Self-reported abstinence from alcohol did not significantly differ between groups. Unexpectedly, patients assigned to ATM were more likely to be assigned a representative payee or a conservator than control participants during the follow-up period (10/47 vs. 2/43). One patient in ATM assaulted the therapist when his check had not arrived.
Conclusions: ATM is an efficacious therapy for the treatment of cocaine abuse among people with concomitant psychiatric illness but requires protection of patient autonomy and staff safety.
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EARLY RESULTS OF A PROTOCOL TO USE BUPRENORPHINE FOR CHRONIC PAIN IN PATIENTS WITH ABERRANT DRUG-RELATED BEHAVIOR.

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Aims: To test a protocol to transition opioid-treated chronic pain patients displaying aberrant behavior onto sublingual buprenorphine (Bup).
Methods: Through a clinical consensus process, experts in addiction and pain developed Bup treatment guidelines for chronic pain patients with aberrant drug-related behavior. Patients were inducted on Bup using an in-office titration dosing schedule beginning with 2mg. Patients discontinued their full mu-opioid pain medication the day before Bup induction. Pain severity was measured on a 0-10 pt scale. Baseline was pain in the past week. Followup was the mean of interview contacts for pain severity during the past 24 hours during the first 4 post-induction weeks. Wilcoxon used to test for significance.
Results: Seven subjects were inducted on Bup. Age ranged from 39-64; 4 were male. Median (M) daily morphine equivalent of opioid medication was 120 mg (range 73mg-152mg). The first 2 subjects withdrew from study due to side-effects. Subsequently the induction protocol was revised to use a more cautious loading protocol. E.g, the 2nd induction dose was changed from 4 mg to 2-4 mg and the 3rd from 6 mg to 2-4 mg. Induction dose ranged from 2mg-8mg (M 4mg). Maintenance dose ranged from 2mg Q8H to 8mg Q8H (M 6mg). PRN dosing ranged from 2mg BID to 2-4mg Q4H. Pain severity range & (M) at baseline and at followup for average pain was 2-9 (5) vs. 0-4.25 (3), p=.03; and for worst pain was 3-10 (8) vs. 0-8 (5.5), p=.09. Six subjects showed reductions in average pain (2 100%, 1 43%, 1 40%, 1 20%); 1 showed a 50% increase.
Conclusions: Early clinical pilot testing of these guidelines suggests that chronic pain patients with aberrant behavior can be inducted on Bup with some patients showing clinically significant reductions (>30%) in pain. Tolerable side-effects are more likely to be achieved when a relatively conservative titration schedule is used to induct patients on Bup.
Financial Support: NIDA; R21 DA022675

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STRATEGIES THAT WORK IN OBTAINING ACTIVE CONSENT FOR SCHOOL-BASED ADOLESCENT DRUG STUDIES.

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Aims: Given the documented difficulties in obtaining parental consent when research involves their child's drug use, the aim of this investigation was to determine the best method of achieving active parental consent for a NIDA study dealing with adolescent substance abuse.
Methods: Three methods were used for obtaining consent from parents: Group 1) Consent was mailed with school year enrollment documents with instructions to return it when picking up academic schedule (N= 839); Group 2) Consent was mailed with letter from the superintendent with instructions to return to student's school (N=1845); and Group 3) Consent was mailed with letter from school principal with an addressed, stamped envelope for return of consent directly to researcher (N=1836). After one month, the above strategies were supplemented over a two month period by research staff attendance at parent-teacher conferences, and by personal phone calls to parents.
Results: The three initial methods yielded different return rates: Group 1) 793/839=94.52%, Group 2) 1047/1845=56.75%, and Group 3) 540/1836=29.41%. When researchers attended five sessions of parent-teacher conferences (Group 2), an additional 246 consents (13.33%) were collected. Attendance at one night of parent-teacher conferences (Group 3) yielded 92 additional consents (5.01%). Phone calls by researchers produced a moderate boost in return rate for Group 3, but was less remarkable for the other groups. The final return rate at three months was: Group 1) 819/839=97.62%; Group 2) 1318/1845=71.44%, and Group 3.) 853/1836=46.46%.
Conclusions: The methods employed for Group 1 were the most successful, yielding a notably high consent return rate of 97.62%. Personal contact with parents by researchers both at parent-teacher conferences and by phone also increased return rates.
Financial Support: This study was supported by NIDA grant R01 DA024678 (Boyd, PI).

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L-5-HYDROXYTRYPTOPHAN COMBINED WITH D-AMPHETAMINE AS POTENTIAL TREATMENT AGENTS FOR STIMULANT ADDICTION: INITIAL EVIDENCE.

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Aims: Evidence suggests that increases in synaptic serotonin (5-HT) can reduce the addictive properties of amphetamine-type stimulants. In the present study, we hypothesized that pretreatment with the 5-HT precursor, L-5-hydroxytryptophan (5-HTP), and the peripheral decarboxylase inhibitor, benserazide, would decrease locomotor effects of (+)-amphetamine.
Methods: Drug treatments were administered to rats undergoing in vivo microdialysis in the nucleus accumbens. Extracellular concentrations of dopamine (DA) and 5-HT were measured in conscious rats that were housed in chambers equipped with photobeams to detect ambulation and stereotypy.
Results: (+)-Amphetamine (1.0 mg/kg, i.p.) caused concurrent increases in dialysate DA, ambulation and stereotypy, without affecting 5-HT. 5-HTP/benserazide (30 mg/kg, i.p.) caused elevations in dialysate 5-HT but failed to alter other parameters. Combined administration of (+)-amphetamine and 5-HTP/benserazide elevated extracellular DA to a greater extent than (+)-amphetamine alone, and markedly enhanced extracellular 5-HT. Importantly, 5-HTP/benserazide significantly reduced the ambulation produced by (+)-amphetamine (~50% reduction) without affecting stereotypy.
Conclusions: Our results confirm the hypothesis that 5-HTP can reduce hyperactivity produced by (+)-amphetamine, even in the presence of large elevations in dialysate DA. The data support further evaluation of these clinically-available treatments in preclinical models of addiction, and possibly in human patients.
Financial Support: Intramural Research Program, NIDA, NIH.

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PRESCRIPTION OPIOID USE AND HARMS IN AUSTRALIA: A REVIEW OF NATIONAL DATA COLLECTIONS.

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Aims: This paper presents trends in the prescription of morphine and oxycodone in Australia. Unsanctioned use will be reported among the general population and regular injecting drug users. Population-level harms related to these drugs, including hospital presentations, will be presented.
Methods: Data from the following will be presented: morphine and oxycodone prescriptions; the Australian Illicit Drug Reporting System, an annual survey of injecting drug users; the National Drug Strategy Household Survey, for unsanctioned use of prescription opioids in the general population; and the Alcohol and Other Drug Treatment National Minimum Data Set in relation to episodes for morphine and oxycodone.
Results: Overall, prescriptions for morphine have declined from 38.3 per 1,000 population in 2002/03 to 30.7 in 2007/08, representing a decrease of approximately 20%. In contrast, oxycodone prescriptions have increased markedly (approximately 152%)from 35.3 per 1,000 population in 2002/03 to 89 in 2007/08. Small proportions (approximately 1%) of the population report unsanctioned use of these drugs.Proportions have not changed over time. In contrast, the majority of use among regular injecting drug users in Australia is unsanctioned,and proportions have increased over time.
Conclusions: The available data suggest that unsanctioned use of morphine and oxycodone are occurring among a minority of the Australian population. Unsanctioned use and diversion may be occurring more broadly than among opioid-dependent persons, however, further research is required. The increases in oxycodone prescription suggest that monitoring of the prescription of these drugs is warranted.
Financial Support: This research is a product of the National Illicit Drug Indicators Project, a national monitoring system funded by the Australian Government Department of Health and Ageing. We would like to acknowledge the staff of the Australian Institute of Health and Welfare, all state and territory health departments, and the Australian Social Science Data Archive.

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STRUCTURAL BARRIERS: QUALITATIVE RESEARCH WITH SOCIAL WORKERS IN ODESSA, UKRAINE.

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Aims: This paper reports on the results of in-depth semi-structured interviews with social service personnel in Odessa, Ukraine to gain an understanding of the varied perspectives in which injection drug users (IDUs), specifically those who are HIV infected, are regarded and served.
Methods: Qualitative methods were used to probe the attitudes, knowledge, beliefs and experiences of frontline staff concerning drug users, HIV prevention and antiretroviral treatment, factors that affect how drug laws are enforced and treatment is provided to those infected, and how ecological factors could be changed with respect to IDUs.
Results: A local non-government organization (NGO)in Odessa identified and recruited 6 social workers(SWs)who had experience working with drug users and a population at high risk for HIV/AIDS. The participants averaged 7 years in the social service field and all held supervisory positions. All referred drug users to treatment programs, stating that negotiating with medical clinics for treatment entry as one of the most challenging aspects of their work. Only one SW did not support substitution therapy (e.g., methadone maintenance). They had extensive knowledge of medical treatment for a pregnant woman with HIV and all but one thought that an IDU with HIV should be allowed to carry a fetus through gestation. The SWs recognized the lack of family structure and support as the greatest challenge for IDUs. They also asserted that financial problems due to high unemployment played a major role in disabling IDUs. Most expressed that medical and drug treatment was limited to those with social influence or wealth. Forced or court-ordered treatment was overwhelmingly thought of as "repressive" and ineffective. Implications of these results will be presented and discussed.
Conclusions: Results of this exploratory study help to identify policy and operational barriers to prevent injection drug users with HIV from getting medical services and accessing HIV prevention programs.
Financial Support: This study was supported by the National Institute on Drug Abuse, DA 024590.

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INDIVIDUAL, STUDY, AND NEIGHBORHOOD CHARACTERISTICS ASSOCIATED WITH SUCCESSFUL PEER RECRUITMENT OF DRUG USERS VIA RESPONDENT-DRIVEN SAMPLING IN NEW YORK CITY.

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Aims: We evaluated individual, study, and neighborhood factors associated with successful peer recruitment of drug users in a study using Respondent Driven Sampling (RDS).
Methods: 436 young adult(18-40 years) heroin/crack/cocaine users in New York City (NYC) were recruited via RDS for a cohort study which aimed to identify social risk factors for transitioning from non-injection to injection drug use (2006-2009). Individual-level baseline characteristics (demographics, drug use, and network characteristics) and study factors (# of recruitment coupons provided and attendance at RDS training sessions (RDST) on peer recruitment) were ascertained. Aggregate measures of neighborhood opinions about drug use and HIV were obtained from an anonymous NYC resident random-digit-dial survey (2002) and linked with baseline data by zipcode. Descriptive statistics and multilevel modeling were used to compare those who recruited >=1 eligible network vs. those who did not.
Results: Before adjusting for study factors, those recruited from neighborhoods with more factual information on drug dependence (AOR=2.6;CI95:1.1-6.3) and positive opinions about sterile syringe availability for drug users (AOR=2.7;CI95:1.3-6.4) were more likely to recruit eligible peers; heroin users were less likely (AOR=0.6;CI95:0.4-0.9) and HIV positive participants were more likely (AOR=2.7;CI95:1.0-7.3) to recruit eligible peers. After adjustment, heroin users (AOR:0.5;CI95:0.3-0.8) were less likely, while those attending RDST (AOR=5.5;CI95:2.9-10.6) and those who received additional recruitment coupons (AOR=2.9;CI95:2.0-4.2) were more likely to recruit eligible peers.
Conclusions: Our data highlight the importance of neighborhood factors and suggest that RDS may not be as effective in areas characterized by negative attitudes about drug use. Group-facilitated peer training sessions may be helpful in countering negative neighborhood social norms when implementing RDS studies among drug users.
Financial Support: NIDA

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GABAA RECEPTOR MODULATORS AS MEDICATIONS FOR METHAMPHETAMINE ABUSE.

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Aims: γ-Aminobutyric-acid (GABA) systems inhibit dopamine systems. Increasing GABA activity may result in greater inhibition of dopamine systems and thus attenuate the behavioral effects of methamphetamine thought to contribute to its abuse. Preclinical and human laboratory experiments have demonstrated that high-efficacy GABAA receptor modulators attenuate the behavioral effects of stimulants under a variety of behavioral arrangements. This study determined the behavioral and cardiovascular effects of methamphetamine during maintenance on a high-efficacy GABAA receptor modulator, alprazolam. We predicted alprazolam maintenance would attenuate the behavioral effects of methamphetamine. We also predicted methamphetamine would be well tolerated during alprazolam maintenance.
Methods: Two alprazolam maintenance conditions were completed in counterbalanced order (0 and 1 mg/day). After 3-5 days of alprazolam maintenance, volunteers were administered ascending doses of intranasal methamphetamine across two experimental sessions (0, 5, and 10 during the first session; 0 20 and 30 mg during the second session). Methamphetamine doses were separated by 90 minutes. Repeated measures analysis of variance (ANOVA) was used to analyze the data.
Results: Eight volunteers completed the study. Methamphetamine alone (i.e., during placebo maintenance) produced prototypical behavioral (e.g., increased ratings of Good Effects and Like Drug) and cardiovascular effects (e.g., increased blood pressure). The cardiovascular effects of methamphetamine alone were not clinically significant. Alprazolam maintenance attenuated some of the positive subjective-rated effects of methamphetamine. Alprazolam maintenance did not alter the pressor-increasing effects of methamphetamine.
Conclusions: These results are concordant with those of preclinical experiments and suggest GABAA receptor modulation may be a viable target for developing medications for methamphetamine abuse
Financial Support: Supported by NIDA R01 DA025591.

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DETERMINING THE EFFECTS OF BENZYLPIPERAZINE ON REWARD PATHWAYS IN COMPARISON TO DEXAMPHETAMINE AND PLACEBO USING A GAMBLING TASK AND FUNCTIONAL MAGNETIC RESONANCE IMAGING.

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Aims: Party pills containing BZP have been marketed as safe and legal alternatives to illicit recreational drugs, such as 3,4-methlenedioxymethamphetamine (MDMA) or methamphetamine. BZP is a stimulant with similar subjective effects to DEX. There is a paucity of information known about the effects of BZP in humans. This study is a randomized double blinded cross-over trial that used a Gambling task to determine the effects of BZP on reward pathways in comparison to DEX and Placebo using fMRI
Methods: 10 healthy participants aged 18-40, were recruited from the Auckland area. Subjects were imaged by fMRI, at the Centre for Advanced MRI, at the University of Auckland. Imaging was performed whilst participants undertook a Gambling task 90minutes after an oral dose of BZP (200mg), DEX (20mg) or Placebo. The participants were tested with each condition on a separate occasion. Echo-planar images were collected on a MRI scanner (Siemens Magnetom Avanto 1.5 T, Germany).Data was pre-processed, analyzed with SPM8 and then used to identify regional activation
Results: BZP and DEX caused similar changes in activation in comparison to placebo. Both drugs caused activation ($p<0.01$) within the mesolimbic reward pathway, including the striatum (caudate and putamen) and the fronto-striatal networks. BZP and DEX also caused similar physiological effects in subjects; increased systolic and diastolic blood pressure, heart rate and decreased body temperature
Conclusions: This study is the first to investigate the effect of BZP on the mesolimbic reward pathways using a gambling task during fMRI. Our results suggest that BZP displays characteristics that are similar to that of other psychostimulants such as DEX in the effect within the mesolimbic reward pathway, and its physiological effects
Financial Support: School of Pharmacy, The University of Auckland

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RE-ENTRY MTC— PRELIMINARY FINDINGS ON REINCARCERATION AT 12-MONTH FOLLOW-UP.

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Aims: The study aimed to determine the effectiveness of an experimental condition, a Re-entry modified therapeutic community (MTC) for offenders with co-occurring disorders, relative to a control condition of parole supervision/case management, and hypothesized better reincarceration outcomes for the Re-entry MTC.
Methods: Data for this report came from 76 men with co-occurring disorders who were referred to treatment services in the community when released from prison.
Inmates included in this report were randomly assigned to the Re-entry MTC (n=49), with a planned duration of 6 months, or to the control condition (n=27); the duration of services for the control group was variable. Baseline data were obtained within a day or two of the offender's release from prison. This article reports outcomes at 12 months post-baseline and focuses on measures of reincarceration, which are of critical importance to the criminal justice system.
Results: Multivariate regression revealed significant differences favoring the Re-entry MTC condition for "reincarceration" and "days until reincarceration" 12 months after assignment to aftercare treatment. Offenders in the Re-entry MTC group (n=49) were significantly ($B=-1.12$; $p<0.05$) less likely to be reincarcerated for a new offense (22.4%) than those in the control group (n=27; 40.7%). Survival techniques revealed another significant difference (Breslow 5.83; $p<0.02$) favoring the Re-entry MTC group, which had a mean of 211 days until reincarceration versus 108 days for the control group.
Conclusions: The transition from prison to the community is a critical point at which continued treatment can sustain and solidify gains achieved during prison treatment. These preliminary findings suggest the effectiveness of the MTC as a re-entry strategy for offenders with co-occurring disorders, which would expand their treatment options.
Financial Support: Supported by NIH, National Institute on Drug Abuse (NIDA), Grant # 5-R01-DA-019982

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WOMEN'S TC— PRELIMINARY PSYCHOLOGICAL FINDINGS AT 12-MONTH FOLLOW-UP.

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Aims: This study was a rigorous evaluation of the effectiveness of a prison TC for female offenders with substance use problems. The study hypothesized that the experimental condition (TC treatment) would produce better outcomes than the control (cognitive-behavioral treatment) condition, and that the TC would be more effective for women with problems of higher severity.
Methods: This report analyzed data from 427 incarcerated human subjects (female) who were randomly assigned to a TC (n=235) or to a control condition (n=192). Over two-thirds had a lifetime diagnosis of severe mental disorder and, while virtually all reported exposure to trauma, nearly half were diagnosed with post traumatic stress disorder (PTSD); i.e., the population had a high proportion of co-occurring disorders.
Baseline data were obtained on study entry (assignment to treatment condition) and follow-up data were collected at 6 and 12 months after subjects were returned to the community.
Results: A linear mixed model analysis at 12-months post prison release found significantly better outcomes ($p<0.05$) for the TC group on 3 standard measures of mental health. For the TC group, Beck Depression Inventory, 2nd Edition (BDI-II) scores of 18.7 (standard deviation [SD]=11.5) at baseline fell to 12.0 (SD=12.2) at 6 months, and 12.4 (SD=11.9) at 12 months post release. In contrast, control group BDI-II scores were 18.2 (SD=11.9), 14.2 (SD=12.2), and 12.4 (SD=11.8), at baseline, 6 and 12 months post release, respectively. The Brief Severity Index (BSI), and the Posttraumatic Symptom Scale (PSS) produced similar results.
Conclusions: These preliminary findings suggest that prison TC treatment was effective in improving mental health symptoms for female offenders with substance use disorders, and underscore the importance of focusing treatment on mental health issues.
Financial Support: NIH, National Institute on Drug Abuse (NIDA), Grant # 5-R01-DA-014370

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IMPLICATION OF EPIGENETIC MODULATION IN REDUCED MESOLIMBIC DOPAMINERGIC ACTIVITY UNDER A NEUROPATHIC PAIN-LIKE STATE.

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Aims: Neuropathic pain reduces mesolimbic dopaminergic activity, which leads to a loss of motivation with decreasing the quality of life. Like dopaminergic dysfunction, the continuous release of endogenous beta-endorphin induces the dysfunction of mu-opioid receptors on the GABAergic neurons in the VTA under a chronic pain. There is now growing evidence that epigenetic mechanisms are attractive candidates for molecular substrates that mediate long-lived changes in brain, such as drug addiction and relapse. In terms of epigenetic modification, microRNAs are small, non-coding RNAs that can control the translation of target messenger RNAs, thereby regulating critical aspects of synaptic plasticity. The present study was then undertaken to investigate the possible epigenetic modulation of central dopaminergic system under the neuropathic pain induced by sciatic nerve ligaion in mice.
Methods: We investigated a possible change in tyrosine hydroxylase (TH) activity in the VTA of sciatic nerve-ligated rats using immunohistochemical study. Furthermore, the expression of several miRNAs in the VTA of mice with nerve ligation was evaluated by qRT-PCR-miRNA assays.
Results: The phosphorylated-TH positive neurons in the VTA, which directly projects to the N.Acc. were dramatically decreased by sciatic nerve ligation. This effect was abolished in mice that lacked the beta-endorphin gene following sciatic nerve ligation. Under these conditions, chronic pain stimulation significantly increased the expression level of miR9 in the VTA of mice ($p<0.01$ vs. sham operated).
Conclusions: These findings suggest that the dysfunction of central dopaminergic neurons along with an increased miR9 expression may be responsible for the impairment of motivation under the neuropathic pain-like state by sciatic nerve ligation. This epigenetic modulation could also explain the molecular mechanism that underlies the suppression of opioid dependence under a chronic pain.
Financial Support: Grants from the Ministry of Education, culture, Sports, Science and Technology of Japan.

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NANOTHERAPY FOR NEUROAIDS AND OPIATE ADDICTION.

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Aims: Drugs of abuse such as opiates are known to exacerbate HIV neurotoxicity thereby accelerating the progression of NeuroAIDS. Currently, no effective treatment exists for NeuroAIDS, which is mainly attributed to the poor penetrability of HAART across the blood-brain barrier (BBB). In the present study, we hypothesize that magnetically guided nanocarrier simultaneously bound to AZT 5'-triphosphate (AZTTP; active form of azidothymidine) and CTOP (a μ opioid receptor antagonist) would be able to deliver the drug across the BBB under the influence of an external magnetic field.
Methods: Magnetic nanoparticles were prepared by chemical co-precipitation of Fe+2 and Fe+3 ions in alkaline condition. Binding of AZTTP and CTOP to magnetic nanoparticles was performed by mixing different ratios of reactants. The anti-HIV activity was performed using an in vitro HIV infection model using PBMCs by p24 antigen and HIV-LTR amplification. Morphine induced apoptosis was done using caspase 3 apoptosis detection kit. BBB model was constructed using a transwell insert by growing human brain microvascular endothelial cells on the upper side whereas human astrocytes were grown on the underside.
Results: Results obtained shows that AZTTP and CTOP can efficiently bind to the magnetic nanoparticles (MP). MP bound AZTTP exhibited significant anti-HIV activity, whereas MP-CTOP prevented morphine induced apoptosis in PBMCs. Furthermore, we performed encapsulation of MP-AZTTP in the liposomes and checked its transmigration across an in vitro BBB model. The result shows significantly higher amount of magnetic AZTTP liposomes transmigrated across the in vitro BBB model in presence of an external magnetic field.
Conclusions: Thus, the proposed magnetic nanocarrier is anticipated to deliver the AZTTP and CTOP across the BBB, thereby simultaneously reduce NeuroAIDS and Opiate addiction in HIV infected patients who are opiate addicts. Currently, studies in our lab are being pursued to simultaneously encapsulate MP-AZTTP and MP-CTOP in liposomes.
Financial Support: This work was supported in part by National Institute on Drug Abuse grant R37DA025576 and RO1DA027049.

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TEST OF ASSOCIATION BETWEEN 10 SNPS IN THE OXYTOCIN RECEPTOR GENE AND CONDUCT DISORDER UTILIZING A SAMPLE OF CLINIC REFERRED YOUTH WITH SERIOUS SUBSTANCE AND CONDUCT PROBLEMS, CONTROLS AND AVAILABLE FIRST DEGREE RELATIVES.

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Aims: Animal and human studies have implicated oxytocin (OXT) in affiliative and prosocial behaviors. We sought to test whether genetic variation in the OXT receptor (OXTR) gene was associated with conduct disorder (CD).
Methods: Utilizing a sample of 419 adolescent patients recruited from an adolescent substance abuse treatment program, 441 parents of patients, 269 siblings of patients, 193 control adolescents, 278 parents of controls and 150 siblings of controls (total sample n=1,750), we conducted three tests of association with CD and 10 SNPs (single nucleotide polymorphisms) in the OXTR gene: (1) case-control comparison of adolescent patients with CD and controls without CD; (2) family-based comparison utilizing the entire sample; and (3) case-control comparison of parents of patients and parents of controls.
Results: No tests reached statistical significance while strictly controlling for the number of statistical comparisons ($\alpha = 0.05/30$ tests $= 0.002$).
Conclusions: In this sample, genotype for 10 SNPs in the OXTR gene were not associated with conduct disorder.
Financial Support: NIDA grants DA016314, DA09842, DA11015, and DA12845, and NIAAA grant AA015336.

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YOUTHFUL TOBACCO SMOKING FOR MALES AND FEMALES IN BRAZIL.

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Aims: Objectives: Determinants of tobacco smoking for boys and girls are not always the same. The research aim is to investigate these hypothesized male-female differences.
Methods: Methods: After probability sampling of private schools in Sao Paulo, Brazil, questionnaire assessments were obtained from 2691 school-attending youths on tobacco smoking and suspected causal determinants, with a focus on religious beliefs, leisure activities, family structure, and parental monitoring. Estimates are from weighted contingency table and regression models.
Results: Results: In this study population, there is no male-female difference in prevalence of recent smoking (14-15%), and 'going out with friends' was a smoking associated behavior for both sexes. Increasing age also was associated with recent smoking. Adolescents who often went out at night were more likely to be tobacco smokers. For girls, the data support causal models in which second-hand exposure is operative ($p<0.05$), as well as parenting, religious activities in the behavioral repertoire, and park/mall activity (all $p<0.05$). For boys, the modeling supports frequency of family meals as an inverse association with smoking, as is the case of 'having a religion' and having alive parents ($p<0.05$).
Conclusions: Conclusion: More than one in seven boys and girls in this study population have become recent tobacco smokers. Age and going out at night with friends are correlates. For girls, smoking behavior may be influenced more by parenting, by park/mall activity, and by facets of religion in the behavioral repertoire. For boys, family meals may be more important; the frequency of religious activities may be less important than religious affiliation.
Financial Support: Financial support: FAPESP and AFIP

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PREVALENCE OF HEPATITIS C AMONG A COHORT OF HISPANIC INJECTION DRUG USERS.

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Aims: The primary goals of the study are:
1) To estimate the prevalence of the hepatitis C virus (HCV) infection among Hispanic IDUs in Miami-Dade County, Florida.
2) To estimate the comorbidity of HCV, HBV, and HIV infections among this same population.
3) To identify sociodemographic and behavioral factors associated with Hepatitis C infection among Hispanic IDUs.
Methods: This study recruited and interviewed 240 Hispanic drug injectors across Miami-Dade County, FL between February 2005 and December 2006 using a targeted snowball sampling strategy. A nested sample of 25 participants were selected for in-depth ethnographic interviews.
Blood was drawn to estimate the prevalence of HCV, HBV, and HIV infections.
Eligibility: to be eligible for the study a participant must have injected opiates and/or cocaine and/or amphetamines for at least 3 months, and used at least weekly for the past 30 days. Age greater than or equal to 18 years.
Results: Among the 240 respondents enrolled in the study, 84.1% tested positive for HCV. Among those who tested positive for HCV, 13.6% also tested positive for HIV.
Prevalence of HCV (80.3%) is extremely high among Hispanic IDUs.
Comorbidity of HBV and HIV is a serious health problem among HCV+ Hispanic injection drug users. Prevalence of HBV among HCV + Hispanic IDUs is extremely high (74.8%). A majority of Hispanic IDUs who tested positive for HIV (15 of 18, 83.3%) also tested positive for HCV.
More than half of those Hispanic IDUs who tested positive for both HCV and HBV (11 of 18, 61.1%), also tested positive for HIV.
Conclusions: Despite their condition, Hispanic IDUs continue to engage in high risk sexual, injection, and drug use activities that compromise their health status even further as well as the health status of their sexual and injection partners.
HIV prevention interventions among Hispanic IDUs must stress the importance of hepatitis B and hepatitis C testing and the risk of co-infection.
Prevention and intervention campaigns tailored to the specific culture and needs of Hispanic IDUs are necessary.
Financial Support: This study was supported by CDC grant #U65/CCU423371

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IN-HOME-MESSAGING DEVICES FOR VETERANS WITH SUBSTANCE USE DISORDERS.

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Aims: Of the estimated 25 million veterans in the US, approximately 11% are heavy drinkers or dependent on alcohol and drugs, although only 0.8% of veterans received substance abuse treatment in the past year. A variety of barriers (e.g., stigma, rural living) contribute to underutilization of substance abuse treatment, warranting the need to develop innovative strategies for enhancing treatment access. A VA standard of care in internal medicine is the Tele-health In-Home-Messaging-Device (IHMD) which provides assessment and treatment to the patient in their home. For patients with substance use disorders, the aim is to develop this novel approach for delivering evidence-based treatment (EBT) and encouraging self-management through Tele-health technology.
Methods: The IHMD is a small text-messaging device connected via phone to a vendor, then electronically sent to the VA via the internet. This allows interaction between the patient and a VA 'care coordinator' from within a patient's residence. Patients log on to the device to receive a Substance Abuse Recovery Program (SARP) consisting of: 1) alcohol, drug, risk assessment; 2) a daily treatment session consisting of a CBT, motivational interviewing, or 12-step activity. The SARP IHMD dialogues were adapted from the CBI manual (COMBINE; Anton et al., 2006). Messages are displayed on a screen and patients read and respond to questions by pushing buttons. Patient responses alert care coordinators when patients have indicated high, medium, or low alert symptoms (e.g., cravings to use alcohol, use of illicit drugs, suicidal ideation). Depending on the type of alert, the patient may be contacted for further evaluation.
Conclusions: The SARP IHMD may be an innovative approach for providing substance abuse EBT, assessment, and monitoring to a larger number of veterans who would otherwise not receive treatment. Plans to evaluate the SARP IHMD for veterans with substance use disorders will be discussed.
Financial Support: This program of research is supported by VA CSR&D to the PI through a CDA-2.

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GENDER DIFFERENCES IN TREATMENT-SEEKING PRESCRIPTION OPIOID ABUSERS.

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Aims: While prescription opioid (PO) abuse has increased dramatically in recent years, there have been limited scientific efforts to examine potential differences between males and females in terms of baseline demographic variables, drug use characteristics, or treatment outcome. While several studies have reported gender differences in opioid treatment outcomes (Ignjatova, 2009), other data suggest no such differences (Messina, 2000).
Methods: We have an ongoing double-blind randomized trial evaluating brief buprenorphine stabilization and taper for treating PO-dependent adults. While the primary focus of this trial is on opioid abstinence, it provides an opportunity to examine potential gender differences in intake characteristics and treatment outcome.
Results: Thus far, 92 subjects have been enrolled (34% female, 25 yrs) and randomized to receive a 1-, 2- or 4-week buprenorphine taper. Males have several intake characteristics suggesting greater severity, including longer duration of opioid use (6 vs. 4 yrs), greater lifetime IV use (56 vs. 15%), greater lifetime heroin use (69 vs. 26%) and more convictions (6 vs. 1) than females, respectively ($P<.05$). However, fewer males reported having a PO-abusing partner (9 vs. 42%) and had lower medical ASI scores (.19 vs. .37). There were no significant differences in age, education, employment status, number of dependents, prevalence of pain, or other ASI composite scores. Preliminary analyses also suggest potential gender differences in treatment outcome, with fewer females successfully completing the taper than males (32 vs. 44%, respectively).
Conclusions: Preliminary analyses from the ongoing trial suggest that, despite several intake characteristics suggesting greater severity among PO-dependent males, they may fare better in an outpatient brief buprenorphine taper than their females. Data from the completed trial (N=105) will be presented in June and will offer important clinical and scientific information on possible gender differences in demographics, drug use characteristics and treatment needs in the emerging population of PO abusers.
Financial Support: NIDA T32 DA007242 and R01 DA019989

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THE EFFECT OF METHADONE ON EMOTIONAL REACTIVITY.

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Aims: There is considerable evidence implicating opioids in emotional regulation. Animal studies have shown that separation distress is reduced with the administration of opioid agonists. Imaging studies in humans suggest that the activity of endogenous opioid systems in brain areas associated with emotional regulation is modified when inducing emotional states such as sadness. However, there is little research on the effect of opioid administration on emotional reactivity. The aim of this study was to investigate the effect of methadone on emotional reactivity in 18 patients on methadone maintenance treatment (MMT) versus 18 drug-free controls (CTRL).
Methods: Velten's mood induction procedure was used to induce either an elated or a depressive emotional state in MMT and CTRL subjects. Both groups were administered elation and depression induction in a morning and afternoon session, corresponding with trough and peak plasma methadone concentrations in MMT subjects. Subjects either completed both sessions on the same day, or the afternoon session first (to balance for order effects). Emotional reactivity was measured with changes in ratings of elation (ΔVASE) and depression (ΔVASD) on Visual Analogue Scales.
Results: Preliminary results show a trend to a decrease in elation reactivity in MMT subjects at peak plasma methadone concentrations compared to controls (morning MMT ΔVASE=13.0, afternoon MMT ΔVASE=7.8; morning CTRL ΔVASE=12.7, afternoon CTRL ΔVASE=19.5; $p=0.0975$). Depression reactivity in MMT subjects at peak methadone plasma concentrations also showed a decrease versus CTRL subjects (morning MMT ΔVASD=21.8, afternoon MMT ΔVASD=20.3; morning CTRL ΔVASD=22.3, afternoon CTRL ΔVASD=35.5; $p>0.1$). In contrast, MMT and CTRL subjects had similar elation and depression reactivity in the morning session (corresponding to trough methadone blood concentrations in the MMT group).
Conclusions: Preliminary results suggest that MMT subjects show less emotional reactivity at peak methadone plasma concentrations, suggesting that opioids reduce both positive and negative emotional responses.
Financial Support: No external support.

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COMPARING OUTCOMES OF 'VOLUNTARY' AND 'QUASI-COMPULSORY' TREATMENT OF SUBSTANCE DEPENDENCE IN EUROPE.

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Aims: This study evaluates quasi-compulsory drug treatment (QCT) arrangements for substance dependent offenders receiving treatment instead of imprisonment in comparison to voluntary treatment within five European countries.
Methods: A total of 845 participants were interviewed with the European Addiction Severity Index, the ASI-crime module, questions on perception of pressure and self-efficacy, and the Readiness-to-Change Questionnaire at treatment entry and after 6, 12, and 18 months.
Results: Reductions in substance use and crime as well as improvements in health and social integration were observed in QCT and voluntary treatment groups. After controlling for various factors, subjects in the QCT and the comparison group showed similar reductions in substance use and crime over time. Study retention was comparable in both groups.
Conclusions: QCT is as effective as voluntary treatment provided in the same services in reducing substance use and crime.
Financial Support: Funding for QCT Europe was provided by the European Commission (contract number QLG4-CT-2002-01446).

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NON-MEDICAL USE OF EXTENDED RELEASE PRESCRIPTION STIMULANTS: AN EXAMINATION OF AMPHETAMINE AND METHYLPHENIDATE.

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Aims: To examine rates of nonmedical use (NMU) of prescription extended-release (ER) amphetamines and ER methylphenidate, relative to availability.
Methods: Prescribing data were acquired from IMS Health. Data relevant to ER amphetamine and ER methylphenidate were collected from two studies in the RADARS® (Researched Abuse, Diversion and Addiction-Related Surveillance) System (Q3 2007-Q2 2009). First, the Drug Diversion System provides a law enforcement perspective based on surveys of diversion investigators throughout the US. Second, the Poison Center System provides data on exposures to prescription drugs based on spontaneous calls. RADARS System data are presented as rates per 1,000 Unique Recipients of Dispensed Drug (URDD) to account for drug availability.
Results: From July 2007-June 2009, 18,315,404 prescriptions were filled for ER amphetamines, 26,674,152 for ER methylphenidate. RADARS System Drug Diversion trends nearly overlap for ER amphetamine and ER methylphenidate, relative to URDD (running average of 0.042 vs. 0.024 drug diversion reports per 1,000 URDD). Similarly, trends in RADARS System Poison Center calls are generally similar for ER amphetamine and ER methylphenidate, although ER amphetamine trends slightly lower (running average of 0.15 vs. 0.22 intentional exposures per 1,000 URDD).
Conclusions: Trends from the US RADARS System, which controls for utilization rates, suggest diversion and poison center call rates are similar for ER amphetamine and ER methylphenidate.
Financial Support: Supported by funding from Shire Development Inc.

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RELATIVE PERFORMANCE OF SUBJECTIVE MEASURES USED IN HUMAN ABUSE POTENTIAL STUDIES.

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Aims: Human abuse potential is evaluated in crossover studies using subjective measures. This analysis describes distribution, variability, reliability, and inter-correlation characteristics of common abuse potential measures.
Methods: Placebo and active control data from single-dose, randomized, double-blind, crossover studies in recreational drug users (N=18–44 each) were summarized with descriptive statistics for visual analogue scales (VAS) and Addiction Research Center Inventory (ARCI). Data distribution was assessed using Shapiro-Wilk and skewness/kurtosis. Reliability, internal consistency and degree of correlation were assessed using Cronbach's alpha, Pearson and Spearman correlations.
Results: Subjects were primarily male, 19-54 years of age and Caucasian or African descent. A large proportion of subjective endpoints were not normally distributed. Mean pooled placebo response (N=189-208) was lower for Drug Liking VAS (5.4%) compared to High/Good Effects VASs/ARCI MBG (~20-30%); although, median responses were lower and closer to baseline for all measures. Variability (%CV) was also lower for Drug Liking VAS with placebo (30% vs 101.5–133%) and across drugs/classes. Peak Drug Liking VAS was significantly correlated with other positive effects measures, particularly Good Effects VAS (Pearson=0.68–0.92). Correlations with High VAS, ARCI MBG and other measures were significant in most cases, but not as consistent across drugs/doses (0.11–0.82). Drug Liking VAS was either not well-correlated with Bad Effects VAS or showed a weak negative correlation (-0.27–0.41).
Conclusions: These results suggest that subjective abuse potential measures may not be normally distributed and differ in placebo response and variability. However, initial correlations indicate that abuse potential measures are well correlated. These results may affect abuse potential endpoint selection and analysis.
Financial Support: Kendle Early Stage and Pfizer Inc.

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CONDITIONED AVERSION TO ETHANOL IN ADOLESCENT VS. ADULT RATS: IMPLICATIONS FOR FUTURE DRINKING.

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Aims: Many people experiment with alcohol and other drugs of abuse during their teenage years. Epidemiological evidence suggests that younger initiates into drug taking are more likely to develop problematic drug seeking behavior, including binge and other high-intake behaviors. The level of drug intake for any individual depends on the balance of rewarding and aversive effects of the drug. Multiple rodent studies have demonstrated that aversive effects of drugs of abuse are reduced in adolescent compared to adult animals. We therefore addressed two key questions: First, do reduced aversive effects of ethanol in younger rats correlate with increased ethanol consumption? Second, are the reduced aversive effects in adolescents attributable to reduced sensitivity to physiological effects?
Methods: Adolescent and adult rats were tested for ethanol conditioned taste aversion followed by a voluntary ethanol drinking period, including post-deprivation consumption. Multivariate regression was used to assess correlations. In separate experiments, adolescent and adult rats were tested for their sensitivity to the hypothermic and sedative effects of ethanol, and for blood ethanol concentrations (BECs).
Results: We observed that in adolescent rats but not adults, taste aversion was inversely correlated with post-deprivation consumption. Adolescents also exhibited a greater increase in consumption after deprivation than adults. Furthermore, the age effect on conditioned taste aversion was not attributable to differences in hypothermia, sedation, or BECs.
Conclusions: These results suggest that during adolescence, individuals who are insensitive to aversive effects are most likely to develop problem drinking behaviors, and that aversive effects are likely cognitively or perceptually mediated. These results underscore the importance of the interaction between developmental stage and individual variation in sensitivity to alcohol.
Financial Support: Supported by NIDA, DA 020729 to NLSS; DA019114 to CMK

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PHYSICAL, SEXUAL, AND EMOTIONAL ABUSE IN A METHAMPHETAMINE-DEPENDENT TREATMENT FOLLOW-UP SAMPLE.

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Aims: A growing body of evidence demonstrates an association between abuse and drug dependence. Those who experience abuse as children are more likely to suffer from addictive disorders as they age as compared to children who do not experience abuse. In adults, research demonstrates a link between current and past abuse and current drug abuse and dependence.
Methods: This study describes secondary data analysis of 587 methamphetamine-dependent individuals who participated in the "Methamphetamine Treatment Project" (MTP), and completed the 3-year post-treatment follow-up entitled the "Methamphetamine Abuse Treatment Special Studies" (MAT-SS). Data were analyzed to provide details about the association between abuse and drug use, collected with the Abuse and Violence Questionnaire, a measure designed for MAT-SS, which includes sections from the Women's Interagency HIV Study (Cohen et al., 2000). Items address childhood and ongoing emotional, physical, and sexual abuse.
Results: Results indicate that 71.2% of participants report having been abused while growing up, and 19.8% of participants report ongoing abuse. Results from other data used in these analyses, including self-reported drug use collected with the ASI, psychiatric diagnosis collected with the MINI, and HIV high risk behavior collected with the Texas Christian University AIDS Risk Assessment, will be presented and discussed.
Conclusions: Study findings indicate the importance of assessing abuse histories when developing treatment plans in light of the association between the experience of abuse and drug dependence and other behavioral issues such as psychiatric conditions and high risk HIV behaviors.
Financial Support: CSAT 270-01-7089

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THE CPDD SPECIAL CONFERENCE ON RISK MANAGEMENT AND POST-MARKETING SURVEILLANCE OF CNS DRUGS: IMPLICATIONS FOR OPIOID REMS.

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Aims: Controlled Substance Act (CSA) scheduling is a regulatory approach to enable access to medications while providing safeguards to minimize abuse and diversion to patients and non patients. For CNS drugs, including those used to treatment drug dependence, risk management must consider abuse liability and CSA among other factors in developing appropriate risk management. CPDD sponsored a special conference to address the regulatory policy and research needs pertaining to risk management in the fall of 2008 with the proceedings published in Drug and Alcohol Dependence (Vol. 105, Suppl. 1, 2009). Approximately 100 researchers, regulators, pharmaceutical developers, and research institution representatives discussed issues, shared perspectives, and informed the development of recommendations for research and regulation by an Expert Panel representing diverse stakeholders. In 2009, the FDA announced that many extended release and long acting opioids would require a new form of risk management termed Risk Evaluation and Mitigation Strategy (REMS). This presentation will present the implications, conclusions and recommendations of the special conference for the development of risk management in general and the opioid REMS in particular.
Conclusions: The process of REMS development for these opioids has been slow, as the FDA along with the diverse stakeholders representing patients, healthcare providers, pharmaceutical distributors, and researchers have come to appreciate the complexity of the problem and the fact that some "solutions" might cause new problems without addressing those of concern. Consistent with the Expert Panel report, however, there is a science foundation for going forward with REMS implementation including specialized post marketing surveillance to provide rapid detection of potential unintended consequences and to guide interventions.
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A RANDOMIZED TRIAL OF ENTRY INTO METHADONE TREATMENT VIA INTERIM MAINTENANCE: PRELIMINARY FINDINGS.

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Aims: To compare the effectiveness of three levels of counseling at 2- and 4-months post-baseline for new admissions to two Methadone Treatment Programs (MTPs).
Methods: New MTP admissions are being randomly assigned in this ongoing trial to: Interim Methadone (IM – emergency counseling) v. Standard Methadone (SM – counseling-as-usual) v. Restored Methadone (RM – counseling with a reduced case load at one of the two MTPs). The Addiction Severity Index (ASI) and urine drug testing are being administered at baseline, 2-, and 4-month follow-up. Analyses were conducted using Poisson regression for the number of days of heroin and cocaine use and Generalized Estimating Equations for results of urine testing for cocaine and heroin.
Results: To date, 210 participants have been enrolled. Their mean age is 43.1 years old; 70% are male; 75.2% are African American; and 23.3% are White. There were no significant differences among Conditions at baseline in terms of demographics or the number of days of heroin (29.2 days) or cocaine (5.7 days) use. Treatment retention rates in all three Conditions at 4-month follow-up were high (IM, SM and RM:100%; 90.3% and 87.5%, respectively). The Condition by Time interaction for self-reported number of days of heroin use at 2 and 4 months was not significant ($p > .08$), although all three Conditions showed a sharp decline from baseline. The Condition by Time interaction was significant ($p < .05$) for the number of days of cocaine use at baseline, 2, and 4 months, favoring the IM and RM groups. The Condition by Time interactions for drug testing results failed to reach significance.
Conclusions: Preliminary findings indicate that in early treatment, patients receiving methadone alone (IM) reduced their heroin and cocaine use as much as those patients in standard methadone treatment. These data, along with prior findings on the negative effects of being placed on a "waiting list" (Schwartz et al., 2007), strengthen the argument that barriers to interim methadone should be revisited.
Financial Support: NIDA R01DA13636

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ADDING VOUCHER-BASED INCENTIVES TO CRA IMPROVES OUTCOMES DURING TREATMENT FOR COCAINE DEPENDENCE.

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Aims: The dissemination of effective treatments for cocaine dependence is an important public health priority in Spain. This study is an extension of a previous work. The purpose of the present study was to compare the efficacy of CRA with or without an incentive program for achieving cocaine abstinence, treatment retention and psychosocial functioning, and to assess whether incentives improved treatment outcome.
Methods: Fifty-eight cocaine addicts enrolled on an outpatient program for cocaine dependence were randomly assigned to one of two treatment conditions, CRA or CRA plus vouchers. Subjects in the CRA plus vouchers program received incentives for cocaine-negative urine samples during weeks 1 through 24 while the CRA group received no vouchers during that period. The CRA was implemented according to the manual published by Budney and Higgins (1998) with one difference: most of the CRA therapy components were applied in group-based sessions in both treatment conditions.
Results: 69% of patients in the CRA plus vouchers group completed six months of treatment versus 58,6% in the group without vouchers. At Month 6, 65,5% of patients in the CRA plus vouchers group were abstinent, compared to 44,8% in the CRA group. The CRA plus vouchers group showed greater improvement on several areas of functioning assessed with the Addiction Severity Index than the no-voucher group.
Conclusions: CRA and CRA plus vouchers treatments are effective for retaining outpatients in treatment and achieving cocaine abstinence in a community setting in Spain but retention and consumption rates are better in the CRA plus vouchers group than in the CRA group. Longer-term studies with larger samples are necessary in order to confirm these results.
Financial Support: Spanish National Plan on Drugs (Ref. MSC-06-01) and the University of Oviedo.

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IMPLEMENTATION OF ROUTINE HIV RAPID TESTING IN A METHADONE PROGRAM.

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Aims: To assess whether HIV rapid testing provided by the physician/PA as routine medical care in a MMTP without pretest counseling increases HIV testing and diagnosis of new HIV+ cases.
Methods: HIV testing in the MMTP was done by referral to HIV counselors, with pretest counseling using an HIV rapid test and incentive $4 subway card. We trained physician/PA's on the revised 2006 CDC HIV testing recommendations and to provide the HIV rapid test. An HIV rapid test (Uni-Gold Recombigen) was offered on admission, at the annual exam or if risky behavior. Literature was provided, pretest counseling was not required. Consent was signed prior to HIV testing(required in NY). Results were available in 10 mins and given to the patient. If HIV+, a confirmatory blood test was sent to lab. The MMTP interdisciplinary team provided case management. Incentives were discontinued.
Results: During the 12 months prior to routinization 1,559 rapid HIV tests were conducted. Of these, 3 were newly identified HIV+ with a prevalence of 0.19%, 95% CI (0.049,0.52). During the 12 months after routinization 2,810 rapid HIV tests were performed. Of these 8 were HIV+ with a prevalence of 0.29%, 95% CI (0.13,0.54). Before and after routinization 100% of patients received their rapid HIV test results. All HIV+ rapid tests were confirmed as true postives. Of the 3 confirmatory tests conducted prior to routinization only 1 patient received the confirmatory result and none of the 3 patients adhered to first HIV care appointment. After routinization all 8 patients received their confirmatory test result and 5 adhered to first HIV care appointment.
Conclusions: This study supports the feasibility of routine HIV rapid testing performed by the physician/PA in a MMTP. The program increased HIV testing, increased patient awareness of their HIV status, and identified new HIV+ patients, most of whom were successfully linked to HIV Care. HIV status was obtained for program planning/resource allocation. Elimination of pretest counseling may facilitate expanded testing. Provision of incentives may further increase routine testing.
Financial Support: BIMC/AI/NYCDOHMH/OASAS

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REWARDING PROPERTIES OF HEROIN DIFFER BY DOSE AND ACROSS INDIVIDUALS OF AN INBRED RAT STRAIN.

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Aims: Differences in individuals' motoric and reward-related responses following acute exposures to drugs of abuse can provide critical insights into the progression to drug dependence and propensity to relapse. We examined heroin-induced locomotion and concomitant heroin reward in individuals of an inbred rat strain (Fischer-344) to examine the degree to which inbred individuals varied in their sensitivity to heroin's reward-related and motoric properties.
Methods: Drug-naïve male Fischer rats (n=17) learned to associate heroin and saline with distinct chambers in a conditioned place preference (CPP) procedure. On Day 1, subjects were exposed to the CPP apparatus for 30min (pre-conditioning). On Days 2-5, subjects were injected i.p. with saline (9am) and heroin at a dose of 0.0, 0.25, 1.0, or 2.5 mg/kg (3pm) and confined to distinct conditioning chambers for 30min each. Locomotion was recorded during each session. On Day 6, subjects could again access all three chambers for 30min (post-conditioning); an increase in time spent in the heroin-paired chamber indicated heroin CPP.
Results: Heroin evoked strong CPP in all subjects conditioned with the 1.0 mg/kg dose ($P<0.05$), whereas lower and higher heroin doses elicited strong attraction to or avoidance of the heroin-paired chamber in subsets of individuals. Locomotor responses to each dose of heroin did not differ from saline responses, remained consistent across conditioning, differed minimally between individuals, and did not predict the strength of heroin CPP.
Conclusions: Male Fischer rats were highly responsive to the rewarding effects of a moderate heroin dose compared to higher or lower doses tested. However, higher and lower doses revealed substantial variability in individuals' responsiveness to heroin reward within this inbred rat strain. In all cases, heroin's rewarding effects were not predicted by its motoric effects. Further work will explore possible neural substrates mediating these differences.
Financial Support: NIH-NIDA-P60-DA05130 to MJK

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COMPARISON OF PSYCHOSOCIAL CHARACTERISTICS OF SUBJECTS WHO VOLUNTEER FOR RESEARCH INVOLVING PET SCANS VS. THOSE WHO DECLINE PARTICIPATION.

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Aims: Functional neuroimaging methods, such as positron emission tomography (PET), are increasingly used to study how individual differences in neural function influence development and course of drug abuse. These methods often involve moderate risks associated with radiation exposure, invasive procedures, and drug administration. There is prior evidence that research volunteers may be more conscientious and have less neuroticism than those who do not volunteer. Willingness to take risks may be another factor that influences study participation. Self-selection in human research may present a challenge to interpretation and generalizability of outcomes. The aim of this study is to evaluate the potential influence of such confounds in PET research. Our hypothesis is that PET volunteers will be no different from non-volunteers in terms of demographics, personality traits, or psychosocial characteristics.
Methods: Thirty-five, healthy M, F subjects, ages 18 to 29 years were recruited by posted flyers and newspaper ads to complete diagnostic screening and an extensive battery of self report measures of personality, mood, anxiety, psychological symptoms, and stress. Subjects also completed the Iowa Gambling Task, a measure of risk-taking behavior. Upon completion, the volunteers were invited to participate in a second study involving [11C] raclopride PET scans and intravenous amphetamine administration.
Results: PET volunteers differed from non-volunteers on only three subscales. They scored higher on experience seeking ($p=.040$) and competence ($p=.007$) and lower on trait anxiety ($p=.044$). No other statistically significant differences were identified.
Conclusions: Although results should be interpreted with caution given the small sample size, our findings suggest that healthy adults who volunteer for PET studies are similar to those who volunteer for research in general and that the use of PET technology in drug abuse research does not itself limit generalizability of findings.
Financial Support: NIH (R01 DA022433)

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EFFECTIVENESS OF A MASS MAIL-OUT DISTRIBUTION OF NICOTINE REPLACEMENT THERAPY TO SMOKERS IN ONTARIO, CANADA: GENDER DIFFERENCES IN CESSATION AND RELAPSE RATES.

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Aims: Findings from randomized trials suggest that the efficacy of nicotine replacement therapy (NRT) declines more rapidly among women than men. We examined whether there were any gender differences in the effectiveness of NRT distributed on a population-based level to participants enrolled in the Smoking Treatment for Ontario Patients (STOP) study.
Methods: 13,143 smokers in Ontario, Canada (55% female; mean age = 44 years) received 5-weeks of NRT in the mail along with self-help materials.
Results: While end-of-treatment quit rates (N=4437) did not significantly differ between women and men (54.6% vs. 53.9%, ns), quit rate at 6-month follow-up (N=2583) was significantly lower among women (19.7% vs. 23.7%, $p<.05$). Lower quit rates at 6-months were due to increased incidence of relapse among women compared to men (68.5% vs. 61.4%, $p<.01$). More women than men indicated that a household smoker or hospital discharge lead to relapse, whereas more men replied that drinking alcohol caused a return to smoking. Women who relapsed were also more likely than men to cite weight gain, depression, and anxiety as challenges encountered with respect to smoking during the past 6 months.
Conclusions: Thus, our findings are consistent with those of randomized trials and indicate that NRT may be less effective for women over longer periods of time due to increased likelihood of relapse. Women may benefit from greater ongoing cessation support to prevent relapse, including support to address concerns related to weight gain and mood, and strategies for maintaining abstinence from smoking when other household members smoke or following hospital discharge.
Financial Support: This research was funded by the Ontario Ministry of Health Promotion.

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WOULD CB1 NEUTRAL ANTAGONISTS BE NON-DYSPHORIC?

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Aims: To determine if a neutral antagonist of the cannabinoid CB1 receptor would be free of the dysphoric effects demonstrated by CB1 inverse agonists.
Methods: Computational modeling to design neutral antagonists. Synthesis to provide test compounds. Calcium channel assay to establish neutral antagonism. Electrical brain stimulation reward threshold assay to discern dysphoria.
Results: Modeling suggested that hydrogen bonding to the carbonyl of the CB1 inverse agonist rimonabant is responsible for stabilization of the inactive state of the constitutively active CB1 receptor and that its removal would afford a neutral antagonist. Synthesis of ligands without the carbonyl but otherwise conformationally equivalent to rimonabant provided analogs that were neutral antagonists as shown by calcium channel assay. The highest affinity ligand (Ki = 17 nM, hCB1) was examined in rats and showed the absence of a shift in the electrical brain stimulation reward threshold assay indicative of the absence of dysphoric effects. This is in contrast to dysphoric shifts seen with rimonabant.
Conclusions: The structural modification of a ligand leading from an inverse agonist to a neutral antagonist of the CB1 receptor causes a loss of dysphoric response while retaining receptor blockade. This has potential implications in the development of treatments for appetitive disorders including food intake, smoking and drug abuse that are free of dysphoric side effects, which have kept the inverse agonists from global markets.
Financial Support: RO1 DA003934 and KO5 DA021358 (PHR); Intramural Research Program, NIDA, NIH (ELG).

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ONE TINY REASON TO QUIT: A PRENATAL SMOKING CESSATION CAMPAIGN IN RICHMOND, VA.

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Aims: In Richmond, VA, rates of infant mortality (IM) are 4-5 times higher among African-Americans (AA) than among whites. A prevention communication campaign was planned as part of a large research center initiative to address this disparity. Two years of community-based participatory strategic planning and formative data gathering led planners to a smoking cessation focus and identified effective communication channels. The resulting intervention, One Tiny Reason to Quit, was a social marketing campaign encouraging pregnant AA women to call 1-800-QUIT-NOW for smoking cessation counseling and support.
Methods: The campaign ran from late June-September 2009 and utilized a two-pronged communication strategy, media and outreach. Media placements were made on an urban radio station, print ads ran in city buses, and billboards were displayed in high-risk communities. Fifty outreach workers were recruited from local organizations that serve at-risk pregnant women and trained to deliver campaign messages face-to-face, distribute give-aways, and arrange to have posters displayed in venues frequented by target audience members.
Results: Preliminary chi square analyses of quitline call data from the cessation counseling service have been conducted. In the month following the campaign launch (compared to the same month the previous year), there was a 357% increase ($p<.001$) in the number of pregnant callers from counties in the radio station coverage area. There were marginally significant increases (150% & 200%) for August and September over the same months last year as well. Similarly, statewide call data show a 258% increase ($p<.001$) in pregnant callers for July 2009 vs. July 2008. Caller characteristics are being explored in further analyses that will be complete prior to the June presentation.
Conclusions: Media campaigns, when combined with face-to-face peer outreach efforts, can prompt at-risk pregnant women to call an evidence-based quitline for smoking cessation counseling and support.
Financial Support: Research supported by NIH National Center for Minority Health and Health Disparities

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PREVALENCE OF SUBSTANCE USE AND DEPENDENCE IN THE WORKPLACE. A CROSS-SECTIONAL STUDY IN FRENCH OCCUPATIONAL MEDICINE CENTERS, AQUITAINE, FRANCE, EU.

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Aims: To screen substance use in a sample of employees attending occupational medicine centers in Aquitaine, France, in October, 2009.
Methods: All consecutive employees attending occupational medicine centers were asked to answer anonymously a self-questionnaire. Socio-demographic and substance use-related data were collected. Lifetime and current use, amount, frequency, modality of use and motivation for use were assessed for tobacco, alcohol, cannabis, opiates, cocaine and amphetamines. Problematic use, request for help and past or current treatment were also explored.
Results: 1,200 questionnaires were analysed. Lifetime prevalence was 93% for tobacco and/or alcohol use and 40% for illegal substances. Prevalence of current use was 62% for tobacco and alcohol use and 8% for illegal substances. Among current users, the prevalence of problematic use ranged from 10 to 12 % (for illegal and legal substances respectively). Among problematic users, the rate of those who were currently in treatment or had ever been treated for a substance-related disorder varied across substances from 20% to 40% for legal substances and from 2% to 100% for illegal substances. Problematic use was significantly more prevalent in some sectors such as building and civil engineering, catering trade, and transportation.
Conclusions: Current use of addictive substances was relatively high among employees, but problematic use was more prevalent in some sectors of activity. A majority of problematic users had never been treated. Screening for substance-related disorders and counselling could be improved in occupational medicine centers.
Financial Support: MILDT 2009.

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EFFECTS OF CHRONIC NEONATAL NICOTINE EXPOSURE ON DECISION MAKING IN ADULTHOOD.

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Aims: Approximately 20% of pregnant women smoke cigarettes, which is associated with adverse outcomes in offspring including cognitive deficits and symptoms of ADHD. However, it is difficult in humans to separate the contributions of maternal smoking from genetic and other environmental factors to these neurobehavioral outcomes. To address this issue, we used a chronic neonatal nicotine exposure model (CNN) in rats, which models exposure to nicotine in the human third trimester of pregnancy. The purpose of this study was to determine how CNN affects decision-making in adulthood.
Methods: Male Sprague-Dawley rats were given nicotine (6 mg/kg/day) or milk formula vehicle (n=12/group) via oral gastric intubation during post-natal days 1-7, and then left undisturbed until 60 days of age. They were then trained in a risky decision-making task in standard operant chambers, in which they were given choices between pressing one of two levers. One lever produced a small, "safe" food reward, and the other produced a large, "risky" food reward, which was accompanied by the possibility of a mild footshock, the probability of which increased over the course of a test session in blocks of trials. Rats were tested at different shock intensities across multiple test sessions.
Results: Rats in both CNN and control groups decreased preference for the large reward as risk of punishment increased over the course of a session (i.e. – risk of punishment discounted the value of the large reward). However, CNN had no effect on reward preference at any shock intensity.
Conclusions: The results suggest that despite prior evidence for adverse cognitive outcomes of perinatal nicotine, it has no effect on risky decision-making. Ongoing experiments are investigating the effects of CNN on other forms of decision-making. These results may have implications for understanding the etiology of altered decision-making in individuals exposed perinatally to nicotine via maternal smoking.
Financial Support: Supported by DA024671 (BS) and DA016487 (UWS)

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REINFORCING EFFECTS OF D-AMPHETAMINE: INFLUENCE OF NOVEL RATIOS ON A PROGRESSIVE-RATIO SCHEDULE.

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Aims: Progressive-ratio procedures have been used in non-humans and humans to study the reinforcing effects of abused stimulants. Previous human laboratory studies have shown that d-amphetamine significantly increased break points relative to placebo levels. However, the magnitude of the increase was modest which may be attributable to rather high levels of placebo responding. In the present study, we utilized novel response requirements under the modified progressive-ratio schedule and hypothesized that the altered range of response requirements would decrease responding for placebo and increase responding for d-amphetamine.
Methods: Eight participants with a history of stimulant use completed the study. The participants first sampled oral doses of d-amphetamine (0, 8, 16 and 24 mg). In subsequent sessions, subjects were offered the opportunity to work for the sampled dose on a modified progressive-ratio procedure with response requirements ranging from 400 to 1800 mouse clicks. A battery of participant-rated drug-effect questionnaires, a performance measure and cardiovascular measures were included to more fully characterize the effects of d-amphetamine.
Results: Placebo maintained low levels of responding. The intermediate dose of d-amphetamine increased responding significantly above placebo levels. d-Amphetamine produced prototypical subject-rated drug effects that were an orderly function of dose (e.g., increased ratings Like Drug).
Conclusions: The present data are concordant with previous human laboratory findings and suggest that the modified response requirements resulted in lower levels of placebo taking and a larger separation between number of placebo and d-amphetamine capsules earned.
Financial Support: This research was supported by DA017711 to CRR.

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PREDICTORS OF FAMILY REUNIFICATION AND CHILD MALTREATMENT RECURRENCE AMONG SUBSTANCE ABUSING FAMILIES.

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Aims: The purpose of this study was to identify predictors of the recurrence of child maltreatment and family reunification among a two year cohort of families engaged in a substance abuse treatment program targeting families engaged in the child welfare system.
Methods: Administrative and programmatic data from a statewide, interagency substance abuse treatment program, representing approximately 9,700 families were reviewed. These data include historical records of child neglect and abuse charges including type and risk severity, treatment and service utilization of substance abuse and associated supportive services, and clinical assessment and diagnostic information. Statistical analyses sought to identify predictive variables from clinical intakes and patterns of treatment and service utilization that correlate with patterns of recurrent child maltreatment and/or family reunification.
Results: Among the study population polysubstance use appeared to be the norm, with Methamphetamine, Marijuana, and Alcohol being the more frequently identified substances of abuse. Rates of child maltreatment recurrence were found to be positively associated with longer and more chronic patterns of substance abuse, more severe forms of child maltreatment, and treatment non-completion.
Conclusions: Effective early identification and efficacious treatment of substance abusing parents is critical to breaking the cycle of child neglect and abuse. These findings provide provocative implications for effective collaboration between child welfare and substance abuse treatment systems and suggest promising areas for future research.
Financial Support: This study was supported, in part, by a contract from the Arizona Department of Economic Security.

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EXAMINING GENDER DIFFERENCES IN SUBSTANCE USE AND AGE OF FIRST USE AMONG RURAL APPALACHIAN DRUG USERS IN KENTUCKY.

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Aims: Aim: Research suggests that gender differences may play a role in the first opportunity to use drugs and that men/women abuse different drugs. This study examines differences in self-reported lifetime and past 30 day substance use as well as age of first use among rural Appalachian drug users.
Methods: Methods: Data are from a community-based study of prescription drug users in rural Appalachia (N=308). Self-reported drug use was recorded via an interviewer-administered questionnaire with questions from the Addiction Severity Index.
Results: Results: Chi-squares and t-tests were used to examine gender differences in substance use and age of first use. More than half of the participants were male (60%) and the median age was 31 years (range = 26 - 38). Consistent with the population in rural, Appalachian Kentucky, the majority of participants were white (93.2%). More males reported lifetime use of: crack cocaine (82% vs. 69%, p<.05), heroin (44% vs. 29%, p<.01), and methamphetamine (51% vs. 33%, p=.001). Additionally, more males reported past 30 day use of marijuana (70% vs. 55%, p<.01), alcohol (63% vs. 44%, p=001), and heroin (9% vs. 2%, p=.01). There was only one significant difference in age of first use, males reported a significantly younger age for first alcohol use (13.7 vs. 14.8, p<.01). There were no significant gender differences in use or age of onset for any prescription drugs.
Conclusions: Conclusion: Findings suggest more men report lifetime and past 30 day use of "street" drugs including: crack cocaine, heroin, methamphetamine, and marijuana. However, there were no gender differences in prescription drug use. Further, findings suggest few differences in age of first use, with the exception of alcohol. Understanding gender differences in substance use as well as other differences among individuals living in rural, Appalachia presents important opportunities to incorporate this knowledge into substance abuse prevention and treatment efforts.
Financial Support: This research is supported by: NIH/NIDA R01DA024598 (PI: Jennifer Havens).

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SMOKING CESSATION IN A LOW-INCOME URBAN SETTING: LESSONS LEARNED.

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Aims: Low-income and socially disadvantaged ethnic groups are still smoking at very high rates in the US. The current study examines smoking behavior of a group of low-income urban residents and perceptions of the community residents with regard to cessation services.
Methods: Through community based participatory research, Morgan State University partnered with community-based organizations to enhance tobacco treatment interventions. The Partnership was formed in 2002 and 1,489 residents of a low-income residents were interviewed through the "Community Urban Health Project". Data from a participatory needs assessment including intercept surveys and focus group discussions from an additional 350 community residents were gathered through standardized questionnaires and analyzed using quantitative and qualitative methodologies. Covariates included demographic, psychosocial, and environmental characteristics as well as key community partners perceived community strengths and barriers.
Results: Data indicated that 55% of the respondents were current smokers and tobacco was among the top priority community health problems. The odds of being a current smoker vs. non-smoker were lower among African Americans and higher among those with Major Depression Episode (MDE). Data from intercept surveys showed high levels of interest in smoking cessation within the next six months among current smokers (60-80 percent) specially if a treatment program is offered at no or low cost (75-85 percent). The main challenges have been maintaining a full, equitable partnership; the lack of consensus about alternative interventions, such as auricular acupuncture; and the issue of fostering trust.
Conclusions: Integrating CBPR principles with rigorous scientific methodology presents unique strengths and challenges with potential to create scientific knowledge and translate them into meaningful practices.
Financial Support: Acknowledgements. NIDA grants DA012390, DA019805; NCMHD grants MD000217 and MD002803.

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A LATENT CLASS ANALYSIS OF ADOLESCENT SUBSTANCE USE AND CHILDHOOD SEXUAL ABUSE.

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Aims: Children who have exposure to childhood sexual abuse (CSA) are at particular risk for developing substance abuse in adolescence, but the extent to which CSA may shape patterns of adolescent substance use remains uncertain. The aim of this paper is to characterize the variations in patterns of adolescent substance use and to examine the association between CSA and qualitatively distinct patterns of adolescent substance use.
Methods: The current study is a quantitative secondary data analysis of the Patterns of Youth Mental Health Care in Public Service Systems Study (POC), a longitudinal study that includes 1,019 adolescents (13-18 years of age) who were active in one or more of the following five publicly-funded service systems in a large metropolitan area: alcohol and drug treatment, child welfare, juvenile justice, mental health, and public school-based mental health. We performed latent class analysis (LCA) based on lifetime use and dependence of six illicit substances: alcohol, cannabis, amphetamines, cocaine, opiates, and hallucinogens.
Results: Different patterns of latent class structures were identified in boys and girls: a 4-class solution for girls (Bayesian information criterion (BIC) = 1643.04; Lo-Mendell-Rubin adjusted likelihood ratio test (LMR): five classes (p) = .1731), and a 3-class solution for boys (BIC = 3302.27; LMR: four classes (p) =.1624). CSA was associated with an increased risk of being a heavy polysubstance user in girls, even after adjustment of age, race/ethnicity, parental substance use, sibling use, peer use, psychopathology and other forms of childhood maltreatment including physical abuse and neglect.
Conclusions: Findings indicate that female victims of CSA who are involved with public service systems are at high risk for developing multiple substance use in adolescence.
Financial Support: The Patterns of Youth Mental Health Care in Public Service Systems Study was supported by grant U01-MH55282 from the National Institute of Mental Health.

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EVIDENCE FOR TOLERANCE TO THE BEHAVIORAL EFFECTS OF COCAINE AFTER LONG-TERM SELF-ADMINISTRATION BY RHESUS MONKEYS.

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Aims: Chronic cocaine exposure has been reported to result in either the development of tolerance to cocaine's behavioral effects or behavioral sensitization. To explore further the behavioral effects of long-term cocaine self-administration, we examined changes in behaviors induced by repeated intravenous (i.v.) cocaine self-administration.
Methods: Rhesus monkeys were implanted with i.v. catheters and allowed to self-administer cocaine (0.03 mg/kg/injection) for 1 hour/day or a daily maximum of 100 injections under a fixed ratio 1 schedule. An additional group (yoked control) received a passive infusion of saline coinciding with each cocaine injection. Duration of cocaine exposure was 48 days (cumulative dose of approximately 150 mg/kg). Twenty species-typical behaviors were measured by trained observers immediately before and after the daily sessions.
Results: A modest increase in cocaine self-administration was apparent as measured by the number of injections per session and rate of responding (responses/min) across the 48 sessions. The majority of behaviors did not change including stereotypic behavior (repetitive pattern of behavior lacking function). However, a significant decrease in locomotor activity was observed as a result of daily cocaine exposure. Scratching, body spasms and "present" (presentation of part of body) also decreased significantly with repeated exposure to cocaine self-administration. Cocaine self-administration resulted in significantly decreased yawning; however, this behavior did not change across sessions.
Conclusions: In conclusion, monkeys self-administering cocaine show increases in drug taking across daily exposures, consistent with an "escalation" effect. In contrast, species-typical behaviors either decreased (e.g., locomotor and scratching) or did not change (e.g., stereotypies) with chronic self-administration. The decrease in observable behaviors suggests the development of tolerance to cocaine-induced behaviors, with no evidence for behavioral sensitization.
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DSM-IV AND FAGERSTROM NICOTINE DEPENDENCE: RELATIONSHIP IN AN ISRAELI GENERAL POPULATION SAMPLE.

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Aims: To investigate the relationship of the DSM-IV and Fagerstrom measures of nicotine dependence in an Israeli general population sample.
Methods: Adult household residents were administered in-person interviews that included translations of the AUDADIS DSM-IV nicotine dependence module and Fagerstrom nicotine dependence scale. Smokers (≥100 cigarettes; N=727) were included in factor and item response theory (IRT) analyses.
Results: DSM-IV dependence criteria fit a unidimensional model (CFI 0.996, RMSEA 0.018), with better model fit after tolerance was expanded to include first cigarette of the day having a stronger effect than previously, and dizziness or nausea no longer occurring after smoking. Fagerstrom items also formed a unidimensional model (CFI 0.989, RMSEA 0.048). The Fagerstrom has been hypothesized to tap physiological aspects of withdrawal, so DSM-IV nicotine withdrawal and Fagerstrom items were factor analyzed. A two-factor model fit the data well (CFI 0.999; RMSEA 0.016) with moderately correlated factors (0.41); one consisted of DSM-IV withdrawal and the other of Fagerstrom items. Analyzing all DSM-IV dependence criteria and Fagerstrom items together also resulted in two moderately correlated (0.52) factors (CFI 0.987, RMSEA 0.029), with DSM-IV dependence criteria as the first factor, and Fagerstrom items as the second. Giving up activities to smoke loaded poorly on both factors, while smoking just after being in situations where smoking was prohibited loaded with DSM-IV dependence. IRT total information curves suggested that DSM-IV nicotine dependence provided moderate information over a wide severity range, while Fagerstrom provided sharply higher information over a more limited, higher severity range.
Conclusions: DSM-IV and Fagerstrom measured moderately correlated but different constructs. Studies are warranted to determine the differential relationships of these measures to smoking history, comorbidity and genetic variants related to nicotine dependence.
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THE EFFECTS OF KETAMINE, PENTOBARBITAL AND ISOFLURANE ON COCAINE SENSITIZATION IN FEMALE RATS.

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Aims: Many behavioral studies require the use of anesthetics. There is emerging evidence that anesthetics act on the same neurotransmitter systems as many drugs of abuse. Previous work in our laboratory suggested that Isoflurane exposure during the course of repeated cocaine administration dampened cocaine sensitization in female (not male) rats (Siegal et al 2009). The primary molecular targets of Isoflurane and other volatile anesthetics are the GABAA, glycine and kainate receptors (Yamakura et al 2001). Isolated rat cortical neurons exposed to Isoflurane increase GABA release and decrease glutamate release, resulting in increased inhibition and decreased excitation overall (Westphalen et al 2006). Since Isoflurane and cocaine exert opposing effects primarily on the GABAA system, this raises the question of whether Isoflurane is the best choice for an anesthetic to be used in experiments focused on the effects of cocaine on GABA/glutamate systems. The results of the Isoflurane study led us to ask whether other anesthetics had similar effects on cocaine sensitization in female rats.
Methods: In the current experiments, we exposed adult, female Sprague-Dawley rats to 5 days of repeated cocaine administration (15 mg/kg ip); in experiment 1, rats underwent a 6-day withdrawal followed by a single exposure to one of three anesthetics on day 11, and a challenge dose of cocaine (10 mg/kg ip) on day 12. In experiment 2, the rats received one of three anesthetics on day 6 (after 5 days of repeated cocaine), underwent a 6-day withdrawal and received a challenge dose of cocaine (10 mg/kg ip) on day 12. Locomotor activity and stereotypic behaviors were analyzed on day 12 of each experiment.
Results: Results indicated that a single exposure to Ketamine (80mg)/Xylazine (12mg)/ml, Isoflurane, or Pentobarbital (50mg/ml) dampened sensitization upon cocaine challenge.
Conclusions: Our data suggest that the short and long-term effects of three of the most commonly used anesthetics interfere with the behavioral changes associated with repeated cocaine administration in female rats.
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PARAMETRIC EVALUATION OF BUPRENORPHINE TAPER DURATION FOR PRESCRIPTION OPIOID ABUSE.

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Aims: Despite alarming increases in prescription opioid (PO) abuse, little is known about effective treatments. Some initial data suggest that PO users may be less severe than heroin users and may avoid maintenance therapies due to the stigma associated with them. Thus, while extended agonist maintenance may eventually be deemed necessary, it is important to know if a meaningful subset of PO abusers may not require long-term maintenance, especially for younger and/or less severe patients. This ongoing 12-week trial evaluates a brief outpatient buprenorphine taper for treating PO abusers.
Methods: PO-dependent outpatients receive brief buprenorphine stabilization and random assignment to a 1-, 2- or 4-week taper, followed by oral naltrexone for those who successfully taper. All receive double-blind, double-dummy medication administration, intensive behavioral therapy and urinalysis testing.
Results: Thus far, 92 subjects have been enrolled (28 yrs old, 90% Caucasian, 34% female). Most report oxycodone as the primary drug of abuse (57%), intranasal as the primary route (69%) and a mean daily dose of 104 mg. By the end of stabilization, 80% of subjects are opioid-negative. By Week 6 (treatment mid-point), 64%, 41% and 33% of subjects in the 4-, 2- and 1-week taper groups, respectively, are retained, opioid-abstinent and on naltrexone. By Week 12 (end of treatment), 48%, 14% and 17% of the 4-, 2- and 1-week groups, respectively, remain opioid abstinent and on naltrexone. Opioid abstinence is significantly greater in the 4- vs. 1- and 2-week groups ($p<.05$).
Conclusions: Preliminary data suggest that a taper may be effective for some PO abusers, with most favorable outcomes among the 4-week taper group. However, many PO abusers do not respond to a brief taper and thus may require longer-term maintenance treatments. Data from the completed trial (N=105) will be presented in June 2010, as well as an examination of the baseline demographic and drug use characteristics which may predict treatment response.
Financial Support: NIDA R01 DA019989 and T32 DA007242

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PROPENSITY TO WORK AMONG CHRONICALLY UNEMPLOYED ADULT DRUG USERS.

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Aims: Chronic unemployment among illicit drug users is common. Interventions designed to increase employment in this population have had limited or no beneficial effects, and illicit drug users frequently remain unemployed over long periods of time. Interestingly, research on a novel employment-based treatment for drug addiction called the therapeutic workplace has shown that chronically unemployed drug users will attend a workplace very consistently over extended periods of time. Analyses were conducted to determine if unemployed drug users attend the therapeutic workplace at higher rates than they work in the community.
Methods: Participants were enrolled in four different randomized controlled clinical trials (N=154), and were assigned to either a treatment or control group. Participants were paid a modest wage in the form of vouchers exchangeable for goods and services, typically averaging about $10 per hour. Rates of attendance in the Therapeutic Workplace were compared to rates of work attendance in the 30 days prior to intake, and rates of work in the 30 days prior to a 6-month follow-up assessment.
Results: Participants attended the therapeutic workplace ($M = 11.85$ days per month) at significantly higher rates (Wilks' $\Lambda = .227$, $F(1,151) = 513.30$, $p < .001$) than they worked before intake ($M = 0.64$ per month), and six months after therapeutic workplace participation ($M = 5.85$ per month, Wilks' $\Lambda = .749$, $F(1,150) = 50.21$, $p < .001$). Rates of employment were also higher after participation in the therapeutic workplace than before (Wilks' $\Lambda = .799$, $F(1,150) = 37.81$, $p < .001$). These effects were consistent for both treatment and control group participants, as no interactions terms were significant.
Conclusions: These data suggest that drug users will attend work when offered the opportunity to engage in paid work, and suggest that the failure to obtain employment in the community does not result from lack of interest in work.
Financial Support: NIDA Grants RO1 DA019386, RO1 DA019497, RO1 DA013107,& RO1 DA012564

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DOES SOMATIC MORBIDITY INCREASE AFTER TERMINATION OF OPIOID MAINTENANCE TREATMENT?

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Aims: Some studies have found increased mortality after termination of OMT, compared to both the pre- and in-treatment periods. However, most of the patients leaving OMT may be "difficult" patients, and the increased post-treatment mortality could therefore be influenced by selection bias. Somatic morbidity prior to, during and after OMT is yet not systematically studied. Interruption/termination of treatment may be considered as a proxy variable for "problems in treatment". The innovative aim of this study is to investigate morbidity patterns in these "problem" patients with interrupted/terminated OMT.
Methods: Acute/sub-acute somatic disease incidents leading to hospital treatment before, during and after OMT in a sample of 200 Norwegian OMT patients were studied, comparing the group with interrupted/terminated treatment (n=51) with the rest (n=149). Hospital records covering five years before and up to five years during and after OMT were scrutinized. Disease incidents were categorized as 1) drug-abuse-related, 2) not drug-abuse-related or 3) injuries, and pre-during-after OMT incidence rates (IR= incidents per 100 patient years) were calculated.
Results: Both groups show reduction in overall and drug-related IR during OMT, but those with interrupted treatment show less reduction. These, however, show a great increase in overall and especially drug-related IR after OMT compared to both before and in treatment.
Conclusions: These findings indicate that somatic morbidity among patients with interrupted/terminated OMT is reduced during OMT compared to before OMT, but increased after OMT compared to both the pre- and in-treatment periods. The study thus reveals important morbidity patterns that may have implications for how to respond to "difficult" patients in OMT programmes.
Financial Support: The study is financed by Helse Sør-Øst, Oslo, Norway

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SMALL CHANGES – BIG RESULTS: THE EFFECTS OF A REORGANIZATION OF INTAKE PROCEDURES ON ACCESS TO TREATMENT.

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Aims: Delayed access to treatment hinders clients' efforts to get needed treatment. Furthermore, accurate assessment of a client's disorder makes it easier for providers to meet the clients' needs. The primary goal of this poster presentation is to show how, by using NIATx principles of process improvement, a statewide systems change effort made assessment and treatment more accessible for clients with co-occurring problem gambling.
Methods: Nine community based treatment centers (CTP), all of which provide treatment for substance use and co-occurring problem gambling disorders, and the Help line (1-800-BETS-OFF), were recruited to participate in this project. All CTPs and the Help-Line participated in individual "walk-throughs." A coach led frequent coach calls with each of the providers as well as a monthly coach call with all providers together. Each CTP and the Help Line assessed baseline and follow-up data.
Results: A thorough assessment of the intake procedures in all 9 CTPs and their relationship to the HELP Line showed that systems level change starting with calls made to the state-wide Helpline (1.800.BETS-OFF) was crucial. Significant reductions in paperwork, an increase in the transition from the Helpline to providers, and an increase in initial and continuation appointments were achieved.
Conclusions: "Walk throughs" in all the CTPs and the Help-line made clear where the challenges to the process were. After addressing the challenges in the process, clients were able to receive their treatment in a much more timely fashion.
Financial Support: This project was supported by Center for Substance Abuse Treatment (CSAT) and Substance Abuse and Mental Health Services Administration (SAMHSA) and the Iowa Department of Public Heath

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A RANDOMIZED CONTROLLED TRIAL OF A BRIEF CARE COORDINATION INTERVENTION FOR INDIVIDUALS WITH A MENTAL HEALTH AND SUBSTANCE ABUSE PROBLEM.

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Aims: Aims: Individuals with a serious mental illness have high rates of co-occurring substance abuse that often results in a severe illness course and poor treatment engagement. In an effort to improve outcomes, we previously developed and piloted Time-Limited Case Management TLC, an eight-week integrated care coordination intervention to augment traditional inpatient and outpatient care and to assist with the treatment engagement process. We currently report on a randomized trial targeting 102 acutely hospitalized patients who were randomly assigned to TLC or treatment-as-usual plus equally matched attention (TAU+A).
Methods: Subjects included were seriously mentally ill substance abusing individuals entering acute psychiatry at the New Jersey VA and randomized to TLC or TAU+A. Preliminary data include treatment initiation, attendance in treatment for both inpatient and outpatient session, and patient's engagement in treatment.
Results: Compared to TAU+A, the TLC group had a significantly higher rate of inpatient treatment attendance (4.2 vs. 1.4; p<.01). TLC subjects were more likely than TAU+A subjects to attend their initial outpatient appointment (50.0% vs. 12.2%, p<.01) and the TLC group had a higher mean attendance rate at outpatient study treatment sessions (7.2 vs. 1.5; p<.01). Subjects in the TLC group also had significantly higher rates of engagement in treatment as compared to those in the TAU+A group (30.3% vs. 7.7%, p=0.1).
Conclusions: These preliminary data are consistent with our earlier non-randomized trial and suggest that TLC assists with treatment attendance and engagement. These preliminary findings have important implications for developing clinical strategies to improve the care of veterans with a serious mental illness and a co-morbid substance abuse disorder. Although preliminary, this data also lends additional support for the efficacy of the TLC intervention.
Financial Support: This work was supported by a VA HSR&D Merit Review Grant IIR-020-145.

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(WO)MAN VS. MACHINE: A COMPARISON OF A COMPUTER- VS. INTERVIEWER-DIRECTED ASSESSMENT OF PERINATAL DRUG USE AND HIV/STD RISK BEHAVIORS.

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Aims: While interview and self-report methods have generally been used to assess for substance use/abuse and HIV/STD risk factors, research suggests that stigma may lead to underreporting. When the respondent is a pregnant woman, the risks for minimization become even more pronounced and often create missed opportunities for intervention. A promising alternative may be computer-directed assessment. The present study compared rates of various substance use and sexual risk behaviors in pregnant women assessed via a computer- or interviewer-administered assessment.
Methods: Pregnant women attending an urban OB clinic were recruited from the waiting area. Consented individuals completed the Sexual Experiences and Risk Behaviors Assessment Schedule (SERBAS) on two occasions. They were randomized to complete either the computer or interviewer assessment at time 1 and then the alternate method at time 2 (average interval =9 days). The SERBAS asked about health behaviors in past 3 months.
Results: Participants were predominantly African American (82%), with a mean age of 25 years, and in their 3rd trimester(59%). For the majority of behaviors, there were no consistent differences between the two methods. However, women were more likely to report perinatal substance use via computer-based assessment (14.5%) than by face-to-face interview (11.1%; $\chi 2(1) = 49.9$, $p < .01$). Interestingly, more women endorsed recent condom use during the face-to-face vs computer-based assessment (18.3 vs 15.9%, respectively). In contrast, more women reported being at risk for HIV infection through recent sexual experiences during face-to-face as compared to computerized assessment (28.4 vs 19.4%).
Conclusions: Although self-report was relatively consistent across time/modality, preliminary analyses suggest computer-directed methods may facilitate self-disclosure of prenatal substance use, a behavior that can have substantial legal and health consequences.
Financial Support: Research was support by NIH grants 1P60MD002256-01 and R36 DA025808-01.

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USING TECHNOLOGY TO ASSESS SUBSTANCE USE BEHAVIORS IN A LOW INCOME PRIMARY CARE CLINIC.

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Aims: To explore the usability and reliability of a touch screen computer for assessing smoking and alcohol use for low SES, minority patients attending a primary care clinic.
Methods: Data was collected from 100 patients attending a low income primary care clinic. Patients checking in with the receptionist were referred to a nearby office where the research staff obtained consent. The patient was asked to use a touch-screen tablet PC to answer questions about current smoking and alcohol use, partner smoking and alcohol use, and demographics. Next, the participant completed a paper survey assessing the same topics, as well as the ease-of-use of the touch-screen tablet PC. The patient was then returned to the waiting room. African Americans made up the majority of the sample (81%). Twenty three percent of the sample had less than a high school education and nearly two-thirds (58%) was currently unemployed.
Results: The majority of participants replied that the laptop was "very easy" (83%) to use. The majority also reported that the touch-screen was much easier to use than a keyboard (84%), and most preferred the computer input over the paper. When asked what the participants liked best about the computer survey, 41% mentioned that it was easy (e.g. "very easy, clear to see"). Self-reported smoking rates and partner smoking rates were reliable between the paper and the touch-screen surveys (Cronbach's alpha = 0.95, 0.95 respectively).
Conclusions: Using a touch-screen tablet PC, we were able to quickly, easily, and reliably assess smoking and alcohol use in a low SES population. Importantly, this occurred in a busy medical practice without interfering with normal clinic operations, suggesting that this approach is a viable option for research and clinical endeavors that require a quick assessment of substance use.
Financial Support: Dept. of Health Behavior, SPHHP, SUNY at Buffalo

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EFFECTS OF AEROBIC EXERCISE ON REINSTATEMENT OF COCAINE-SEEKING BEHAVIOR.

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Aims: Aerobic exercise decreases cocaine self-administration in laboratory animals and may be an effective treatment intervention in human substance-abusing populations. Using an animal model of relapse, we examined whether exercise decreases drug-primed reinstatement of cocaine-seeking behavior after a period of abstinence.
Methods: Male Long-Evans rats were obtained at weaning and divided into two groups immediately upon arrival: sedentary rats were housed individually in standard laboratory cages that permitted no exercise beyond normal ambulation; exercising rats were housed in similar cages but with a running wheel affixed to the interior of the cage. After 6 weeks under these conditions, rats from both groups were surgically implanted with intravenous catheters and trained to self-administer cocaine (0.5 mg/kg/infusion) under positive-reinforcement contingencies. After 14 days, saline was substituted for cocaine for a period 7 days (i.e., abstinence), after which cocaine-primed reinstatement was examined in both groups (i.e., relapse).
Results: Both groups maintained similar levels of responding during the 14 days of cocaine self-administration, but the exercise group decreased responding more quickly and to a greater extent when saline was substituted for cocaine during the abstinence phase. During tests of reinstatement, responding was lower in exercising rats than sedentary rats following priming injections of both low (15 mg/kg, ip) and high (30 mg/kg, ip) doses of cocaine.
Conclusions: These data indicate that aerobic exercise decreases reinstatement of cocaine-seeking behavior and may be effective at preventing relapse in substance-abusing populations.
Financial Support: This study was supported by grants DA014255 and DA027485 from the National Institutes of Health, by grant 52006292 from the Howard Hughes Medical Institute, and by funds from The Duke Endowment.

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MANIPULATION OF GLT1 ALTERS CUE-INDUCED COCAINE REINSTATEMENT.

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Aims: Relapse to cocaine-seeking behavior depends on increased glutamate transmission in the nucleus accumbens (NAc) and prefrontal cortex (PFC). We previously reported that treatment with 200 mg/kg ceftriaxone, a β-lactam antibiotic previously shown to increase GLT1 expression, blocks cue-induced cocaine reinstatement (Sari, Smith et al., 2009). Aim 1. We investigated the effects of increased GLT1 expression before and following two weeks of cocaine self-administration (SA). Because extinction training induces changes in glutamate signaling, we hypothesize that ceftriaxone will have no effect on cocaine SA. Aim 2. Because long periods of cocaine SA decrease GLT1 expression in NAc but not PFC (Knacksteadt et al., 2009), we are also testing the effects of GLT1 blockade in NAc following ceftriaxone treatment on cocaine reinstatement. If increased GLT1 expression in NAc is responsible for the attenuated reinstatement response, blocking NAc GLT1 should increase cocaine seeking during reinstatement.
Methods: Aim 1. Two groups of Sprague-dawley male rats (14/group) were trained to SA cocaine (0.125 mg per iv infusion) in a daily two-hour session for 14 days. One group was treated with 200 mg/kg ceftriaxone or vehicle before SA had begun whereas the other group was treated following 14 days of SA and tested subsequently for SA.
Aim 2. Following 200 mg/kg ceftriaxone treatment, dihydrokainate acid, a GLT1 blocker, or vehicle is injected bilaterally into the NAc of male Sprague-dawley rats before reinstatement.
Results: Aim 1. Preliminary data indicate no effects of ceftriaxone treatment on both groups.
Conclusions: Our results suggest that up-regulation of cortical GLT1 plays a key role in the reinstatement of cocaine-seeking behavior, but may not interfere with the onset or continuation of cocaine SA.
If blocking NAc GLT1 increases reinstatement, this would suggest that up-regulation of cortical GLT1 plays a key role in the reinstatement of cocaine-seeking behavior and may be specifically due to increased GLT1 within the NAc.
Financial Support: Supported by R01 DA 02451 and T32 DA024628

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PROLONGED COCAINE SELF-ADMINISTRATION DOES NOT RESULT IN ALTERED CONCENTRATIONS OF DOPAMINE D1 RECEPTORS IN NONHUMAN PRIMATES: AN AUTORADIOGRAPHIC ANALYSIS.

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Aims: Previously we have described alterations in the dopaminergic system in monkey striatum following 3.3 months of cocaine self-administration, including elevations in [3H]SCH 23390 binding to D1 receptors in the pre-commissural striatum which persist into early abstinence. Although these exposure times are relatively long for animal models, they are considerably shorter than the durations of use reported by addicts. Therefore, in order to characterize the ongoing influence of cocaine upon the dopamine (DA) system we have extended these studies to include a more prolonged period of cocaine access.
Methods: Rhesus monkeys (n=4) self-administered cocaine (0.3 mg/kg/inj, 30 reinforcers per session) for 15 months (total intake ~2750 mg/kg). Control monkeys (n=4) responded for food reinforcement under an identical schedule. Following the final session monkeys were sacrificed and brains were processed for [3H]SCH 23390 autoradiography.
Results: Following 15 months of cocaine self-administration [3H]SCH 23390 binding to DA D1 receptors was not different from control at any level of striatum measured, including both pre- and post-commissural caudate and putamen as well as the nucleus accumbens core and shell.
Conclusions: These results, taken together with our earlier findings, suggest that D1 receptors are susceptible to the effects of cocaine during the earlier stages of both self-administration and abstinence, after which they normalize to control levels. Furthermore, this finding is also consistent with our previous report of *decreases* in D1 receptors following 18 months of cocaine self- administration interspersed with periods of abstinence, indicating that regulation of this receptor system may undergo further changes as the duration of exposure progresses. These data highlight the importance of a clear understanding of the temporal course of the effects of cocaine exposure in considering potential treatment strategies for addiction.
Financial Support: DA09085 DA06634

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NEUROBEHAVIORAL AND DEVELOPMENTAL EFFECTS OF PRENATAL EXPOSURE TO STRESS AND/OR TOLUENE IN MICE.

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Aims: Prenatal stress alone or in combination with abused drugs can lead to deleterious effects in the offspring. Inhalant abuse is prevalent among women in reproductive age. The aim of this study was to evaluate whether prenatal stress in combination with toluene would increase neurobehavioral and developmental effects in pups compared with the effects of either exposure alone.
Methods: Pregnant Swiss Webster mice were subjected to chronic mild stress (CMS) or restraint stress (RS) alone or with toluene. CMS consisted in subjecting the animals to different stressors 8 h/day from gestational day 1 (GD1) to GD19. The stressors used were food-water deprivation, damp bedding, cage tilting, no bedding, restraint for 30 min and reversed light/dark cycle for 48 h. RS was produced by confining each mouse to a ventilated restriction chamber for 30 min, 3 times a day, from GD7-19. Animals were exposed to toluene (tol, 8000 ppm) in a static exposure chamber 30 min, twice a day from GD7-19. Control animals were exposed to air. After parturition, mortality and malformations were assessed. Pups growth was monitored from postnatal day 4 (PN4) to PN30. At PN30, male mice were tested in the forced swimming test (FST), in the open-field test and in the rota-rod test for depressive-like behaviour, general activity and motor coordination, respectively.
Results: The results show that three prenatal treatments: RS, RS+tol and CMS+tol were associated with a significant decrease in weight gain and an increase in mortality when compared to control pups. Malformations were only observed in the RS+tol group. Animals that were exposed in uterus to CMS+tol showed a decrease in motor activity and less immobility in the FST in comparison with control animals. Neither treatment affected motor coordination.
Conclusions: Taken together, these results indicate that prenatal exposure to RS+tol produces the most severe deleterious neurobehavioral and developmental effects.
Financial Support: Supported by grant 50636-M (CLR) and fellowship 210070 (PSC) from CONACyT.

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DISSEMINATION AND IMPLEMENTATION OF COGNITIVE BEHAVIORAL THERAPY FOR STIMULANT DEPENDENCE IN SOUTH AFRICA.

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Aims: Cognitive behavioral therapy (CBT) has been established as an efficacious treatment for stimulant use disorders. However, it is not yet clear how to successfully disseminate and implement CBT in ways that will ensure fidelity to the intended approach. This study evaluated clinician adherence and competency after receiving one of three training methods for CBT. We hypothesized that the two experimental conditions would demonstrate superior outcomes compared to the control condition.
Methods: The study consisted of 143 clinicians randomly assigned to: 1) in-vivo training, 2) distance learning training, and 3) manual-only training. Data were collected at baseline, 4-, 8-, and 12-weeks and again at 24-weeks post training.
Results: Clinician adherence during the 12-week implementation phase differed significantly between groups, $F(2, 120) = 25.53$, $p < .001$, with in-vivo ($M=2.30$, $SD=0.39$) and distance learning ($M=2.33$, $SD=0.40$) groups showing higher levels of skill implementation compared to the manual only group ($M=1.75$, $SD=0.44$). Clinician competence did not differ between groups, $F(2, 120) = 1.43$, $p = .243$. However, when the five most frequently implemented CBT techniques were analyzed separately, differences were found at week 12, $F(2, 92) = 3.29$, $p = .04$, with the in-vivo group showing the greatest skill ($M=4.20$, $SD=0.55$), the distance learning group showing less skill ($M=3.89$, $SD=0.62$), and manual-only group showing the lowest level of skill ($M=3.80$, $SD=0.82$).
Conclusions: These findings suggest that in-person and distance-learning training produces a greater application of CBT compared to the no-training condition. Yet overall, clinicians in the two experimental conditions did not implement the CBT skills more competently than those who did not receive training. However, when selecting only those skills implemented in 70% or more of the sessions, greater competency emerges in the in-vivo group. This finding suggests that skills may be better learned in a face-to-face environment.
Financial Support: "Cognitive Behavioral Therapy for South Africa" is funded by NIDA R01 DA019063-02.

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PATTERN OF OXYCONTIN® USE IN OPIOID ABUSERS EXPERIENCED IN TAMPERING WITH THE FORMULATION: A RETROSPECTIVE ASSESSMENT OF DRUG ADMINISTRATION METHODS FROM THE FIRST USE TO THE CURRENT PREFERRED METHOD.

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Aims: Although various methods of tampering with controlled release (CR) opioid formulations have been reported including chewing, snorting, and intravenous injecting, there is limited information on how the preferences change with drug use experience. The aim of this analysis was to characterize the pattern of OxyContin® (OC) use by drug users experienced in tampering with the formulation.
Methods: The data were collected as part of a study designed to evaluate whether a novel CR formulation that is difficult to crush would be less preferred and have lower street value to abusers who currently tamper with OC. Participants were asked about the pattern(s) of their drug use and the method(s) they had employed to tamper with CR opioids, particularly OC or its generics, for the purpose of abusing them.
Results: Forty participants were recruited for this study [65% male, 72% white, mean age 43 years (24 to 57 years)]. On average, participants had used OC for about 5 years (<1 to 20 years). When OC was used for the first time, most participants reported swallowing the tablet intact (n=18, 45%) or chewing it (n=14, 35%). A lower proportion of participants reported snorting (n=5, 13%) OC or injecting it upon first use (n=3, 8%). Of the participants who initially swallowed the tablets, 14 (78%) indicated snorting as the currently preferred route of administration, followed by injecting (n=2, 11%) and chewing or drinking it as a solution (n=1, 6%, each). Of those who initially chewed the tablets, 50% still preferred chewing it (n=7), followed by snorting (n=6, 43%) and injecting (n=1, 7%). Although history of heroin use was correlated with OC injection, no significant correlation was found between the duration of drug use and the method of OC administration.
Conclusions: The preferred route of drug administration and method of tampering is altered with experience in administering the drug.
Financial Support: Grünenthal GmbH, Germany

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DRINKING OUTCOMES BY ORDER OF ONSET IN A PLACEBO CONTROLLED TRIAL OF ACAMPROSATE IN ANXIOUS OR DEPRESSED ALCOHOLICS.

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Aims: Several studies have found order of onset (1° vs. 2°) to have prognostic implications in the treatment of alcoholics with comorbid psychiatric disorders. The study aim was to evaluate the effect of acamprosate in alcoholics with comorbid anxiety or depression by order of onset.
Methods: There were three research sites in the 12 week, multi-site trial. Participants were seen weekly. Substance use and psychiatric diagnoses were determined by the MINI International Neuropsychiatric Interview. Age of onset was defined as the age in which a participant first met DSM-IV diagnostic criteria for a disorder. Alcohol use was assessed using the TimeLine Follow-back and breathalyzer readings.
Results: 243 individuals were screened and 90 (55 M, 35 F) were randomized, with an equal distribution between acamprosate and placebo groups. All met criteria for alcohol dependence, and 93.3% (n=84) had major depression. The majority of participants (n=64) also had lifetime comorbid generalized anxiety disorder. There were no statistically significant differences in demographics between intervention groups, however there were site differences. The average age was 44.1 (9.3) years and the majority of participants were Caucasian (76.7%; n=69) and employed (62.2%; n=56). When controlling for baseline drinking and site differences, there no overall group differences. In the acamprosate group, those with primary alcoholism had fewer percent days drinking (p=0.03), drinks per day (p=0.045) and drinks per drinking day (p=0.043) than those with secondary alcoholism.
Conclusions: Although there were no differences between acamprosate and placebo, analysis of those who received acamprosate suggests that those with primary alcoholism, i.e., prior to the onset of a psychiatric disorder, may benefit from acamprosate therapy.
Financial Support: This study was sponsored by Forest Laboratories

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AGONIST REPLACEMENT THERAPY FOR MARIJUANA DEPENDENCE.

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Aims: Agonist replacement therapies are successfully used to treat dependence on opiates and nicotine. There are currently no effective pharmacotherapies for marijuana dependence (MD). MD is gaining recognition as a clinically significant phenomenon. In recent years, increasing numbers of heavy users are presenting at drug treatment clinics seeking help to overcome MD. Clinical and epidemiological evidence indicates that a cannabis dependence syndrome occurs in heavy users, exhibited by a lack of control over use and continued use despite adverse personal consequences. 85% of users seeking treatment report increased irritability, aggressive behavior, depression, nervousness, and craving while abstaining from marijuana. These symptoms undermine one's ability to quit using marijuana. 65% of treatment-seekers admit to using marijuana to relieve withdrawal symptoms, suggesting that agonist replacement therapy deserves further consideration.
Stimulation of CB1 receptors in the brain by delta-9 tetrahydrocannabinol (THC) produces the "high" associated with marijuana smoking and suppresses withdrawal symptoms. The best candidate for agonist treatment of MD is orally administered THC (O-THC). Like oral methadone or buprenorphine for opiate addictions, O-THC can provide a slow-onset, long acting substitute for the THC inhaled with marijuana smoke. Unlike methadone, however, O-THC should decrease withdrawal symptoms at less intoxicating dose levels and allow short-term tapering that would avoid chronic maintenance.
There are two FDA-approved O-THC products: MARINOL® (dronabinol) Capsules and CESAMET® (nabilone) Capsules, neither of which is indicated for the treatment of MD. Sativex® is an oral spray containing THC derived from the marijuana plant. It is marketed in Canada and the UK and is under development in the U.S. Each of these products should be tested as agonist pharmacotherapies for MD.
Conclusions: Controlled oral administration of a CB1 agonist should minimize withdrawal symptoms when one stops marijuana use, thus minimizing the risk of relapse.
Financial Support: NIDA

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GENDER DIFFERENCES AMONG URBAN AMERICAN INDIANS IN SUBSTANCE ABUSE TREATMENT.

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Aims: Little is known about gender differences in drug use patterns and treatment outcomes among urban American Indian and Alaska Native (AI/AN) populations. The current study takes advantage of treatment data from the Los Angeles County Participant Reporting System. The purpose of this study is to 1) describe the characteristics of AI/AN adult men and women receiving treatment in the county, and 2) examine treatment processes and outcomes by gender.
Methods: We analyzed treatment admission and discharge data for all AI/AN admissions for the period 2001 to 2008 (N=2,759). Treatment providers collect the data at treatment entry and discharge.
Results: Among treatment admissions, 57.2% were men and 42.8% were women. We found no significant differences in age and educational level. A greater proportion of women reported a mental illness (22% vs. 14%). At admission, women had higher rates of past 30-day use of heroin (26.5% vs. 19.1%), methamphetamine (28.2% vs. 18.9%), and cocaine/crack (28.2% vs. 18.9%). Men had higher rates of alcohol (38.6% vs. 22%) and marijuana (11.3% vs 7.6%). A higher proportion of women reported using needles in the past 12 months (33.7% vs. 25.5%). A higher proportion of women were treated in day care (14% vs 4.8%), detox residential (9.3% vs 7.4%), and adolescent residential programs (8% vs. 5.9%). More men received treatment in outpatient counseling (33.6% vs 30.4%) and residential treatment (38.9% vs 24.7%) programs. No significant gender differences were found with respect to treatment retention and completion. Among both men and women, approximately 39% completed their treatment regimens.
Conclusions: Urban AI/ANs are a vulnerable and understudied population in drug treatment research. This study found gender differences in primary drug abuse. AI/AN men and women appear to have comparable rates for treatment completion. Subsequent analyses will examine additional treatment outcomes and determine whether predictors of treatment completion and reduction in use vary for men and women.
Financial Support: Supported by LA County Ph-000179 (PI: Crevecoeur-MacPhail) and NIDA DA 07272-16A1 (PI: Rawson)

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PROGESTERONE IN COCAINE ABUSE: GENDER DIFFERENCES.

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Aims: The aim of this inpatient human laboratory study was to examine the effect of progesterone on cocaine use and response to cocaine and to compare these effects between men and women. Gender differences at screening were also examined.
Methods: This study was a double-blind, placebo-controlled, cross-over design in men and women with cocaine abuse and conducted over two inpatient four day stays. Subjects were randomized to progesterone or placebo and crossed over to other condition the following stay. Two experimental sessions were conducted during each admission: one day with active smoked cocaine dose options and the other, inactive cocaine. Subjects could elect to keep an earned token for $5 or exchange for a dose of cocaine. Recorded were physiological measures, number of doses taken, and subjective measures including craving.
Results: At screen (414 total), women used smoked cocaine more days/week than men($p<.001$), 63% of women endorsed exchanging sex for cocaine. Thirty-eight subjects completed the study (21 men, 17 women). During the experimental sessions, women chose to use cocaine slightly less than men (44% vs. 56%, ns) and progesterone did not have an effect on number of doses used in either men or women. There were no gender differences on choice to take active cocaine (65%) vs. inactive cocaine (32%). Our previous analysis reported craving to be significantly reduced in the progesterone condition ($p<.001$). In general, women experienced more craving than men ($p=.013$). Higher progesterone levels were associated with lower craving ($p<.001$). Men experienced greater heart racing, and more feelings of high and stimulation than women in response to cocaine. Systolic BP was found to be significantly lower in the progesterone condition.
Conclusions: Women have different use patterns, consequences, and responses to cocaine. These findings highlight the importance of studying gender in cocaine trials. Progesterone impacts craving but not use. An inpatient laboratory offers a unique setting to test effects of medications for cocaine abuse.
Financial Support: NIDA RO1-14573 and GCRC, U of MN

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PROBING ACUTE OPIOID EFFECTS IN BIPOLAR DISORDER.

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Aims: Mood disorders may influence the experience of opioid drug effect. Previous opioid agonist challenge studies in unipolar and bipolar depressed subjects support trends of transient global improvements in depressive symptoms, however they are limited by very small sample sizes and mixed patient groups. In addition, although hypothalamic-pituitary-adrenal axis and immune system dysregulation is prevalent in major depression it has not been well studied in bipolar disorder. The objective of this study was to compare the behavioural, psychomotor and physiological effects of a single 6mg oral dose of hydromorphone in bipolar depressed (n=8), bipolar euthymic (n=11), and healthy volunteer subjects (n=11).
Methods: This was a double-blind, placebo-controlled, randomized, crossover study. Each subject attended 2 study days, receiving in random order either oral hydromorphone 6mg or placebo.
Results: Repeated measures ANOVA detected drug*time*group interactions ($p<0.05$) for POMS Depression-Dejection (improved mood with hydromorphone in bipolar depressed), VAS Good Effects (higher with hydromorphone in bipolar groups compared to controls, with significant placebo effect in depressed group), VAS Bad Effects (higher in bipolar euthymic and control groups with hydromorphone compared to bipolar depressed group). Basal cortisol, IL-6, IL-10 and IL-12 levels did not significantly differ among subjects groups. Bipolar depressed subjects had significantly higher basal IL-8 levels than control and euthymic subjects. Morning IL-6 was significantly elevated in the depressed group compared to the euthymic group. Hydromorphone did not significantly influence cortisol or pro-inflammatory cytokine levels in any subject group.
Conclusions: These results may contribute to understanding the pharmacological effects and influences of opioids in bipolar disorder.
Financial Support: None.

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NEIGHBORHOOD ENVIRONMENT, DISTANCE, AND INDIVIDUAL FACTORS PREDICTING INITIAL OUTPATIENT TREATMENT ATTENDANCE FOLLOWING ACUTE INPATIENT CARE.

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Aims: To examine the influence of the neighborhood environment, distance to treatment, and individual factors in predicting initial outpatient attendance for dually diagnosed patients discharged from acute inpatient care.
Methods: Data were extracted from the medical records of 342 dually diagnosed patients discharged from an inpatient unit. City census data were factor analyzed and produced five independent nieghborhood factors: Concentrated Disadvantage, Ethnic Diversity, Hispanic Residence, Crime, and Residential Instability. Data relating to each patient's discharge address and outpatient program location was then geocoded using GIS, and indices of neighborhood environment were computed using the five factors. Stepwise-forward logistic regression modeling was utilized to identify predictors of outpatient treatment attendance. Independent variables included individual characteristics, distance to outpatient treatment, and neighborhood environment indices. The analysis tested for the influence of the neighborhood environment and accessibility to treatment while controlling for individual demographic and clinical (mental health and substance use) characteristics.
Results: Patients were less likely to attend initial outpatient treatment if they had a chief complaint of bizarre behavior (OR=0.37), had greater driving distance to outpatient treatment (OR=0.42), and lived in areas with higher rates of crime (OR=0.27). They were more likely to attend programs that were located in areas with less crime than the neighborhood they lived in (OR=1.70).
Conclusions: Given the importance of continuity of care for dually diagnosed patients discharged from acute inpatient treatment, aftercare planning should take into consideration the neighborhood environment to which patients live as well as the location of outpatient programs to which they are referred. Distance to treatment and the prevalence of crime in patient neighborhoods seem to be especially important considerations for discharge planning.
Financial Support: Support was provided by the Temple University College of Liberal Arts and Grant in Aid funds.

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DOPAMINE RECEPTOR INVOLVEMENT IN ENRICHMENT-INDUCED DIFFERENCES IN METHAMPHETAMINE DRUG DISCRIMINATION IN RATS.

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Aims: Rats raised in an enriched environment show a decrease in sensitivity to the subjective effects of the psychostimulant d-amphetamine. The purpose of the present study was to determine if environmental enrichment during development alters the subjective effects of the more commonly abused drug methamphetamine.
Methods: Male Sprague-Dawley rats were raised in either an enriched condition (EC) or an isolated condition (IC). EC and IC rats were trained on a two-lever operant procedure to discriminate 1.0 mg/kg (i.p.) methamphetamine from saline administered 15 min. prior to the 15-min session. Following acquisition of the discrimination (80% appropriate responding) a methamphetamine generalization curve (0.1-1.0 mg/kg) was determined. Following completion of the methamphetamine generalization curve, pretreatments with either the dopamine D1 receptor antagonist SCH23390 (0.0075-0.06 mg/kg) or the dopamine D2 receptor antagonist eticlopride (0.01-0.3 mg/kg) were administered prior to the training dose of methamphetamine. Finally, the ability of nicotine (0.05-0.5 mg/kg) to generalize and the ability of the nicotinic receptor antagonist mecamylamine (0.125-0.5 mg/kg) to antagonize the discriminative stimulus effects of methamphetamine were also determined.
Results: Results from this study indicate that both EC and IC rats acquired methamphetamine drug discrimination and EC rats were less sensitive to the discriminative stimulus effects of a moderate methamphetamine dose compared to IC rats. EC rats were more sensitive to the antagonistic effects of SCH23390 on methamphetamine discrimination compared to IC rats, while there were no environmentally-induced differences in the effects of eticlopride. Nicotine failed to significantly generalize to the effects of methamphetamine in either EC or IC rats.
Conclusions: These results suggest that environmental enrichment decreases sensitivity to the discriminative effects of methamphetamine and the differences may be mediated through changes in the D1 dopamine receptor.
Financial Support: Support was provided by Creighton University Faculty Research Fellowship Program

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CONTINGENCY MANAGEMENT FOR ADOLESCENT MARIJUANA ABUSE: CACE MODELS.

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Aims: An ongoing randomized clinical trial is comparing two CM interventions to a control condition for adolescent marijuana abuse. Complier Average Causal Effects analyses were used to test the effects of CM vs. no CM and to simultaneously assess and control effects of compliance, severity, SES, and ethnicity on outcomes.
Methods: Treatments last 14 weeks, include twice weekly urine drug testing (parents receive results), and all youth receive individual MET/CBT, plus some form of contingent incentives. The control condition (CONTROL) included incentives for attendance. The CM treatments include abstinence based incentives plus parent involvement.
Results: To date, 66 adolescents (67% African American) have completed treatment (CONTROL=22; CM=44). All youth met DSM-IV criteria for marijuana abuse or dependence and either reported marijuana use in the past 30 days or provided a THC positive urine drug test. By June 2010, we expect that n=100 youth will complete treatment and 80 will have completed the 3 month follow up. The primary outcome measure is the number of consecutive weeks of marijuana abstinence during treatment. Intent to treat (ITT) analyses showed a small but significant effect of CM (Std B=.28). CM effects increased in CACE analyses across increasingly stringent definitions of compliance (>10, >19, >26 of 28 urine samples provided) from Std B=.38 to .63. A total of 43% of the CM group attended >26 UAs. In addition to CM effects, severity was related to outcome, and low SES was related to poorer participation. Effects of ethnicity were not significant on either outcome or compliance when SES was controlled. CACE analyses also showed CM related improvements on youth externalizing, maternal monitoring, and curfew not found in ITT analyses.
Conclusions: CACE analyses showed increased effect sizes for CM compared to ITT analyses. CACE results were strongest using attendance in the last week of treatment as the definition of compliance. CACE analyses showed CM effects on parenting and teen psychopathology not evident in ITT analyses.
Financial Support: NIDA DA015186, NIAAA AA016917, Arkansas Tobacco Settlement Proceeds

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REINFORCING EFFECTS OF D-AMPHETAMINE IN LIGHT AND MODERATE DRINKERS.

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Aims: The results of previous laboratory experiments with humans suggest that light and moderate drinkers respond differently to the effects of stimulants. The purpose of this study was to determine whether light and moderate drinkers differ in their sensitivity to the reinforcing and subject-rated effects of d-amphetamine. We hypothesized that moderate drinkers (i.e., participants that reported consuming at least seven alcohol-containing beverages per week) would be more sensitive to the reinforcing and positive subject-rated effects of d-amphetamine than light drinkers.
Methods: Data from four studies that employed similar d-amphetamine self-administration procedures and subject-rated drug-effect measures were included in the analysis. Light (N=17) and moderate (N=16) drinkers sampled placebo, low (8-10 mg) and high (16-20 mg) doses of oral d-amphetamine administered in eight (8) capsules. Following sampling sessions, participants worked for a maximum of eight capsules, each containing 12.5% of the previously sampled dose, on a modified progressive-ratio schedule of reinforcement. A mixed model ANOVA and planned comparisons were used in the statistical analyses with Drinking Status and Dose as the factors.
Results: Both active doses of d-amphetamine functioned as a reinforcer in the moderate drinkers while only the high dose did so in the light drinkers. The moderate drinkers worked for significantly more capsules that contained the high dose of d-amphetamine than did the light drinkers. d-Amphetamine produced prototypical stimulant-like subject-rated effects (e.g. dose-dependent increases in ratings of Like Drug). Moderate drinkers reported significantly greater subject-rated effects than the light drinkers.
Conclusions: These results are consistent with those from previous laboratory experiments and suggest that moderate alcohol consumption may increase vulnerability to the abuse-related effects of stimulants.
Financial Support: NIDA Grants DA010325, DA012665, DA021155, DA02559 and DA025032 (CRR).

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PATTERNS OF USE SITUATIONS AMONG ACTIVE CLUB DRUG USERS.

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Aims: Research has suggested that the situations in which individuals use substances may inform treatment planning. We examined data from a sample of active club drug users in order to test for the presence of clusters of drug use situations and the utility of clusters to predict dependence beyond factors already identified in the literature.
Methods: A sample of young adult (18-29 years old) active club drug users, stratified by gender and sexual orientation, was recruited using time-space sampling from venues in NYC. Participants completed surveys at baseline and 12 month follow-up (N=295).
Results: K-means cluster analyses were conducted on subscales of the Inventory of Drug Taking Situations (IDTS) using 12 month follow-up data. A three-cluster solution provided the best fit. Groups constituted "Restricted Users" (limited use in all situations; N=132), "Broad Users" (extensive use in all situations; N=37), and "Pleasure Driven Users" (extensive use only in situations involving enjoying pleasant times with others; N=127). Broad Users had the highest anxiety/depression scores followed by Pleasure Driven and then Restricted Users. Rates of substance dependence were higher among Broad (81.0%) and Pleasure Driven (66.1%) Users compared to Restricted Users (34.8%).
Accounting for baseline dependence, amount of current use, and current anxiety/depression, Pleasure Driven Users had a higher likelihood of substance dependence relative to Restricted Users (OR = 2.35; p<.01). The full model accounted for 37% of variance in dependence at 12 months.
Conclusions: Patterns of club drug use were observed and these patterns were associated with dependence above and beyond factors already identified in the literature. Provides evidence for the usefulness of tailoring interventions to account for the situations in which people use substances.
Financial Support: Research supported by NIDA grant R01-DA014925-02.

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INCREASING ACCESS TO SERVICES FOR RURAL RE-ENTERING OFFENDERS USING TELEMEDICINE.

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Aims: A large number of prison inmates report hazardous use of alcohol prior to incarceration, yet few receive treatment. Thus, many hazardous drinkers who did not get treatment in prison re-enter the community on parole to rural areas where services are limited. The purpose of this project is to examine the feasibility of using telemedicine technology to deliver an evidence-based alcohol intervention to rural offenders re-entering the community from prison.
Methods: A process evaluation is used to describe treatment implementation through qualitative interviews with supervisors, parole officers, and treatment providers in two rural parole districts. The interviews were conducted face-to-face, lasted about 30 minutes, and were content analyzed for themes related to alcohol and other drug use as barriers to offenders' success during re-entry. In addition, the interviews included perceptions of telemedicine as a strategy to increase treatment access for re-entering rural offenders.
Results: Findings from the process evaluation indicated that the majority (85%) of re-entering rural offenders are referred for a substance abuse assessment and treatment by the parole board. Respondents agreed that the number of available community services in their areas were limited in serving the number of individuals in need of treatment, and some have to wait as long as 3 months to enter outpatient treatment. Because re-entering offenders have limited resources for treatment including money and transportation, this is a population at increased risk for relapse in the absence of targeted services.
Conclusions: Findings suggest that a number of re-entering offenders need alcohol and drug treatment, have limited service opportunities in rural parole areas, and face consequences of continued use including parole revocation. The long-term objective of this study is to increase access to effective treatment approaches for rural re-entering offenders in order to promote alcohol abstinence and reduce recidivism.
Financial Support: Project supported by R21-AA017937.

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CATECHOL-O-METHYL TRANSFERASE AND CORTICOTROPIN-RELEASING HORMONE RECEPTOR GENE VARIANTS MAY IMPACT OPIOID ABSTINENCE INITIATION AND WITHDRAWAL SYMPTOMS IN HEROIN-DEPENDENT VOLUNTEERS.

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Aims: A functional SNP in the COMT gene (val158met) alters endogenous dopamine and opioid function and pain sensitivity. Gene knockout and pharmacological antagonism studies suggest that disrupting CRHR1 function decreases opioid dependence signs. This ongoing study examines whether COMT and CRHR1 variations influence opioid withdrawal symptoms and abstinence initiation.
Methods: During standardized outpatient buprenorphine 8mg/day induction, withdrawal symptoms and abstinence (% or any opioid-free urines) are measured 6x over 2 weeks in heroin-dependent volunteers (total n=52; n=25 AA), genotyped with the Golden Gate assay. ANOVAs and regression were used to test genotype associations with withdrawal symptoms and abstinence.
Results: All variants reported are independent of race. COMT met carriers (n=33) vs. val/val homozygotes (n=17) show a lower proportion of opioid-free samples, 5 vs. 23%, $F(1,49)=7.78$, $p<.01$, and fewer met carriers achieve any abstinence (18 vs. 41%, p=.08); and marginally higher withdrawal symptoms (p=.19). Four CRHR1 intron-1 SNPs with MAFs>0.3 are in linkage disequilibrium ($\chi 2$ tests, ps<.05). CRHR1 rs242924 A-allele carriers (n=32) vs. C/C homozygotes (n=19) show a lower proportion of opioid-free samples, 5 vs. 23%, $F(1,50)=8.17$, $p<.01$; fewer achieve any abstinence, $\chi 2(1,51)=6.03$, $p<.02$; and report more withdrawal, $F(1,39)=4.29$, $p<.05$. CRHR1 rs173365 'A/A', 'A/G' and 'G/G' carriers (ns=10, 28 and 13) show progressively lower proportions of opioid-free samples (21, 14 and 0%), $F(2,50)=6.04$, $p<.01$; any abstinence (60, 29 and 0%), $\chi 2(2,51)=10.26$, $p<.01$; withdrawal scores did not differ. Logistic regression, controlling for withdrawal on induction days 1 and 3, found that only CRHR1 rs173365 predicted any opioid abstinence (r2=15%).
Conclusions: These preliminary findings suggest that COMT and CRHR1 SNPs may be related to opioid reinforcement/dependence processes.
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METHAMPHETAMINE-USING PREGNANT WOMEN IN CALIFORNIA DRUG TREATMENT: CHARACTERISTICS, REFERRAL SOURCE, PROGRAM COMPLETION AND PRENATAL CARE.

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Aims: This study explores characteristics of 174 methamphetamine-using pregnant women regarding drug treatment entry and program completion.
Methods: Descriptive statistics and Chi-square assessed 407 pregnant women, of whom 42% (174) identified MA as their primary drug of choice. These women entered California public substance abuse treatment programs during 2000-2002.
Results: Compared to pregnant women who used alcohol or other drugs (AOD), MA-using women were more likely to enter treatment from a criminal justice system (CJS) referral ($P<0.0001$) and had significantly more prior drug treatment episodes ($P<0.001$). Among the pregnant women, similar psychiatric comorbidities were identified; however, MA users with CJS referrals reported more lifetime suicide attempts than MA users who had community referrals ($P<0.04$). The onset of prenatal care for pregnant MA-using women is comparable to AOD women; approximately 18% reported no prenatal care and 32% entered care late in pregnancy. However, CJS-referred MA pregnant users were more likely to have lost parental rights than other MA-using pregnant women ($P< 0.002$). Lastly, CJS-referred pregnant MA users had a greater likelihood of successful drug treatment completion than MA-users referred by other sources ($p<001$).
Conclusions: Findings suggests ethical and public policy implications regarding MA-using pregnant women who entered treatment via the criminal justice system rather than healthcare or social services. It suggests the need for coordination of services through the CJS for pregnant MA-using women regarding prenatal services, drug treatment, and psychosocial support services. Likewise, it obviates the need for longitudinal studies to evaluate the efficacy of cumulative episodes of substance abuse treatment for MA-using women.
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ALTERED RESTING STATE FMRI DEFAULT MODES IN METHAMPHETAMINE USERS.

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Aims: Methamphetamine (Meth) abuse is known to be associated with cognitive deficits and altered brain activation from prior Blood-oxygenation-level-dependent functional MRI (BOLD-fMRI) studies. However, whether Meth alters the resting state brain function is unknown. This study aim is to use resting state BOLD-fMRI to evaluate the default mode (DM) networks in current and abstinent Meth users.
Methods: Resting state BOLD-fMRI was performed in 14 healthy non-drug users, 7 current, and 7 abstinent (for at least one month) Meth users. Each subject had one or two 4-minute fMRI scans on a 3 Tesla Siemens MRI scanner. Images were acquired with a spiral in/out gradient-echo sequence to achieve a higher signal-to-noise ratio. The subjects were instructed to rest motionless with their eyes closed. The Melodic FSL software tool was used to perform probabilistic Independent Component Analysis (ICA). A set of ICA spatial maps and time courses were obtained identifying the major sources of variation in the entire group. A linear model was used to assess the statistical significance of each ICA to each group.
Results: The DM's were identified by visual inspection and corresponded to previously observed DM networks in the literature. The resting network for executive function appeared to be activated less in the current and abstinent users, suggesting a down regulation of this network, compared to non-drug user controls ($p < 0.00000$).
Conclusions: The resting state DM networks involved with executive function appeared to be down regulated in Meth users. These preliminary results suggest that the resting state brain network may be altered by Meth use or Meth-associated brain injury. Correlations with cognitive performance and the DM network also will be performed.
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ROLE OF VENTRAL MEDIAL PREFRONTAL CORTEX IN CONTEXT-INDUCED REINSTATEMENT OF HEROIN SEEKING.

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Aims: In humans, exposure to environmental contexts previously associated with heroin intake can provoke drug relapse but the neuronal mechanisms mediating this relapse are largely unknown. Using a drug relapse model, we previously found that re-exposing rats to heroin-associated contexts following extinction of drug-reinforced responding in a different context reinstates heroin seeking. This effect is attenuated by inhibition of glutamate transmission in ventral tegmental area and accumbens shell, and by blockade of dopamine D1-like receptors in accumbens shell and dorsolateral striatum. Here, we examined the potential contribution of prefrontal cortex (mPFC) in this reinstatement by testing the effect of reversible inactivation of ventral or dorsal mPFC.
Methods: Rats were trained to self-administer heroin for 12 days; drug infusions were paired with a discrete tone-light cue. Subsequently, the heroin-reinforced responding was extinguished in the presence of the discrete cue in a context that differed from the drug self-administration context in terms of visual, auditory, tactile, and circadian cues. During subsequent tests for context-induced reinstatement, we inactivated the ventral or dorsal mPFC by local injections of muscimol+baclofen (0.1+1.0 mM per side) and then re-exposed the rats to the original heroin self-administration context.
Results: Inactivation of ventral mPFC decreased context-induced reinstatement of heroin seeking; experiments on inactivation of dorsal mPFC are ongoing and results will be presented at the meeting.
Conclusions: Based on our previous data on the role of glutamate in accumbens shell in context-induced reinstatement of heroin seeking, we speculate that the glutamate projection from the ventral mPFC to accumbens shell contributes to this reinstatement.
Financial Support: IRP/NIDA

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DOPAMINE RECEPTOR AGONISTS MODIFY THE DISCRIMINATIVE STIMULUS EFFECTS OF RIMONABANT IN Δ9-THC TREATED RHESUS MONKEYS.

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Aims: Clinical studies suggest that depression is a component of the marijuana withdrawal syndrome, yet treatment with the antidepressant and catecholamine transport inhibitor bupropion worsens mood in abstinent marijuana users. To examine the pharmacological mechanism(s) by which bupropion enhances marijuana withdrawal, the effects of bupropion and pharmacologically related drugs were tested in a pre-clinical assay of cannabinoid withdrawal.
Methods: Cannabinoid dependence and withdrawal were indexed with a drug discrimination assay, i.e., rhesus monkeys discriminating the cannabinoid antagonist rimonabant (1 mg/kg i.v.) while receiving daily treatment with Δ9-THC (1 mg/kg/12 h s.c.).
Results: Cocaine (0.1-1 mg/kg), amphetamine (0.1-0.32 mg/kg), and bupropion (1-5.6 mg/kg) produced a maximum of 54, 33, and 31% responding on the rimonabant lever, respectively. Cocaine and amphetamine produced leftward shifts in the rimonabant dose-response curve. The involvement of dopamine receptor subtypes was then investigated; the dopamine D1- and D2- like receptor agonist apomorphine (0.32-1 mg/kg) produced a maximum of 38% rimonabant-lever responding and shifted the rimonabant dose-response curve leftward. The D2-like antagonist haloperidol (0.01-0.1 mg/kg), on the other hand, produced a maximum of 4% responding on the rimonabant lever and did not shift the rimonabant dose-response curve leftward. Thus, there was some pharmacological specificity in the effects of dopamine receptor agonists to produce rimonabant-like effects and to increase the potency of rimonabant.
Conclusions: Dopamine receptor agonism appears to enhance cannabinoid withdrawal. Therefore, ligands that increase dopamine neurotransmission appear to be contraindicated as therapeutics for marijuana dependence.
Financial Support: Supported by USPHS grant DA 19222 and DA 26781.

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EARLY SUBSTANCE USE AND RISKS ASSOCIATED WITH FATHER ABSENCE.

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Aims: We examine alcohol, tobacco, and cannabis use by age 14 and risks, both familial and extra-familial, associated with father absence during childhood.
Methods: Data were drawn from child samples of the National Longitudinal Study of Youth, including 1798 female and 1873 male youth, aged 14-28 years, with non-missing substance use histories and data used to code father absence. Following univariate logistic regression predicting early substance use from father absence, multivariate logistic regression was conducted including maternal monitoring at ages 12-13 and perceived peer pressure to use alcohol, tobacco, or cannabis, also assessed at ages 12-13. To examine differences by gender, all models were conducted separately for female and male youth.
Results: For female youth, we observed a significant univariate association between father absence and smoking (OR=1.52) and cannabis use (OR=1.87). For male youth, a similar pattern was observed for smoking(OR=1.65) and cannabis use (OR=1.71). Associations between father absence and alcohol use were nonsignificant for both females and males. In multivariate analyses, father absence remained a robust predictor of smoking (female OR=1.64; male OR=1.52). Maternal monitoring was associated with 29% decreased risk for females (OR=.71), with nonsignificant effects observed for males. Peer pressure was associated with over three times increased risk of smoking for females (OR=3.35), and over two times increased risk for males(OR=2.40). Father absence also remained predictive in multivariate analyses of cannabis use, with pronounced effects for females (OR=2.03), compared with males (OR=1.60). Maternal monitoring was associated with 26-30% decreased risk of cannabis use [female (OR=.70); male (OR=.74), with peer pressure associated with over three times increased risk for females (OR=3.50), and over four times increased risk for males (OR=4.21).
Conclusions: Results for both female and male youth confirm the importance of father absence, and familial and extra-familial risks associated with father absence, as significant predictors of early smoking and cannabis use, especially.
Financial Support: none

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ADULT SUBSTANCE ABUSERS WITH ADHD SHOW HIGHER PREVALENCE OF MARIJUANA AND COCAINE USE.

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Aims: Once most studies have investigated substance abuse and attention deficit and hyperactivity disorder with adolescent samples this study aims to compare prevalences of substance abuse among adults with and without attention deficit and hyperactivity disorder (ADHD).
Methods: A cross-sectional multi-center sample of 285 current adult substance abusers from in- and outpatient clinics was collected at three research centers located in Brazilian state capitals. Subjects were evaluated with the Adult ADHD Self-report Scale (ASRS), the sixth version of the Addiction Severity Index (ASI6) and the MINI-Plus. Ninety eight subjects who screened positive for ADHD were compared to negatives (n=187), using multivariate analysis in order to minimize confounding factors.
Results: Individuals with ADHD showed more prevalence of marijuana (54.1% vs 37.2%, p=0.009) and cocaine use (58.2 vs 43.6, p=0.027) when compared to individuals without ADHD. Use of marijuana (OR 1.786, p=0.03) and cocaine (OR 1.939, p=0.025) were higher in the last 30 days in the ADHD group even when controled by confounding factors. Other psychiatric disorders such as depressive disorder, suicidal risk, manic episodes and general anxiety disorder were also higher in this sample.
Conclusions: This is one of the first studies conducted with an adult sample that demonstrates that ADHD may be associated to marijuana and cocaine use. Most of the studies in this area suggest that marijuana could be used for restlessness and cocaine for inattention improvement as a self-medication strategy, which could explain the higher prevalence in this population. On the other hand ADHD symptoms may be also a consequence of marijuana and cocaine use related to the acute and withdrawal symptoms or the brain damage caused by these drugs. Further research among adult ADHD population could elucidate this question.
Financial Support: National Secretariat for Drug Policies

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THE REINFORCING EFFECTS OF INTRANASAL COCAINE ON A PROGRESSIVE RATIO SCHEDULE.

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Aims: Even though many cocaine users report initiating cocaine use by the intranasal route and some prefer that route, the reinforcing effects of cocaine have largely been tested in humans using smoked or intravenous administration. The purpose of the present experiment was to measure the reinforcing effects of intranasal cocaine using a progressive-ratio schedule in which subjects chose between doses of cocaine (4 [placebo], 15, 30 and 45 mg) and an alternative reinforcer ($0.25). We hypothesized that cocaine would maintain responding to a greater degree than placebo and that the alternative reinforcer would suppress choices of lower cocaine doses.
Methods: Six current cocaine-using humans completed the protocol. During each session, the subjects first sampled the dose of cocaine available that day and then made six choices between that dose and money. To earn their first choice, subjects had to make 400 responses. The response cost for each subsequent choice of each option increased by 200 responses (i.e., a second choice of cocaine would require 600 responses whereas the responses for a money choice following an initial cocaine choice would require 400 responses). Data are analyzed using repeated-measures ANOVA.
Results: Break points for active cocaine doses were higher than those for placebo, and the alternative reinforcer failed to effectively decrease self-administration of active cocaine doses. Cocaine also produced prototypical stimulant-like effects (e.g. increased heart rate and blood pressure; increased ratings of drug liking).
Conclusions: These data demonstrate that intranasal cocaine functions as a reinforcer under a progressive ratio schedule in humans. Future research will test higher values of money to determine whether they can suppress cocaine self-administration behavior under progressive-ratio schedules.
Financial Support: NIDA Grant R21 DA 024089 (WWS).

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YOUNG ADULT SUBSTANCE USE AND WORKPLACE POLICIES AND CONDITIONS.

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Aims: Workers between the ages of 18-25 have been found to have the highest rates of substance use. The aim of this study is to examine differences in recent substance use by workplace conditions and the awareness of substance use policies and programs among an urban sample of employed young adults

Methods: Approximately 75% of two consecutive cohorts of children entering first grade of a public school system of a large mid-Atlantic city in the mid 1980s were followed into young adulthood (mean age 21). Interviews were conducted at their place of residence and 66% of the participants indicated they were currently employed (n=1020: 46% male and 64% African American).

Results: Approximately one-third of the working young adults had used tobacco (32%) and 41% had consumed alcohol in the prior month. An estimated 29% had used an illicit drug in the year preceding the interview. Awareness of workplace policies restricting smoking and for alcohol and drug use was quite common (79% and 87%, respectively). Over half worked for employers who did drug testing (58%). Employers sometimes had assistance programs (EAP, 39%), offered wellness programs such as stress reduction (34%) but less commonly offered smoking cessation programs (20%). Tobacco use was less common among those who were aware of an official workplace smoking restriction policy (29% vs 45%, p<.001) and in sites where employers offered cessation programs or wellness classes (22% vs 38%, p<.001). Alcohol consumption and the use of illicit drugs was also less common among those aware of a written policy about drug and alcohol use at their worksite (alcohol: 39% vs 53%, p=.06; illicit drugs: 26% vs 54%, p<.001) and if their employer had a drug testing program (alcohol: 37% vs 47%, p=.002; illicit drugs: 22% vs 39%, p<.001). The availability of EAP or wellness classes was associated with less illicit drug use (p<.001) but no differences were noted for alcohol use (p>.1).

Conclusions: The workplace may be an appropriate venue for establishing substance use prevention and interventions for young adults.

Financial Support: Supported by grants MH71395, DA09897, DA04392, and DA019805.

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ACCEPTANCE AND COMMITMENT THERAPY AS AN ADJUNCT TO METHADONE DETOXIFICATION.

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Aims: Methadone maintenance is the most successful approach to the management of heroin/opioid dependence. While some individuals choose to remain on methadone for the duration of their lives, many wish to be drug-free. Various medication and dosing strategies for opiate detoxification have been tested, however long-term success rates are dismal. Anxiety, fear, and intolerance of physical withdrawal symptoms are certain to affect outcomes negatively, however, few behavioral therapies have been developed to target these common detoxification symptoms. The aims of this stage I study were to develop and test an opiate detoxification behavioral therapy based on Acceptance and Commitment Therapy (ACT).

Methods: Methadone patients (N = 52) between the ages of 25 and 60 who were attending a licensed clinic were randomized to receive either 24 individual therapy sessions of ACT or Drug Counseling (DC) while undergoing a 6 month linear dose reduction program.

Results: Mixed effects logistic regression identified linear and quadratic trends over time. Evaluation of treatment effects and their interaction with time failed to identify statistically reliable differences, likely due to sample size constraints. Effect sizes for the main effect of treatment may be more meaningful. Collapsing across time, participants in the DC condition demonstrated higher odds of being opiate positive (O.R. = 1.82, 95% C.I. 0.24-14.01) relative to the ACT condition. Similarly, evaluation of the Treatment Effectiveness Score (TES; number of opiate negative urine screens across treatment) as a function of intervention condition indicated that TES decreased for participants in the DC condition by a factor of 0.77 (95% C.I. 0.44-1.35) (i.e. 23% reduction in TES for the DC relative to the ACT condition).

Conclusions: Although caution must be used in interpreting these preliminary data, results indicate that the ACT intervention is successfully reducing opiate use during methadone detoxification relative to an equally intensive drug counseling condition.

Financial Support: Supported by NIDA #019436

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ADVERSE CONSEQUENCES FOR CHILDREN OF COCAINE-DEPENDENT PARENTS.

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Aims: Parental substance dependence is known to have negative consequences for children including neglectful parenting, abuse, and child psychopathology. The purpose of these analyses were to examine parental reports of behavioral problems and other adverse outcomes in children (e.g., foster care, special education) among cocaine dependent cases and community-based controls.

Methods: As part of the Family Study of Cocaine Dependence, cases were recruited through substance abuse treatment centers and were required to meet DSM-IV criteria for cocaine dependence. Nearly 60% also met dependence criteria for other illicit substances. Community-based controls were identified through the Missouri driver's license registry and matched to cases on gender, race, age, and zip code; controls were not dependent on tobacco, alcohol, or any other substance. Only subjects who had at least one biological child were included in the analyses. The total sample consisted of 740 participants: 395 cases (60% African American, 42% Male) and 345 controls (59% African American, 35% Male). All subjects completed a semi-structured assessment of substance dependence and other psychiatric disorders, as well as questions about their children.

Results: Chi-square analyses indicate that cocaine dependent cases were significantly more likely than community-controls to have children in special education (27.3% v. 18.3%), have children who were suspended or expelled from school (42.5% v. 27.8%), have deceased children (9.9% v. 2.6%), have child welfare services check on their children (35.7% v. 9.3%), and have their children placed in foster care (19.7%v. 1.4%). Regression analyses confirm that parental cocaine dependence was a significant predictor of adverse consequences in children.

Conclusions: These results suggest that that there are adverse consequences for children beyond familial transmission of dependence. Treatment centers and policy makers need to acknowledge the social and behavioral child outcomes in a familial systems approach.

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OPIATE DEPENDENCE, ALCOHOL DEPENDENCE AND ASPD AMONG AGE COHORTS: A TRIPLE THREAT TO THE SERVICE SYSTEM.

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Aims: Practitioners and researchers are increasingly concerned about the emerging health problems and complex substance dependence treatment needs among methadone clinic patients with a history of alcohol dependence (Dobler-Mikola et al, 2005; Stenbacka et al., 2007; Rosen et al., 2008; Ryder et al., 2009). As this population with reduced access ages, their health problems may become increasingly difficult to treat. A public health response is needed to increase relevant services with low barriers to care, including a work force with expertise in geriatrics and substance dependence (Rosen et al., 2008; Simoni-Wastila & Yang, 2006). Antisocial personality disorder has been found to be as high as 61% in this population (Darke et al., 1994); ASPD further complicates the public health response.

Methods: In a study of 235 men and 174 women aged 18 – 65 with prescription drug misuse (opiates, sedatives or stimulants), we had the opportunity to consider the "triple threat" of Opiate Dependence (prescription and/or heroin), Alcohol Dependence and Antisocial Personality Disorder.

Results: Among men and women, by age group, the rates of the "triple threat" varied from 4 – 9% in each age group except among men aged 26 – 49, who had more than double the rate (20%). These individuals were more likely to have been arrested, and to have had fewer physician check-ups in the last year than those without the "triple threat."

Conclusions: The number of women with this comorbidity is concerning (Magura et al., 1998). Service providers need to consider the possibility that ASPD may be elevated in women with alcohol and opiate dependence histories. Middle aged men in this sample had an elevated rate and will be investigated further. Adding to the literature, our findings strengthen the call from methadone clinics to ensure that the services and expertise needed by this population will be available to meet their unique needs as they continue to age.

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MICE THAT SOLELY EXPRESS NON-EDITED 5-HT$_{2C}$ RECEPTOR ISOFORM EXHIBIT AN ANXIETY-LIKE PHENOTYPE.

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Aims: Serotonin 2C receptor (5-HT$_{2C}$R) functions and subcellular expression are modulated by RNA editing, a post-transcriptional mechanism that alters the coding properties of the mature mRNA. 5-HT$_{2C}$R pre-mRNA editing can generate isoforms that differ in agonist binding properties and functional activity. A new line of genetically-modified mice that solely express the protein isoform encoded by the non-edited mRNA (5-HT$_{2C}$-INI) provides a unique opportunity to explore the neurobiological importance of editing in vivo. Here, we characterized the general health and behavioral phenotype of heterozygous 5-HT$_{2C}$-INI mice compared to wild-type (WT) littermates.
Methods: WT C57BL/6 (n=16) or 5-HT$_{2C}$R-INI (HET) female mice (n=18) were screened on several behavioral assays: anxiety-like behavior (elevated plus maze, EPM); locomotor activity (open field exploration, OF); motor skill acquisition (rotarod task, RR); depressive-like behavior (tail suspension test, TST).
Results: WT and HET mice express similar general health characteristics, levels of OF exploration, and time spent immobile or struggling in the TST. In EPM, HET mice entered the open arms significantly fewer times (5.9 ± 0.39 entries) than WT mice (7.4 ± 0.37 entries) ($p < 0.05$, t-test. HET mice did not show the same level of improvement in the RR test as observed in WT, indicating a motor learning deficit.
Conclusions: Mice that solely express the 5-HT$_{2C}$R-INI isoform exhibit an anxiety-like phenotype and motor learning impairment. Thus, expression of only the fully functional non-edited 5-HT$_{2C}$R provides an innovative animal model to further our understanding of the role of the 5-HT$_{2C}$R in complex neuropsychiatric diseases.
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CUE-INDUCED RESPONSE-POTENTIATION IN A RUNWAY MODEL OF IV HEROIN AND COCAINE SELF-ADMINISTRATION.

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Aims: Response-reinstatement of goal-seeking behavior has been widely utilized as an animal model of drug "relapse." In this work, rats with an "extensive" history of self-administration reinstate their drug-seeking behavior upon presentation of a drug-paired cue following a period of abstinence. The current study aimed to assess whether similar cue-induced effects would be observed in rats with a "casual" history of drug exposure.
Methods: Rats were trained to run a straight alley once a day for a single IV injection of heroin or cocaine upon goal-box entry. Each drug was associated with a distinctive olfactory cue and was present throughout the runway apparatus. All rats were also exposed to the alternate (i.e., non-drug paired) scent in their home cages, 2-hr prior to runway training. After 15 reinforced trials/days, extinction trials were initiated during which both the scent and reinforcer were removed from the apparatus. Each rat was subsequently tested for its response to the drug-paired or non-paired cue after either 7 or 21 extinction trials.
Results: The results confirmed previous findings that rats running the alley for IV heroin exhibited a strong positive response, while cocaine-reinforced rats exhibited slower response times and a high frequency of approach-avoidance "retreat" responses. In contrast, after 3-weeks of extinction, only the cocaine-paired cue produced a robust potentiation in drug-seeking behavior. Furthermore, rats exposed to the cocaine-cue exhibited fewer "retreats" suggesting that their elevation in drug-seeking may have been due to a weakening of their negative associations with the goal box.
Conclusions: Together, these data suggest that in animals running once a day for a single drug injection, the motivation to seek heroin is stronger than that for cocaine; however, once the drug is removed for a period of time, the cocaine-paired cue produces a more robust potentiation in drug-seeking behavior. Thus, the propensity to "relapse" may not be reliably predicted by the pattern and extent of prior drug self-administration.
Financial Support: PHS NIDA grant DA05041 awarded to AE

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THE ADDED RISK OF OPIOID PROBLEM USE AMONG TREATMENT-SEEKING YOUTH WITH MARIJUANA/ALCOHOL PROBLEM USE.

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Aims: To determine the added risk of opioid problem use (OPU) in youth with marijuana/alcohol problem use (MAPU)
Methods: 475 youth (ages 14-21 years) with OPU+MAPU were compared to a weighted sample of 475 youth with MAPU only (i.e., no OPU) before and after propensity score matching on gender, age, race, level of care, and weekly use of marijuana/alcohol. Youth were recruited from 88 U.S.drug treatment sites. At treatment intake, participants were administered the Global Appraisal of Individual Need to elicit information on demographic, social, substance, mental health, HIV, physical and legal characteristics. Odds ratios with confidence intervals were calculated.
Results: The added risk of OPU among MAPU youth was associated with > comorbidity: higher rates of psychiatric symptoms and trauma/victimization; > needle-use and sex-related HIV-risk behaviors and physical distress. The OPU+MAPU group was < likely to be African American or other race and > likely to be age 15-17 years, Caucasian; report weekly drug use at home and among peers; engage in illegal behaviors and be confined longer; have > substance abuse severity and poly drug use; and use mental health and substance abuse treatment services.
Conclusions: These findings expand on the existing literature and highlight the substantial incremental risk of OPU on multiple comorbid areas, among treatment-seeking youth. Further evaluation is needed to assess their outcomes following standard drug treatment and to evaluate specialized interventions for this subgroup of severely impaired youth.
Financial Support: This research was supported by grant K12DA000357 (Subramaniam, P.I.) from the National Institute on Drug Abuse (NIDA) and American Academy of Child and Adolescent Psychiatry, prior to Dr. Subramaniam's employment at NIDA. This project was also supported by the Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration (SAMHSA) contract 270-07-0191 using data provided by several grants and contracts from CSAT

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IMPAIRED FRONTO-AMYGDALAR CONNECTIVITY: A MARKER OF POOR BEHAVIORAL CONTROL IN COCAINE DEPENDENCE?

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Aims: We recently found that "relapse-prone" cocaine patients (characterized by cocaine-positive urine status at the end of screening) evidenced poor connectivity between the amygdala (AMYG) and dorsal cortical regions when attempting to inhibit cocaine craving. To examine the behavioral significance of our findings, we examined a relationship between AMYG connectivity and ability to inhibit behavioral responding in a novel Affect-congruent GoNoGo task.
Methods: Nineteen cocaine-dependent patients were scanned after 7 days in a controlled therapeutic setting to ensure stable, cocaine-free state. The novel GoNoGo task was administered off-magnet. ASL (arterial spin-labeled) perfusion fMRI at 3 Tesla was used to measure rCBF while watching a cocaine video and attempting to decrease subjective craving. Perfusion data were pre-processed within SPM2, using functional connectivity analyses with amygdala as the reference region. The relationship between the connectivity and errors of commission (i.e., NoGo errors) was examined using a single regression analysis.
Results: The mean errors of commission score was 5.70 (s.d.=3.2). Functional connectivity analyses (cluster-corrected whole brain) demonstrated a striking absence of frontal-AMYG connectivity and strong intra-limbic connectivity with AMYG during attempts to inhibit cocaine craving (p corrected<0.001; cluster size => 20 contiguous voxels). Regression analysis revealed an inverse relationship between NoGo errors and dorsal PFC-AMYG connectivity (peak voxel: -6, -24, 48; cluster size=94 voxels; t=6.64).
Conclusions: Poor connectivity between frontal modulatory region and AMYG predicted greater difficulty with response inhibition. Impaired fronto-limbic connectivity may provide an important marker of greater relapse vulnerability in clinical trials, and a critical treatment target for interventions.
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THE IMPACT OF COCAINE USE ON OUTCOMES IN HIV-INFECTED PATIENTS RECEIVING BUPRENORPHINE/NALOXONE.

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Aims: Cocaine use is common in opioid dependent HIV-infected patients. To determine the impact of cocaine use on illicit drug and HIV outcomes among HIV-infected patients receiving buprenorphine/naloxone (BUP) we conducted a prospective study in 299 patients.
Methods: Self-report assessments were conducted at baseline and every 3 months for one year. We evaluated the association between baseline and in-treatment cocaine use on BUP retention, self-reported illicit drug use, antiretroviral adherence, CD4 counts, Log10 HIV RNA levels, and HIV risk behaviors.
Results: Sixty-six percent (N=197) of 299 patients reported baseline cocaine use and 65% (N=173) of 266 patients with follow-up data reported in-treatment cocaine use. Baseline and in-treatment cocaine use did not impact BUP retention. Baseline cocaine use was associated with a 14.8 (95% CI=9.0-24.2) times greater likelihood of in-treatment cocaine use (95% CI=9.0 - 24.2; p<.001), a 1.4 times greater likelihood of in-treatment opioid use (95% CI=1.02 - 2.00; p=.04), and higher Log10 HIV RNA levels (p< .016). Patients with in-treatment cocaine use were 1.4 times more likely to report using opioids (95% CI=1.01-2.00; p=.04). Antiretroviral adherence, CD4 lymphocyte counts, and HIV risk behaviors did not differ significantly over time based on baseline or in-treatment cocaine use.
Conclusions: Interventions that address cocaine use in HIV-infected opioid dependent patients may augment the benefits seen with BUP treatment.
Financial Support: Supported by the Health Resources and Services Administration (HRSA) (1H97HA03800)

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OPIOID PRESCRIBING PRACTICES FOR ADOLESCENTS WITH CHRONIC PAIN.

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Aims: The goals of this survey were to characterize the opioid prescribing practices of adolescent pain management providers, and identify possible barriers to addiction risk assessment.
Methods: Respondents (N=114) included medical and surgical pediatric providers. Prescribing practices for adolescent non-cancer chronic and subacute post-operative pain conditions were the focus of this study. Outcomes included self-reports of pain diagnoses for which opioids are prescribed, screening and monitoring practices, and perceptions regarding barriers to prescribing opioids.
Results: The vast majority (22/23)of practitioners prescribed opioids for a limited number of pain conditions including headache, musculoskeletal/limb pain, and inflammatory/rheumatologic pain. Relative to functional pain, the odds of an opioid being prescribed for musculoskeletal with no identified pathology (OR=3.09, p=.001); neuropathic pain (OR=3.14, p=.005); musculoskeletal with identified pathology (OR=12.3, p<.0001); and post-operative pain (OR=20.9, p<.0001) conditions were significantly higher. Most opioid-prescribing practitioners conducted confidential interviews with adolescents presenting with chronic non-malignant pain (81.5%), whereas almost half (46.2%) of practitioners omitted this practice when prescribing opioids for sub-acute post-operative pain. Among practitioners with established pain patients, only 10.7% reported collecting random toxicology screens at least once a year. Non-prescribers differed significantly from prescribers with respect to their concerns about addiction (X21=3.92, p=.05) and lack of knowledge of which narcotic to use (X21=4.41, p=.04).
Conclusions: Limited training in opioid pain management, as well as fears of engendering addiction, may limit the appropriate use of opioid analgesics for pediatric chronic and sub-acute pain populations. Important opportunities to assess for addiction risk in this population are lost because of practices of non-confidential interviewing as well as the lack of urine toxicology screening.
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DECREASED N-ACETYLASPARTATE LEVELS IN ADOLESCENTS CONCURRENTLY USING BOTH METHAMPHETAMINE AND CANNABIS.

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Aims: The impact of concomitant heavy methamphetamine (MA) use and cannabis (CA) use is not well understood. While there is limited evidence that MA is neurotoxic to the brain, CA use has been associated with both neuroprotective and neurotoxic effects. It is therefore not known what the combined effects of MA and CA use will be on the developing brain. To evaluate the effect of concurrent use of MA+CA, this study utilized single voxel magnetic resonance spectroscopy (MRS) and compared in vivo brain metabolite levels in three adolescent groups from Cape Town, South Africa:1) MA-alone, 2) MA+CA and 3) healthy controls.
Methods: Single voxel MRS was acquired in nine MA dependent (age=15.1±1.26, 3 female), eight MA+CA dependent (age=15.8 ±1.39, 3 female) adolescent subjects and ten healthy subjects (age=16.3±0.49, 3 female). Imaging was completed on a 3.0 Tesla Siemens, using PRESS (point-resolved spectroscopy), TR=1500 ms, TE=30 ms, NA=128, ROI=2x2x2cm. Spectroscopic data were analyzed using LCModel for fully automated quantitation of metabolite levels of N-acetylaspartate (NAA), myo-inositol and choline and reported as metabolite ratios to creatine (Cr). Analysis of variance (ANOVA) was performed for each metabolite ratio to detect between-group differences.
Results: The MA+CA group showed a significant reduction in the brain NAA/Cr ratio (primarily an indicator of neuronal viability and function) compared to both healthy controls by 7.2% (p=0.011) and to the MA-alone group by 6.9% (p=0.018). The MA-alone group did not show a statistically significant difference in NAA/Cr ratios compared to the control group.
Conclusions: It is surprising that the MA-alone cohort did not demonstrate reductions in the NAA/Cr ratio. However, our preliminary results suggest that combined MA+CA abuse may synergistically interact to induce biochemical abnormalities and neuronal dysfunction. A larger scale study is warranted to confirm the altered NAA levels in adolescent MA+CA dependence.
Financial Support: Research supported by funding from NIH R21 DA 021422 and 1R01 DA020269

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ABRUPT DISCONTINUATION AFTER CHRONIC TREATMENT WITH SSRI AND SNRI INDUCES WITHDRAWAL SYNDROME-LIKE SIGNS IN MICE AND RATS.

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Aims: Early discontinuation or dosage reduction during first several weeks of treatment with the selective serotonin reuptake inhibitor (SSRI) and selective serotonin-noradrenaline reuptake inhibitor (SNRI) caused the discontinuation syndrome. In clinical settings, this syndrome was characterized by symptoms including dizziness, dysphoria, and gastrointestinal upset. However, the mechanism of action underlies this syndrome remained unclear.
Methods: We treated mice and rats with fluvoxamine (SSRI) (mice: 0.1-3.2 mg/g of food, rats: 0.5-5.0 mg/g of food) or milnacipran (SNRI) (mice: 0.05-1.6 mg/g of food, rats: 0.2-3.6 mg/g of food) for 4 weeks using drug-admixed food (DAF) method. The treatment was abruptly discontinued by replaced the mixed food with normal food.
Results: We found that abrupt discontinuation after chronic treatment with SSRI or SNRI did not change general locomotor activity and motor coordination in mice. Interestingly, milnacipran, but not fluvoxamine, treatment group showed greater body weight loss compared to control group (P<0.05). Milnacipran group also showed the tail-shaking-like behavior when softly touched by hands. This behavior mimicked to sensory hypersensitivity. Furthermore, we found that the fluvoxamine and milnacipran treated groups showed significantly higher scores (P<0.05) for emotional/sensory-sensitive and autonomic behavioral, but not on motor behavioral changes after discontinuation. Present RT-PCR analysis in the frontal cortex after chronic treatment with SSRI or SNRI showed no change in the gene expressions of serotonin receptor 1A, 2A, 2C, 3A, 4 and 7 subtypes.
Conclusions: These results suggest that abrupt discontinuation after chronic treatment with SSRI and SNRI using DAF method causes withdrawal syndrome-like signs in rodents. Furthermore, the sensory-sensitive and autonomic behaviors changes are the most observed behavior during the syndromes.
Financial Support: Grants from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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UP IN SMOKE? COGNITIVE-BEHAVIORAL MOTIVATIONAL ENHANCEMENT +/- NICOTINE REPLACEMENT THERAPY FOR ADOLESCENT SMOKERS.

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Aims: To assess the uptake and early efficacy of a smoking cessation program tailored for adolescents and young adults (ages 14-21) that provides six sessions of cognitive behavioral motivational enhancement therapy in conjunction with optional open-label nicotine replacement therapy.
Methods: The intervention was based on current guidelines for smoking cessation and tailored using youth-oriented materials and peer-to-peer delivery. Youth seeking smoking cessation were offered six weeks of one-on-one therapy using cognitive behavioral motivational enhancement and offered optional 4 weeks of nicotine replacement therapy (NicoDerm CQ). Participants completed baseline measures to assess physical health, personality and mental health functioning, smoking history, and neurocognitive measures. Youth were recruited from schools, community health clinics, youth organizations, and via the Internet and local newspapers.
Results: Forty-one youth consented to participate in the trial from January 2008 to March 2009. In total, 34 youth enrolled in the trial. 71% were male, 29% female. The average age was 18.8 years old. The average number of cigarettes smoked per day at entry to the trial was 12.7 (s.d. 7.9) with 94% smoking daily. 81% of youth accepted NRT. Youth attended an average of 4.3 counseling sessions and 73% provided data for the final session. Youth exhibited significant declines in smoking dependence and nicotine withdrawal by the end of the intervention period.
Conclusions: Youth-focused, clinic-based smoking cessation programs are acceptible, but the uptake of same is slow. In low smoking prevalence areas, such as California, young smokers seeking cessation experience high rates of psychiatric comorbidities, which present additional challenges to cessation research. Youth who participate are motivated to quit smoking, though non-clinic based approaches (e.g., Internet, cell phone) may represent more acceptable venues for treatment.
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MTEP DRUG DISCRIMINATION: PSYCHOACTIVE EFFECTS SELECTIVELY INDUCED BY MGLUR5 ANTAGONISTS.

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Aims: Glutamatergic transmission is mediated via ligand-gated ionotropic receptors (iGluR) and G protein coupled metabotropic receptors (mGluR). Fenobam (McN-3377) is a potent, noncompetitive antagonist of the mGluR5 receptor (Porter et al, J Pharmacol Exp Ther 2005) is analgesic in animals (Montana et al, J Pharmacol Exp Ther 2009) and anxiolytic in man, causing adverse events including "derealization phenomena [—] characterized by a feeling of unreality as in a dream-like state" (Pecknold et al, J Clin Psychopharmacol 1982). The aim was to evaluate fenobam in a rat PCP drug discrimination (DD) model, and to establish DD using the mGluR5 antagonist 3-((2-methyl-1,3-thiazol-4-yl)ethynyl)-pyridine, MTEP.
Methods: Rats were trained to discriminate PCP (10 μmol/kg, ip, 15 min) or MTEP (10 μmol/kg, ip, 30 min) from no drug in a standard two-lever fixed-ratio (FR10) DD procedure using food reinforcement (Swedberg et al, J Pharmacol Exp Ther 1995).
Results: In rats trained to discriminate PCP, fenobam produced no PCP-like effects up to doses that depressed response rates by more than 50% and MTEP produced less than 20% PCP-like effects, whereas MK-801, ketamine and memantine produced full PCP-appropriate responding. Rats were succesfully trained to discriminate MTEP from no drug. In these rats MTEP caused a dose dependent increase in MTEP-appropriate rsponding with an ED50 of ~1 μmol/kg. MTEP, MPEP (2-methyl-6-(phenylethynyl)pyridine) and fenobam all equipotently (ED50's approximately 1 to 2 μmol/kg) produced full MTEP-appropriate responding, whereas PCP produced approximately 30% MTEP-appropriate responding at 10 μmol/kg, the training dose used in the PCP study.
Conclusions: These data suggest that mGluR5 antagonism does not produce PCP-like effects, and that PCP at a highly discriminable dose produced only a weak mGluR5-like antagonistic effect. Furthermore, these data suggest that mGluR5-antagonism may produce psychoactive and psychotomimetic effects of an idiosyncratic nature relative to NMDA antagonism.
Financial Support: AstraZeneca R&D Södertälje, Sweden

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THE DORSAL HIPPOCAMPUS: A NEURAL SUBSTRATE FOR COCAINE CUE EXTINCTION CONSOLIDATION.

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Aims: The dorsal hippocampus (DH) is an integral neural substrate for the acquisition and consolidation of fear extinction and for the acquisition of cocaine cue extinction. We hypothesize that the DH is also important for the consolidation of cocaine cue extinction.
Methods: Rats were trained to self-administer 1 mg/kg cocaine paired with a discrete light cue and contextual sound cue under a second-order schedule during 1hr sessions. Next, rats received three 1hr extinction sessions (no cocaine, but cues present) and patterns of extinction responding were measured. Because inhibition of protein synthesis has been shown to specifically disrupt consolidation of fear extinction, rats (n=4/tx) received anisomycin (100 μg) or vehicle bilaterally into DH immediately after each extinction session to test our hypothesis. A cocaine-primed reinstatement test was conducted 3 days after the final extinction session.
Results: Self-administration responding did not differ between groups. With post-training vehicle treatment, responses decreased from day 1 to 2 and again from day 2 to 3 of extinction training. This pattern indicates that extinction learning was consolidated by the 3rd session under control conditions. With post-training anisomycin treatment, responses decreased from day 1 to 2, but not from day 2 to 3. Notably, responding during the extinction session on day 3 was greater in anisomycin-treated rats than vehicle-treated rats ($p<0.01$). Overall, these findings indicate that inhibition of protein synthesis in the DH did not affect extinction acquisition, but deterred extinction consolidation. During cocaine-primed reinstatement tests, anisomycin-treated rats exhibited more drug-seeking responses than vehicle-treated rats ($p<0.03$). This finding suggests that cocaine-paired cues were more salient in anisomycin-treated rats than vehicle-treated rats. A greater number of drug-seeking responses would be expected if consolidation of cocaine cue extinction learning was disrupted by post-training anisomycin treatment.
Conclusions: Findings suggest that the DH is an integral neural substrate for consolidation of cocaine cue extinction learning.
Financial Support: DA024315

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RESTING STATE INTRA-LIMBIC CONNECTIVITY PREDICTS AFFECTIVE SYMPTOMS IN MARIJUANA-DEPENDENT SUBJECTS.

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Aims: An association has been observed between marijuana use and symptoms of anxiety and depression. The amygdala is implicated in anxiety and depression, and also in the brain's response to marijuana. There is growing interest in functional studies of the resting state, in the absence of tasks, as task-related activation may be based upon this resting state. One method to probe the interaction of the amygdala with other brain regions is through connectivity analyses, which correlate the time series of amygdala activation with that of other brain voxels. The present study aims to investigate correlations between levels of anxiety and depression and amygdala connectivity within limbic regions of interest.
Methods: 14 subjects underwent perfusion MRI during the resting state. Connectivity maps of the whole brain were generated using voxelwise regression analyses with amygdala as the seed region. The relationship between both Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) scores and amygdala connectivity was examined using linear regression. All subjects had at least a 10-year history of marijuana dependence, smoked at least 2 joints/day, 5 days/week, and did not meet criteria for other Axis I disorders.
Results: Positive correlations between resting amygdala connectivity and BAI score were observed in the lateral orbitofrontal cortex ($r=0.79$ and 0.80 for L and R) and the ventral striatum ($r=0.92$ and 0.81 for L and R). A positive correlation between resting amygdala connectivity and BDI score was also observed in the ventral striatum ($r= 0.78$ and 0.80 for L and R). $P < 0.001$ (uncorrected).
Conclusions: Marijuana patients with greater intra-limbic connectivity at rest reported more affective symptoms, highlighting these brain circuits as potential brain substrates of anxiety and depression. Studies of the resting state may enable the identification of endophenotypes of treatment response to guide therapies for marijuana addiction.
Financial Support: P60DA05186, P5012756, VA VISN 4 MIRECC, P30NS045839

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CHANGES IN PFC GLUTAMATE/HOMER-RELATED SIGNALING FOLLOWING LONG-ACCESS COCAINE SELF-ADMINISTRATION.

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Aims: To examine the potential molecular underpinnings of prefrontal cortex (PFC) abnormalities characteristic of addiction, the present study related cocaine-seeking behavior in rats with the expression and activational state of members of Group 1 mGluR/NMDA/Homer signaling cascades within PFC subregions.
Methods: Rats self-administered IV cocaine (0.25 mg/infusion) for 6 hr/day for 10 days. At 3 or 30 days following the last session, lever-pressing for a cue previously associated with cocaine/saline delivery was assessed under extinction conditions. Immediately following these "cue tests", the animals were sacrificed, their ventral PFC (vPFC) and dorsal PFC (dPFC) harvested and processed by immunoblotting.
Results: Cocaine rats exhibited a time-dependent increase in lever-pressing during the cue tests. At 3 days withdrawal, cocaine rats exhibited increases in vPFC expression of both Homer isoforms and p(Tyr)p85α and decreases in pERK1/2 and pPKCε. While the levels of Homer1b/c returned to control levels by 30 days, the elevated levels of Homer2a/b persisted thus, resulting in an imbalance in Homer2 vs. Homer1 expression. This imbalance in vPFC Homers was accompanied by a significant reduction in mGluR1/5 expression. In the dPFC, cocaine animals exhibited persistent increases in Group1 mGluR expression and a time-dependent increase in NR2b expression that was paralleled by changes in PKCε activity.
Conclusions: A history of prolonged access to cocaine produces changes in the PFC expression and activational state of proteins associated with glutamate receptor/Homer signaling and the time-course and direction of these changes are subregionally distinct. These data are consistent with a role for Group 1 mGluRs and for NR2b in cocaine-seeking behavior and further a relationship between drug-seeking and imbalances between Homer1 and Homer2 isoforms within the vPFC.
Financial Support: Supported by the Academic Senate of UCSB and NIDA grant DA024038 (KKS).

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SUSTAINED LOCOMOTOR ACTIVITY INCREASES MDMA-INDUCED HYPERTHERMIA AND DEATH.

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Aims: Recreational use of (±)3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy") remains common; the lifetime exposure frequency in young adults is similar to those for cocaine and prescription amphetamines. Medical emergency and death is an occasional catastrophic consequence and yet the causes are not well understood. Sustained dancing in the rave environment is an assumed risk factor but has not been tested directly. This study evaluated the body temperature response to MDMA in a rodent model to determine if sustained activity on a running wheel modulated hyperthermia.
Methods: Male Wistar rats were challenged with MDMA (1, 3.2, 5.6, 10 mg/kg s.c.) under varying ambient temperatures (19-30 deg Celsius) either with or without access to a running wheel. Body temperature was measured rectally and by implanted radiotelemetry.
Results: MDMA increased body temperature at low ambient temperature and increased temperature at high ambient temperature in a dose dependent manner. Locomotor activity (home cage and wheel running) was suppressed at lower doses and increased at higher doses. MDMA-induced elevations of activity were associated with exaggerated hyperthermia and increased lethality under high dose and/or high ambient temperature conditions.
Conclusions: These data connect two established findings to provide novel and direct evidence that sustained physical activity can interact with MDMA to produce medical emergency and death.
Financial Support: USPHS Grants DA018418 and DA024705

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NEW YORK STATE POLICY TO ADDRESS TOBACCO DEPENDENCE IN DRUG TREATMENT: PRELIMINARY CLIENT BASELINE-FOLLOW-UP RESULTS.

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Aims: In 2007, the New York (NY) State Office of Alcohol and Substance Abuse Services (OASAS) developed a systemic approach to address smoking in drug treatment programs. The initiative required all OASAS-funded programs to implement a)smoke free grounds, b) no evidence (of smoking) policies for staff, and c) provision of tobacco dependence intervention to clients who request such services.
Methods: A random sample of 10 NY treatment programs were surveyed before the policy was implemented in July 2008. Clients participated in self-administered brief survey about smoking behaviors and services. Baseline surveys were collected in summer of 2008 and follow-up (FU) surveys were collected one year later. Results were available for 8 NY programs.
Results: Demographics were similar at baseline and FU. At FU, clients (n=321) averaged 37 years old, 55% male, 21% Hispanic, 26% African-American, 50% Caucasian, 64% had a H.S. diploma or less, and 58% were current smokers.
Preliminary findings showed decreased smoking prevalence from 66% to 58% (P=.0002). Among quitters (n=114), 51% reported they had quit due to the ban on smoking in facilities and 9% said they quit smoking because of the tax increase. Among smokers (n=181), 20% said recent NY excise tax increases moderately affected their smoking habits. At the same time, clients reported receiving fewer smoking-related services such as counseling and nicotine replacement therapy (P=.0001).
Conclusions: In this sample of programs, client smoking prevalence decreased significantly in the year following implementation of the OASAS smoking policy. Many quitters, reported the policy as a reason for quitting smoking and smoking prevalence decreased even while smoking services also decreased. Preliminary data suggest that smoke-free policies may impact smoking in drug abuse treatment systems as they have been shown to do in other settings.
Financial Support: NIDA R01 DA020705, U10 DA015815, P50 DA009253

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VERBAL MEMORY, LEARNING AND EXECUTIVE FUNCTIONING AMONG YOUNG INHALANT AND CANNABIS USERS.

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Aims: While inhalants are commonly misused by young adolescents, very little is known about how chronic inhalant use affects cognition during this key developmental stage. Several studies have examined cognitive deficits among inhalant users (e.g., learning, memory, executive functioning); however no study has thoroughly addressed the confounding issues frequently associated with inhalant users (e.g., polysubstance use, lack of appropriate controls). The aim of the current study was to examine possible deficits in memory, learning, and executive components of memory among young, regular inhalant users relative to a well-matched non-inhalant drug-using control group (primarily cannabis users) and a community control group.
Methods: Three groups of 21 young people (age 13-24) were recruited: a chronic inhalant-using group, a drug-using control group and a community control group. The inhalant and drug-using controls were matched on demographic, clinical, and substance use measures. All three groups were matched on age, sex, and education. The Rey Auditory Verbal Learning Test (RAVLT) was used to assess learning, memory, and executive components of memory.
Results: Community control participants performed significantly better than inhalant users and drug-using controls while inhalant users were more susceptible to proactive interference relative to drug-using controls.
Conclusions: The difficulty in successful proactive interference resolution demonstrated by the inhalant group may be related to inhalant-specific deficits in executive functioning; however there are several other potential confounds that should be considered (e.g., cumulative effects of polydrug use). These findings raise several important questions regarding the hypothesized toxicity of inhalants and of substance-specific cognitive deficits among regular adolescent substance users.
Financial Support: The study was supported by the Colonial Foundation and the Alcohol Education and Rehabilitation (AER) Foundation. A/Professor Yücel is supported by a NHMRC Clinical Career Development Award (I.D. 509345).

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NEURAL CORRELATES OF HABIT LEARNING AND REWARD PROCESSING IN COCAINE USERS.

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Aims: Remodeling of reward circuits is central to the evolution of the addiction process. In turn, changes in dorsal striatum, which is important in habit learning, participate in the maintenance of addictive behaviors. The interplay between drugs of abuse, the neural processes that underlie habit learning, and reward is not well understood. Using a novel virtual reality-based fMRI assessment of habit learning, we aimed to simultaneously interrogate the neural systems for habit learning and reward processing in cocaine users.
Methods: fMRI scans were acquired from 12 adult chronic cocaine users (abstinent for 2 weeks) and 12 healthy controls during navigation of a virtual 8-arm radial maze where learning to respond to a stimulus (lit arm) leads to a monetary reward. We compared task performance and fMRI signal associated with habit learning and reward processing across groups.
Results: Both groups showed behavioral evidence of habit learning, but markedly differed in brain activity during maze navigation. When searching the maze, control participants engaged broader cortical regions than cocaine users, including anterior cingulate, prefrontal and lateral temporal regions. During receipt of reward, group differences were found in BA25, ventral and dorsal striatum, orbitofrontal, and ventrolateral prefrontal cortices. In failed trials, group differences were detected in BA25, ventral and dorsal striatum.
Conclusions: Our use of rigorously defined and controlled conditions in this virtual reality-based task allowed for the precise investigation of alterations in the neural systems involved in habit learning and reward processing that may be related to chronic cocaine use. We demonstrated that, in the setting of habit learning, cocaine users engage a restricted repertoire of cortical regions and exhibit marked alterations in the neural processing of positive and negative rewards.
Financial Support: NIDA R01 DA020855
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NEW FACTORS TO CONSIDER IN ASSESSING ACCURACY OF SELF-REPORTED DRUG USE IN TREATMENT SETTINGS.

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Aims: Prior research has found that validity of self-reported drug use varies by subjects' characteristics. This study builds on past research by incorporating psychometric, geographic, and environmental predictors, along with traditional demographics, to improve our understanding of self-reporting behaviors during research interviews, particularly when subjects are involved in treatment related activities.
Methods: The study population includes 222 probationers receiving drug treatment in Baltimore City and Baltimore County, MD. Data for this study were obtained three months after the initiation of probation from questionnaires, a daily log of self-reported drug use, and drug test results from cheek swabs. The instruments for this study measure demographic, psycho-social functioning, and criminal history characteristics of the clients. Also, place-based variables were calculated using ArcGIS, and neighborhood socioeconomic characteristics were obtained from U.S. Census block groups.
Results: A total of 67 (30%) clients failed to self-report drug use. Those clients who had a negative drug test at the initiation of probation, but had a positive test at the three month follow-up were 16 times more likely to fail to report drug use (CI.95= 5.16, 52.16; p=.000), and were also less likely to have self-reported crime (p<.01). Subjects who underreported drug use had statistically higher levels of self-efficacy (p<.05) and lower levels of power orientation (p<.05). A strong association was found between those who failed to report drug use and the perception of drug inaccessibility within a client's neighborhood (p<.05).
Conclusions: The results indicate that the validity of self-reported drug use varies based on a range of demographics and community characteristics. Findings from this study can help treatment providers better understand the conditions when clients are more likely to be consistent in their report of self-reported drug use.
Financial Support: Supported by NIDA R01 DA017729.

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CURRENT DRUG SCHEDULING REVIEWS REPORTED BY THE DRUG ENFORCEMENT ADMINISTRATION.

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Aims: As mandated by the Controlled Substances Act (CSA), DEA collects and reviews scientific, medical and other data for substances with abuse potential to determine their appropriate control status for placement into one of five schedules.
Methods: Administrative process for scheduling is currently ongoing for carisoprodol, dextromethorphan, Salvinorin A and hallucinogens such as 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), 5-methoxy-alphamethyltryptamine (5-MeO-AMT), 5-methoxy-N,N-diethyltryptamine (5-MeO-DET), 5-methoxy-N-methyl-N-isopropyltryptamine (5-MeO-MIPT), N,N-diisopropyltryptamine (DIPT), and 4-hydroxy-N,N-diisopropyltryptamine (4-OH-DIPT). Administrative process for several petitions requesting control of tramadol and propofol, decontrol of 6-beta-naltrexol and amendment to CFR so as to allow generic products of dronabinol in sesame oil into schedule III. In order to comply with the 1971 Convention on Psychotropic Substances, administrative process for scheduling is currently ongoing for zipeprol, amineptine, mesocarb, 4-methylthioamphetamine (4-MTA) and brotizolam.
Results: DEA is currently reviewing the data for hallucinogens such as 4-iodo-2,5-dimethoxy-phenethylamine (2C-I), 2,5-dimethoxy-4-ethylthiophenethylamine (2C-T-2), and 2,5-dimethoxy-4-iodoamphetamine (DOI) for possible control under the CSA. Chemical synthesis/pharmacological studies for 2,5-Dimethoxy-4-chloroamphetamine (DOC), 2,5-Dimethoxy-4-chlorophenethylamine (2C-C), 2,5-Dimethoxy-4-methylphenethylamine (2C-D), and 2,5-Dimethoxy-4-ethylphenethylamine (2C-E) are currently ongoing to determine if these substances meet the requirements for possible control under the CSA. In order to comply with the 1971 Convention on Psychotropic Substances, administrative process for scheduling is currently ongoing for zipeprol, amineptine, mesocarb, 4-methylthioamphetamine (4-MTA) and brotizolam.
Conclusions: Administrative process for scheduling is completed for tapentadol, lacosamide and fospropofol.
Financial Support: Drug Enforcement Administration

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ETHANOL/NALTREXONE INTERACTIONS AT THE OPIOID RECEPTOR. CLSM/FCS STUDY IN LIVE CELLS.

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Aims: Mechanisms of ethanol action are not sufficiently well understood at the molecular level and the pharmacotherapy of alcoholism is still in its infancy. Our study focuses at the cellular and molecular level on ethanol-induced effects that are mediated through the mu (MOP), kappa (KOP) and the nociceptin (NOP) opioid receptor, and the effects of naltrexone, a well-known antagonist at MOP that is used clinically to prevent relapse in alcoholism.
Methods: Advanced fluorescence imaging by Confocal Laser Scanning Microscopy (CLSM) and Fluorescence Correlation Spectroscopy (FCS) are used to study ethanol effects on opioid receptor mobility in the plasma membrane and on plasma membrane lipid dynamics in live PC12 cells transformed with the respective receptor.
Results: We observed that relevant concentrations of ethanol (10 - 40 mM) alter MOP mobility and surface density, and affect the dynamics of plasma membrane lipids. Compared to the action of specific ligands at MOP, ethanol-induced effects show complex kinetics and point to a biphasic underlying mechanism. Pretreatment with naltrexone considerably counteracts the effects of ethanol, which is kept "frozen" in the plasma membrane. Ethanol effects on NOP are similar and observable under acute exposure. In comparison, ethanol has no effects on KOP.
Conclusions: We propose a new hypothesis to explain the well established ethanol-induced increase in the activity of the endogenous opioid system. Ethanol acts by affecting the sorting of opioid receptors at the plasma membrane of PC12 cells. Naltrexone exerts opposite effects on opioid receptor sorting, thereby countering the effects of ethanol.
Financial Support: The Swedish Research Council, AFA Insurance, Cancerdegradome, The Brain foundation and The Knut and Alice Wallenberg Foundation.

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INTENSITY OF CARE IS THE ONLY PREDICTOR OF OUTPATIENT OPIATE TREATMENT RETENTION AMONG PREGNANT WOMEN.

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Aims: To compare predictors of outpatient opiate treatment retention between men, women, and pregnant women

Methods: We used the 2006 Treatment Episode Data Set – Discharges, the first year these data are publically available, and limited the dataset to only outpatient admissions for which an opiate was the primary substance of abuse. The primary outcome was treatment retention defined as either treatment completion or transfer to further care. The primary exposure was intensive outpatient treatment defined as at least two hours per day for three or more days a week. Demographic and treatment characteristics were compared with chi-squared and t-tests. Confounding was assessed via a backwards elimination method using change-in-estimate criteria. Logistic regression models were stratified by gender and pregnancy. Results are reported as Odds Ratios (OR) with 95% confidence intervals (CI).

Results: In 2006, 74,220 men, 44,510 non-pregnant women, and 2454 pregnant women were admitted into outpatient opiate treatment. Compared with men and non-pregnant admissions, pregnant admissions were less likely to enter treatment from the criminal justice system, have a high school education, or be employed. They were more likely to have used opiates daily although no more likely to have injected the drug. Although methadone is the expected standard of care for opiate abuse in pregnancy, only 60% of pregnant opiate admissions were slated to receive methadone compared with 50% of men and non-pregnant women. Overall 50% of admissions into intensive outpatient were retained in treatment compared with only 34% of lower intensity treatment. Whereas age, race, education, methadone use, and a criminal justice referral were all associated with treatment retention in men and non-pregnant women, only treatment intensity was predictive in pregnancy (OR 1.4 95%CI 1.1, 1.7).

Conclusions: Unlike in men and non-pregnant women, only treatment intensity appears to predict opiate treatment retention in pregnancy. The expansion of such services for this vulnerable population should be encouraged.

Financial Support: None

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RETAINING PARTICIPANTS IN STARTING TREATMENT WITH AGONIST REPLACEMENT THERAPIES: PERSPECTIVES OF EARLY SUBOXONE DROPOUTS.

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Aims: Retention has long been linked to treatment outcome, with those who remain in treatment longer experiencing more favorable treatment results. A recent study (Starting Treatment with Agonist Replacement Therapies, or START) conducted through the Clinical Trials Network (CTN) of the National Institute on Drug Abuse (NIDA) randomly assigned treatment-seeking opioid-dependent individuals to either methadone or Suboxone (buprenorphine and naloxone) for 24 weeks of pharmacotherapy. It was estimated that 60% of participants would complete the trial; however, within the first year of the study, a pattern emerged that remained relatively stable over the course of the trial. A disproportionately larger number of the Suboxone group, compared to the methadone group, discontinued study participation prematurely, with many dropping out shortly after enrollment (57% Suboxone vs. 27% methadone).

Methods: The current study explored the nature of the different retention rates from the perspective of the patients and providers. One-hour in-depth semi-structured face-to-face interviews were conducted with staff and patients (dropouts, completers) at the 8 outpatient opioid treatment programs participating in START. This analysis highlights results of interviews with 85 individuals (65 Suboxone, 20 methadone) who dropped out of START prior to completing the trial. The interviews were digitally recorded, transcribed, and analyzed (ATLAS.ti).

Results: Examination of these qualitative interviews identified potential barriers and facilitators to treatment retention, including medication-related factors (e.g., dosing), patient factors (e.g., prior treatment, medication preferences, expectations), and life events (e.g., incarceration).

Conclusions: Recommendations offered by patients (e.g., provision of take home meds) may help in efforts to improve treatment retention. Ultimately, findings from this study may inform clinical practice, resulting in improved utilization and integration of buprenorphine within opioid treatment programs.

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HEPATIC SAFETY AND ANTIRETROVIRAL EFFECTIVENESS IN HIV-INFECTED PATIENTS RECEIVING NALTREXONE.

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Aims: Most trials of naltrexone exclude HIV-infected (HIV+) patients. To determine the impact of naltrexone on hepatic enzymes and antiretroviral effectiveness in HIV+ patients we used the Veterans Aging Cohort Study Virtual Cohort.

Methods: Using the Wilcoxon rank-sum test in the overall sample and stratified by receipt of antiretroviral therapy (ART) we compared median AST, ALT, CD4 count and HIV viral load (VL) values at baseline (prior to naltrexone) and within 3, 6, 9, and 12 months of naltrexone initiation in HIV+ patients. We also compared values obtained during exposure to naltrexone.

Results: Of the 214 HIV+ patients on naltrexone, 97% were male, 36% were white, and 65% were on ART. The mean age of the sample was 44 years, and median time on naltrexone was 180 days [interquartile range (IQR) 90-448]. Between baseline and 3 months after naltrexone initiation, median AST (n=70) remained the same at 43 (IQR = 31-62 and 34-64; p=0.7), ALT (n=75) remained the same at 32 (IQR = 21-48 and 19-52; p=0.3), CD4 (n=53) count decreased from 420 to 352 (IQR=230-584 and 208-651; p=0.9), and VL (n=51) decreased from 1326 to 433 (IQR=383-38,643 and 319-8741; p=0.03). Between the first and second values after naltrexone initiation, AST (n=72, median time between draws=69 days) went from 46 to 51 (IQR=37-67 and 36-75; p=0.9), ALT (n=76, time= 53 days) went from 36 to 39 (IQR=22-56 and 27-62; p=0.2), CD4 (n=55, time=82 days) went from 477 to 424 (IQR=247-651 and 266-644; p=0.2) and VL (n=53, time=85 days) decreased from 1686 to 670 (IQR=400-10,475 and 75-12,480; p=0.2). There were no differences in these values over 12 months in the overall sample and when stratified by ART use, although small sample sizes prohibited reliable comparisons.

Conclusions: Naltrexone is not associated with hepatotoxicity and does not have a negative impact on biologic parameters in patients on or off ART. In fact, naltrexone treatment is associated with a VL decrease at 3 months. We conclude that HIV+ patients with alcohol or opioid dependence can safely receive naltrexone.

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CORRELATION OF FETAL HEART RATE AND OPIOID WITHDRAWAL SIGNS IN PREGNANT OPIOID-DEPENDENT WOMEN.

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Aims: The purpose of this study was to investigate whether fetal heart rate(FHR)is correlated with opioid withdrawal as measured by Clinical Institute Narcotic Assessment(CINA)scale in pregnant opioid dependent women during inpatient opioid replacement treatment.

Methods: Informed consent was obtained from 28 opioid dependent pregnant women, 21 of whom were enrolled in the WSU site of the MOTHER study, a multi-site double blind, double dummy trial to examine the safety and efficacy of buprenorphine vs. methadone in opioid dependent pregnant women. The 21 women were opioid dependent according to DSM-IV (SCID-E) and average EGA was 20.35 weeks. All women were treated with immediate-release morphine sulfate (IRM) every 6 hours for 3 to 6 days. Comfort doses were given 2 hours after the scheduled doses for CINA above 5. The FHR was obtained at the same time as CINA using the Bistos HI Bebe fetal Doppler. All CINA scores were divided into high and low groups (<5 vs. ≥5 respectively). We had a total of 441 scores for comparison. The FHR values were compared between high and low CINA groups using t-test. Correlation between FHR and CINA scores was tested using linear regression.

Results: Mean CINA scores were 1.30 and 8.53 for the low and high CINA groups respectively. The average FHR score was 150.56 for the high CINA group and 146.70 for the low CINA group. The difference was not significant (p=0.125). However, FHR measures were correlated with CINA scores (r=0.150, p=0.002). Within the high CINA score sub-group FHR measures were again significantly correlated with CINA scores (r=0.355, p=0.025). We did not find significant correlation within the low CINA sub-group.

Conclusions: Pregnant opioid dependent patients tolerated opioid replacement with IRM. FHR was not significantly increased in those with higher CINA scores. However, increased FHR was significantly associated with higher CINA score.

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NEUROPATHOGENIC MECHANISMS OF HIV-1 CLADE B AND C: ROLE OF DOPAMINE RECEPTOR-2.

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Aims: Aim: Previous studies have demonstrated that infections with HIV-1 clades differentially contribute to the neuropathogenesis of HIV-1-associated dementia (HAD) and HIV-associated neurocognitive disorder (HAND). The dopamine receptor-2 (DRD-2) and tyrosine hydoxylase (TH) leads to down regulation of metabolite such as homovallinic acid (HVA) and Ca2+/CaM-dependent protein kinases (CaMKs) and are known to play a significant role in neuropathogenesis of HAD and HAND. We hypothesize that clade B and C gp120 proteins exert differential effects on human primary astrocytes by down regulation of DRD-2 and CaMK II gene and protein expression as well as the rate limiting enzyme TH and the metabolite of HVA level.
Methods: Methods: RNA extracted from astrocytes treated with HIV-1 clade B- and C- gp120 proteins was reverse transcribed and analyzed by quantitative real-time PCR to determine DRD-2 and CaMK II gene expression. Cell lysates were analyzed by western blot to determine protein expression. The enzymatic activity of TH and the concentration of HVA were measured in cell lysates and culture supernatants respectively.
Results: Results: Our results indicate that HIV-1 clade B gp120 protein significantly down regulated DRD-2 and CaMK II gene and their protein expression, TH enzyme activity, as well as the level of HVA concentration compared to HIV-1 clade C- gp120 protein.
Conclusions: Conclusions: Thus, our studies for the first time demonstrate that HIV-1 clade B- gp120 protein appears to significantly down regulate DRD-2 and CaMK II as compared to HIV-1 clade C- gp120 protein. This suggests a differential effect of HIV-1 clade B leading to increased neuropathogenesis and associated HAD and HAND.
Financial Support: Funding Sources: The present study was supported by grants from National Institute of Health (NIH); DA012366, DA 021537, DA 025576

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PRECLINICAL EXAMINATION OF ENVIRONMENTAL ENRICHMENT AS AN ANTI-RELAPSE STRATEGY.

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Aims: We examined the protective effects of environmental enrichment (EE) introduced at the onset of forced cocaine abstinence on subsequent cocaine-seeking behavior (CSB).
Methods: Rats were trained to press a lever reinforced by cocaine and light/tone cues for 15 d while housed in isolated conditions (IC). Rats were then assigned to live in either IC, pair-housed conditions (PC), or EE for 21 d of forced abstinence. Subsequently, CSB was assessed under extinction for 2 h, followed immediately by a 2-h cocaine-primed reinstatement test. Rats were returned to their assigned living conditions for 9 days and were then tested for cue-elicted CSB. Brains were harvested for Fos IHC after this test. Next, we examined the combined protective effects of extinction training and EE. After self-administration, rats were assigned to either PC or EE and underwent either daily extinction or forced abstinence for 15 d, and were then tested for cue-elicited CSB. To determine whether the protective effects persisted following discontinuation of EE, all rats underwent 7 d of forced abstinence in PC living conditions before retesting for cue-elicited CSB.
Results: EE housing during abstinence attenuated CSB during extinction but not cocaine-primed reinstatement. EE housing also attenuated cue-elicited CSB, as well as Fos protein expression across several cortical and limbic regions that have been implicated in the incentive motivational effects of cocaine-paired cues. The results of our second experiment revealed that the combination of EE and extinction training provided the greatest degree of protection against cue-elicited CSB. However, rats that discontinued EE and/or extinction for 7 d demonstrated equivalent CSB to rats that had lived consistently in PC.
Conclusions: These results suggest that EE has utility in terms of attenuating the incentive motivational effects of cocaine-associated stimuli; however, its protective effects may not persist beyond the period of EE. These findings may have important implications for treatments aimed at reducing drug craving.
Financial Support: DA11064, DA023123, and F31DA023746

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HEPATITIS B AND C PREVALENCE IN OPIOID-DEPENDENT TREATMENT PARTICIPANTS: COMPARISONS BETWEEN HEROIN USERS AND PRESCRIPTION OPIOID USERS.

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Aims: Illicit drug use is associated with infectious diseases, including hepatitis virus, B and C (HBV, HCV). Surveys addressing hepatitis prevalence do not distinguish the type of opioid used. The current study compares HBV and HCV rates by type of opioid used among participants in an ongoing treatment study for opioid dependence.
Methods: A study-specific opioid use questionnaire and lab tests on 90 opioid dependent participants were collected at intake to determine type of opioid used and prevalence of hepatitis.
Results: Responding to the questionnaire, 52.2% (n=47) of the sample reported heroin as their major drug problem; 37.8% (n=34) reported illegally obtained prescription opioids as their major drug problem; 6.7% (n=6) reported legally obtained prescription opioids as their major drug problem; and 3.3% (n=3) reported that methadone as their major drug problem. Rates of positive test results for HBV (Anti-HBc) differed by type of opioid used, with 72.3% of heroin users and 7.5% of prescription opioid users testing positive for HBV. Similarly, 66% of heroin users and 7.5% of prescription opioid users tested positive for HCV. Descriptions of the drug use groups and additional results are presented and discussed.
Conclusions: Findings have important implications for health care and treatment providers, especially in suggesting that hepatitis prevention efforts be tailored to include prescription drug users.
Financial Support: This project is supported by NIDA Grant RO1 DA020210

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WITHDRAWN

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SENSORIMOTOR REPLACEMENT REDUCES CIGARETTE CRAVING, WITHDRAWAL SYMPTOMS AND SMOKING IN SMOKERS WITH SCHIZOPHRENIA.

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Aims: About 70% of people with schizophrenia smoke cigarettes and these smokers have poor cessation rates. We recently reported that smokers with schizophrenia (SWS) were less sensitive than non-psychiatric controls (CON) to transdermal nicotine replacement (NRT), suggesting that novel strategies are needed to reduce smoking in SWS. In this within-subjects placebo-controlled laboratory study, we are comparing the responses of SWS and CON to sensorimotor replacement for smoking (denicotinized cigarettes vs. no cigs) alone and combined with high-dose NRT (42 mg NRT vs. placebo patches).
Methods: In each session, participants undergo one of five study conditions for 5 hours: placebo patches + no cigs, 42 mg NRT + no cigs, placebo patches + denic cigs, 42 mg NRT + denic cigs, or usual brand cigarettes, followed by assessments of craving, nicotine withdrawal symptoms and ad-lib smoking behavior.
Results: The SWS and CON groups are matched on age (M = 47.7 yrs), gender (65% male), daily smoking rate (M = 26.6 cigs/day), and nicotine dependence (FTND) scores (M = 7.2). Results from 18 SWS and 12 CON indicate that sensorimotor replacement decreased 100-mm VAS cigarette craving scores (No cigs: 76.0 ± 28.9 [M ± SD]; Denic cigs: 37.2 ± 35.9; $p < .001$), Minnesota Nicotine Withdrawal Scale scores (No cigs: 27.9 ± 26.4; Denic cigs: 18.0 ± 23.6; $p < .001$) and CO boosts from the 90-min ad-lib smoking period (No cigs: 9.8 ± 7.9; Denic cigs: 3.1 ± 9.9; $p < .001$) to levels comparable to those from participants' usual brands. There is no indication from the preliminary data that NRT enhances the effects of sensorimotor replacement or that SWS and CON differ in their sensitivity to sensorimotor replacement.
Conclusions: These findings indicate that sensorimotor replacement for smoking reduces smoking urges, nicotine withdrawal symptoms and smoking behavior in SWS, suggesting that treatment approaches that include a phase of sensorimotor replacement may improve smoking cessation rates in this population.
Financial Support: Supported by NIDA R01-DA14002 to JWT.

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THE NOVEL MIXED OPIOID RDC-5768 REDUCES THE BEHAVIORAL EFFECTS OF NICOTINE AND D-AMPHETAMINE IN RATS.

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Aims: A novel, highly potent, non-selective opioid receptor modulator, has been evaluated across several in vitro characterization assays and nonclinical behavioral and neurochemical models of nicotine (NIC) and amphetamine (AMPH) administration and reward. We previously demonstrated that RDC-5768 reduces ethanol drinking behavior (Todtenkopf,et.al.,2008;ACER32,s1:291) and AMPH reward in rats as well as reduce AMPH-induced dopamine (DA) release in the accumbens shell (NAs;SFN,2009). Here we further examine effects of RDC-5768 on NIC reward and NIC-induced DA release in rodent models of drug abuse.
Methods: To characterize the ability of RDC-5768 to reduce the reward-enhancing effects of NIC, we used a rate-frequency curve method in the intracranial self-stimulation paradigm to measure brain stimulation reward (BSR). Rats were pretreated with RDC-5768 (0.1-1.0 mg/kg, sc) 30 min prior to NIC administration (0.25 mg/kg, SC). Also, we examined the effects of RDC-5768 pretreatment in the open field activity (OF) paradigm. After repeated treatment with NIC, rats were habituated to the OF chamber and subsequently pretreated with either saline or RDC-5768 (1.0 mg/kg) and challenged with NIC(0.4 mg/kg, SC) immediately prior to testing for 60 min.
Results: In the BSR assay, RDC-5768 dose-dependently decreased NIC-potentiated BSR. In addition, in the OF paradigm, RDC-5768 significantly reduced NIC-potentiated locomotor activity in rats previously exposed to repeated NIC.
Conclusions: We previously reported the ability of RDC-5768 to reduce ethanol self-administration and reduce AMPH reward and AMPH-induced DA release. The data presented here demonstrate that RDC-5768 significantly reduces behavioral and rewarding effects of NIC. In addition, we have previously demonstrated that pretreatment with RDC-5768 reduces AMPH-induced NAs DA release. Studies are currently being conducted to examine the effects of RDC-5768 on NIC-potentiated extracellular monoamine concentrations in the NAs.
Financial Support: All funding was sponsored by the employer. There are no financial conflicts to report for any author.

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PRONOUNCED ATTENTIONAL BIAS IN METHAMPHETAMINE-DEPENDENT SUBJECTS UPON METHAMPHETAMINE CUE EXPOSURE: RELATIONSHIP TO CRAVING.

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Aims: In drug-dependent individuals, exposure to cues associated with an addictive drug can elicit subjective craving and can shift attentional priority toward subsequent drug-related stimuli. The current study assessed whether exposure to methamphetamine (METH)-related visual cues can elicit attentional bias and craving in METH-dependent and control subjects.
Methods: Attentional bias was defined by differences in reaction time, response errors, and inhibition errors on an auditory go-no go task while watching neutral versus METH-related video cues. Craving was assessed with the Within-Subject Rating Scale modified for assessment of METH-dependent subjects.
Results: METH-dependent subjects (n=29) reported significantly more craving upon exposure to METH-related cues than to neutral cues. No cue-induced craving was reported by control subjects (n=30). Both inhibition and response error rates were significantly higher in METH-dependent subjects than control subjects during neutral cue exposure. Upon exposure to METH cues, inhibition errors increased significantly in METH-dependent subjects but not in control subjects. Similarly, differences in response errors between neutral- vs. METH-cue conditions were 4-fold higher in METH-dependent subjects than in control subjects. Reaction times were significantly slower in METH-dependent subjects than control subjects regardless of cue presentation. Further delay in reaction time during METH vs. neutral cue conditions tended to be greater in METH-dependent than control subjects ($p<.07$). Reaction time and response error rates, but not inhibition error rates, were significantly associated with craving scores in METH-dependent subjects.
Conclusions: METH-dependent individuals exhibit impaired inhibitory behavior even during exposure to neutral stimuli and exhibit a significant attentional bias that correlates, at least in part, with severity of craving.
Financial Support: Supported by NIDA grant 5 P20 DA022658 (See, PI; Brady, Co-PI)

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THE RELATIONSHIP BETWEEN PAIN AND TREATMENT OUTCOME DURING METHADONE MAINTENANCE: A PROSPECTIVE STUDY.

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Aims: Pain is thought to complicate the treatment of substance use disorders but few prospective studies have examined this question.
Methods: 177 consecutive treatment-seeking volunteers with DSM-IV cocaine and opioid dependence who qualified for methadone maintenance were enrolled in a 31-week outpatient clinical trial of topiramate for cocaine dependence. Persons with unstable psychiatric or medical illness, benzodiazepine dependence, and contraindication to topiramate treatment were excluded. Pain was collected weekly on a visual analog scale (0-100) and categorized as mild-moderate (5-69), or severe (70+) based upon published guidelines. Self-reported drug use was collected weekly, and urine toxicology was performed thrice weekly. Negative binomial regression models with generalized estimating equations were used to calculate incidence rate ratios (IRRs) for pain and treatment outcomes.
Results: Volunteers were 59% African American, 46% female, mean age of 41.6 years, and 14% had current cannabis dependence. 73 volunteers (41%) had at least mild baseline pain (VAS>4) and the percentage with pain remained between 19-38% throughout the 31-week follow-up. Self-reported pain decreased over the trial (IRR by week 0.985, $p<0.001$). Significant predictors of reporting pain included baseline pain (IRR=2.61, $p<0.001$), weekly self reported cannabis use (IRR 1.08, $p<0.001$), and weekly cocaine positive urine (IRR 1.24, $p=0.02$), but not cannabis positive urine (IRR 0.98, $p=.94$). There was a trend for an opioid positive urine to predict weekly pain (IRR 1.14, $p=.08$). No differences in self-reported pain were seen based upon gender, age, disability status, antisocial personality, or treatment group. Volunteers who reported severe pain at any point during the trial dropped out 30 days earlier (95%CI 12-48) than those who were pain free.
Conclusions: Pain is frequent and associated with worse treatment outcome during methadone maintenance.
Financial Support: DA021808, DA07209.

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D-CYCLOSERINE IN THE NUCLEUS ACCUMBENS PRODUCES A CONTEXT-INDEPENDENT ENHANCEMENT OF EXTINCTION LEARNING TO ATTENUATE CUE-INDUCED REINSTATEMENT IN RATS.

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Aims: Extinction therapy has been proposed as a method to prevent relapse; however, it is not likely to occur in the drug-taking context even though extinction learning is context specific. We have found the systemic administration of d-cycloserine (DCS) after extinction of drug cues in a novel context reduces cue reinstatement in the self-administration context. The aims of the current studies were to 1) determine in which brain region DCS acts to reduce cue-induced reinstatement, and 2) determine if the effect is dependent on the extinction learning experience.
Methods: Male Sprague-Dawley rats were trained to self-administer cocaine in Context A, where each infusion was paired with a light/tone cue. Animals then underwent non-contingent cue extinction in Context B. Controls were placed in Context B, but did not undergo cue extinction. Rats received systemic injections of vehicle or 15 mg/kg DCS or microinjections of vehicle or 10 µg/side DCS to discrete brain regions immediately after these sessions, and were tested for cue-induced reinstatement in Context A 24 hr later.
Results: Vehicle treated rats demonstrated robust cue-induced reinstatement to the same degree as the no extinction control groups. Notably, rats receiving DCS systemically or into the nucleus accumbens core had significantly reduced cue-induced reinstatement. In contrast, rats receiving DCS in the infralimbic or prelimbic cortex, basolateral amygdala, or dorsal hippocampus did not show reduced reinstatement. In addition, rats receiving DCS in the absence of extinction learning showed equivalent reinstatement to the vehicle-treated group indicating that extinction learning was necessary for these effects of DCS.
Conclusions: Our results demonstrate that DCS enhances cue extinction memories such that they can generalize to the drug-taking context, and that this effect is mediated by the nucleus accumbens. Therefore, DCS could provide an innovative method to enhance extinction therapy to reduce cue-induced relapse in addicts.
Financial Support: Research was supported by DA022812-01A1, DA01522 and DA011717.

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RISK FACTORS FOR SUBSTANCE-INDUCED DISORDERS AMONG ILLICIT DRUG USERS.

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Aims: To determine the co-occurrence of independent and substance-induced psychiatric disorders among a sample of drug users recruited from treatment and out of treatment settings; and to characterize substance-induced disorders with respect to independent disorders.
Methods: Secondary analysis of five cross-sectional studies including 629 subjects. Independent and substance-induced DSM-IV psychiatric diagnoses assessed with the Psychiatric Research Interview for Substance and Mental Disorders (PRISM).
Results: Lifetime prevalence of Axis I disorders other than substance use disorder (SUD) was 41.8%, independent major depression was the most prevalent (17%). In multinomial logistic regression analysis, being female (OR 2.41; 95%CI 1.56, 3.71) and having lifetime borderline personality disorder (OR 2.45; 95%CI 1.31, 4.59) remained significant variables in the group with independent disorders. In the group with substance-induced disorders remained: being recruited from an out of treatment setting (OR 4.18; 95%CI 2.12, 8.25), being female (OR 2.69; 95%CI 1.56, 4.64), being infected with hepatitis C (OR 1.95; 95%CI 1.13, 3.35), and the number of SUD (OR 1.30; 95%CI 1.11, 1.51).
Conclusions: Illicit drug users show high prevalence of co-occurrence of mainly independent mood and anxiety psychiatric disorders. Being female increased the risk for both independent and substance-induced disorders. Borderline personality disorder increased the risk for independent disorder; while being recruited from an out of treatment setting, polydrug use or hepatitis C infection increased the risk for substance-induced disorders.
Financial Support: Financial support was received from the Instituto Carlos III (RTA: RD06/0001/1009).

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TREATMENT WITH FLUMAZENIL: COMPARISONS OF TREATMENT OUTCOMES AMONG PATIENTS ACCORDING TO PRIMARY DRUG OF ABUSE.

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Aims: Pharmacotherapy-based addiction treatment should address brain-modifying effects brought about by repeated exposures to substances of abuse. Chronic exposure to stimulants causes disturbances in dopaminergic and GABAergic systems. Dysregulation of both systems stems from and causes disruptions in the release of neurotransmitters, and in the numbers of receptors to which dopaminergic and GABAergic transmitters bind. The study sought to examine whether treatment and management of substance-dependent patients can be enhanced by a medically supervised procedure that addresses this dysregulation.
Methods: The study examined the use of flumazenil in a private practice setting for the treatment of alcohol, cocaine, or methamphetamine dependence (24 cocaine, 41 alcohol, 43 methamphetamine, and 28 polydrug). Flumazenil is a partial agonist at the GABA/BDZ receptor, and in states of chronically low GABAergic transmission, such as may occur in drug dependence, flumazenil modestly increases inhibitory drive, thereby helping to restore the balance of inhibitory/excitatory activity without driving the reward system. Data were collected at all clinic visits (mean number of visits was xx per patient). The sample includes 89 men and 54 women with a combined mean age of 38.67 (sd = 10.8).
Results: After treatment, a total of 55.5% of the sample reported not using their drug of choice, and 21.2% reported still using drug(s) of choice (Information was not collected from 23.3% of the sample).
Conclusions: Further analyses provide a comparison of patients by substance of abuse to examine possible differences in treatment outcomes according to variations in patient characteristics by primary drug used. Findings indicate the potential of flumazenil for the treatment of stimulant dependence and alcoholism.
Financial Support: None

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MULTICENTER STUDY OF THE SWITCH FROM BUPRENORPHINE TO BUPRENORPHINE/NALOXONE IN STABLE PATIENTS.

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Aims: Clinical data on directly switching from Subutex® to Suboxone® are limited and uncontrolled. Thus, a prospective, multicenter, randomized, placebo-controlled trial was conducted at 26 sites in 10 European countries.
Methods: Patients (n=241) stabilized on Subutex maintenance treatment for ≥1 month were randomized (2:3) to continue receiving Subutex (n=98) or be switched to Suboxone (n=143) under double-blind/double-dummy conditions for 1 week, followed by 3 weeks of open-label therapy when patients received their assigned treatments as take-home therapy. The primary objective was non-inferiority between Subutex and Suboxone, defined as the patient proportion not requiring a dose increase during the 1-week blinded switch period.
Results: Suboxone was noninferior to Subutex in the patient proportion not requiring a dose increase (83.2% vs 88.7%, respectively; 95% CI, –14.2, 3.4 [ns]). A minority of patients in both groups received ~30% increases in dose to manage withdrawal symptoms. Subutex, but not Suboxone, was misused intravenously by a few patients. Treatment retention and compliance were excellent. Most adverse events in both groups were mild or moderate. These findings show that most patients can be acceptably and safely switched from Subutex to Suboxone without dosage adjustment. No patients were destabilized due to the switch from Subutex to Suboxone. No misuse of Suboxone occurred despite weekly access to take-home therapy as of week 2.
Conclusions: Suboxone allows stable patients to continue receiving maintenance therapy acceptably and safely with a reduced risk for intravenous misuse.
Financial Support: Supported by Schering Corporation.

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PERSONAL SOCIAL NETWORKS OF WOMEN WITH SUBSTANCE USE AND CO-OCCURRING MENTAL DISORDERS.

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Aims: This study examined the use of a social network mapping instrument to compare social networks of women with substance use disorders only (SUD) and co-occurring substance use and mental disorders (COD).
Methods: Participants were 136 primarily African American and low SES women (50 in community, 41 in residential and 45 in outpatient treatment). SUD and COD were assessed using the Computerized Diagnostic Interview Schedule. Measures included social network structure and composition, and perceived social support. Analysis of co-variance was used to examine group differences; multiple regression examined social networks as predictors of social support. Social networks were visually mapped using a software program, Egonet.
Results: 77(57%) had a SUD and 59 (43%) had a COD. Mean network size was 10.7 (SD=5.5). On average, 48% of the network either used alcohol/drugs or did not support recovery. A higher proportion of family members was associated with the presence of less sobriety support (r =.22, p =.008) and less reciprocity (r =.33, p < .001). COD women reported less concrete (F(1,134) = 6.36, p =.04) and emotional (F(1,134)=4.52, p =.04) support from household members and less emotional (F(1,134)=3.92, p =.05) and sobriety (F(1,134)=3.8, p =.05) support from professionals. Greater percent of critical network members (t =-2.478, p<.05) and presence of COD (t = -2.004, p<.05) were significant in predicting higher perceived social support (F(5.122)=4.45,p<.01, R2=.154). Network visualizations illustrate network structure and composition.
Conclusions: Women with dual disorders may have difficulty recognizing and accessing sufficient social support from their network. Source of support and quality of relationship impact perceived support. Further research to study social network relationships at the various stages of progression during and post treatment is currently underway.
Financial Support: National Institute of Drug Abuse (NIDA) R01 DA13944 (pilot study) and R01 DA022994

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THE EFFECTS OF SLEEP DEPRIVATION ON MARIJUANA CUE-REACTIVITY AND CRAVING.

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Aims: Research suggests that important associations exist between sleep and drug use. Recent reports have begun to study the impact of sleep deprivation (SD) on indices of drug use, craving, and relapse. The present study examines the effects of SD on drug cue-reactivity and craving by collecting EEG event-related potentials elicited by marihuana-related images and subjective drug craving responses in heavy marihuana-using (MH) participants.
Methods: The physiological impact of SD provides a method to examine how sleep loss can influence the objective response to drug-related cues and subjective drug craving. Our preliminary data provide some intriguing insights to the hypothesis that SD results in enhanced drug cue-reactivity and/or craving in MH participants. Three types of images were presented in an odd-ball paradigm: neutral, arousing, or drug-related.
Results: P300 amplitudes were significantly higher in response to arousing [p<0.05] and drug-related [p<0.05] images compared to neutral images in both control (n=2) and MH participants (n=5). SD resulted in reduced P300 amplitudes in response to neutral [p<0.05] and arousing images [p<0.05], but not for the drug-related images. Although not statistically significant, preliminary subjective craving data indicate that MH participants experienced increased marihuana craving on the second study day and that the magnitude of craving was greater in sleep-deprived MH participants compared to those with normal sleep.
Conclusions: These preliminary data support the notion that acute sleep loss can impact drug cue reactivity/craving in heavy marihuana users and highlight the potential for greater objective reactivity to drug cues, in conjunction with heightened subjective drug craving following SD. Collectively, enhanced drug cue-reactivity and craving as a result of SD may perpetuate drug-taking/seeking behaviors, increase drug consumption, and/or increase relapse potential during abstinence.
Financial Support: Supported by NIDA grants K01DA025125, K25DA017712, and K05DA000343

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HEPATITIS C VIRUS INFECTION AND CHRONIC PAIN IN OPIOID-DEPENDENT INJECTION DRUG USERS.

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Aims: Chronic pain is common among opioid dependent injection drug users (IDU) who frequently have hepatitis C virus (HCV) infection. The study aim was to explore an association between HCV and clinically significant chronic pain and discomfort intolerance among opioid dependent IDU.
Methods: Cross-sectional analyses used baseline data from a study of opioid dependent IDU who were initiating office-based buprenorphine treatment. Multivariate regression was used to determine whether self-reported HCV was associated with chronic (present at least 6 months) severe pain, defined as pain that was above the median score using the Visual Analog Scale or caused at least moderate interference with normal activities (single question from the SF-12). Additional analyses evaluated whether HCV was associated with higher ratings of discomfort intolerance using the Discomfort Intolerance Scale. All models were adjusted for age, sex, race, severe depression, current IDU, and initial use of opioids being related to pain.
Results: Among 97 IDUs, 37 (38%) participants reported that they were HCV infected; none reported having HIV. A higher prevalence of chronic severe pain was observed among individuals who were HCV+ compared to those who were HCV- (51% v. 33%). After adjusting for other covariates, the odds of having chronic severe pain was 2.78 (95% CI: 1.06 to 7.27) times higher among participants with HCV. Being HCV infected was also associated with a higher discomfort intolerance score after adjustment for other covariates (β-coefficient= 2.56; 95% CI: 0.03 to 5.09).
Conclusions: In this cohort of opioid dependent IDU, HCV infection was associated with chronic severe pain and pain/discomfort intolerance. More research is needed to understand how chronic viral infections such as HCV impact risk for chronic pain in substance users.
Financial Support: This study was funded by the National Institute of Drug Abuse DA 022207, Clinical Trial # NCT 00475878. Dr. Stein is a recipient of a NIDA Mid-Career Award DA 000512.

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ANABOLIC-ANDROGENIC STEROID EFFECTS ON ACUTE AND CHRONIC NOCICEPTION AND MORPHINE ANTINOCICEPTION.

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Aims: Use of anabolic-androgenic steroids (AAS) has been anecdotally associated with pain reduction as well as opioid abuse. The purpose of the current study was to investigate the effects of AAS on nociception and morphine antinociception in acute pain models, as well as on chronic nociception in an arthritis model, in adult male Sprague-Dawley rats.
Methods: Rats were injected s.c. for 28 days with either 5 mg/kg dihydrotestosterone proprionate (DHT), testosterone proprionate (TP), or stanozolol proprionate (STAN), or safflower oil vehicle (N=16-20/group). Half of the rats in each group were tested on acute thermal and mechanical nociceptive assays on day 28, without and then with morphine. The other half of the rats in each group were injected with mineral oil or complete Freund's adjuvant (CFA) into one hindpaw, and then tested for thermal hyperalgesia and mechanical allodynia intermittently for 28 days. Reproductive organs were harvested on the last day of testing.
Results: AAS treatment did not significantly affect nociception or morphine potency on the acute pain tests. In the chronic pain group, TP-treated rats demonstrated significantly less thermal hyperalgesia (Hargreaves test) in comparison to vehicle-treated rats. However, rats treated with any of the three AAS responded to significantly less force on the von Frey test in comparison to the vehicle-treated groups, suggesting that AAS treatment increased mechanical allodynia. AAS also decreased body weight gain and increased seminal vesicle weight in both acute and chronic pain groups.
Conclusions: Overall, results are inconsistent with some previous research findings obtained in rats, showing that testosterone can decrease nociceptive responses and enhance opioid sensitivity. Possible explanations for the general lack of pain reduction observed in the present study are that (1) rats showed learning effects resulting from repeated testing, and (2) AAS were administered to gonadally intact as opposed to gonadectomized rats.
Financial Support: Supported by WA Initiative Measure Number 171.

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A NOVEL OPIOID RECEPTOR ANTAGONIST, ALKS 33, DEMONSTRATES FULL AND DURABLE BLOCKADE OF REMIFENTANYL.

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Aims: ALKS 33(ALKS33) is a novel opioid modulator characterized in vitro as a potent μ-antagonist and partial δ-agonist. ALKS33 is in development for the treatment of reward disorders. A Phase 1 clinical study was conducted to evaluate the degree and duration of blockade of a selective μ-opioid agonist following single doses of ALKS33. A PK/PD relationship of ALKS33 was explored.
Methods: A single-center, randomized, single-blind, fixed-order, placebo-controlled study was conducted in 24 opioid experienced subjects. PBO was administered on Day 1; ALKS33(10 or 20mg) was administered on Day 2. Five remifentanyl(REMI) and 2 saline(SAL) infusion challenges were administered on Day 1 and Day 2; daily REMI and SAL challenges were administered on Days 3-9. At each challenge repeat PD evaluations were conducted up to 25min post-infusion including pupil diameter and visual analog scales(VAS) scoring for Drug Liking, High, etc. The degree, onset and duration of blockade were determined by statistical comparison of pupil diameter and VAS scores. Safety and tolerability of ALKS33 was assessed. ALKS33 concentrations were determined by LC/MS/MS.
Results: REMI produced significant PD effects on Day 1 ($p<0.001$ vs SAL). ALKS33 10 and 20mg blocked pupil miosis induced by REMI within 1 hr and 0.25hr, respectively; complete blockade persisted for at least 24hr (48hr $p<0.001$ REMI vs SAL). Complete blockade of subjective effects of "Drug Liking" persisted for at least 48hr (72hr $p<0.001$ REMI vs SAL). ALKS33 concentrations of >15 ng/mL were sufficient for full blockade. Partial blockade of physiologic and subjective effects persisted through at least Day 4, even after >99% ALKS33 had been eliminated (t1/2=7hr). Nausea, fatigue and somnolence were reported in >2 subjects each; incidence was not dose related.
Conclusions: ALKS33 was associated with complete blockade of a potent μ-opioid agonist. The duration of blockade was sufficient to support less than daily administration. ALKS33 was well-tolerated after a single dose in opioid experienced subjects.
Financial Support: Study conducted by Alkermes, Inc.

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MEDICAL AND PSYCHIATRIC SEVERITY OF OPIOID-ADDICTED INDIVIDUALS IN- VS. OUT-OF-TREATMENT.

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Aims: To assess and compare the physical and mental health problem severity of opioid-addicted individuals in-treatment *v.* out-of-treatment over the course of one year.
Methods: The Addiction Severity Index (ASI) was administered at baseline and at 6- and 12-month post-entry to 351 opioid-addicted individuals entering one of six Baltimore area methadone programs and 164 opioid-addicted individuals recruited from the Baltimore City streets that were out-of-treatment and not seeking addiction treatment. A one-way ANOVA was conducted to examine baseline differences between the two groups on Medical and Psychiatric composite scores. A mixed model repeated measures analysis was conducted to examine Group (in- *v.* out-of treatment) differences in ASI Medical and Psychiatric composite scores over Time (baseline *v.* 6 months *v.* 12 months).
Results: At baseline, the in-treatment sample had significantly (both $ps < .001$) higher ASI Medical and Psychiatric composite scores ($Ms = .17$ and .09, respectively) than the out-of-treatment sample ($Ms = .10$ and .05, respectively). The Group X Time interaction was not significant for either Medical or Psychiatric composite scores (both $ps > .05$). However, there were mean differences in the Medical composite scores for gender (women $M = .17$ *v.* men $M = .10$), race (Caucasian $M = .16$ *v.* African American $M = .11$); and age was positively associated with Medical composite scores [b = .007 ($SE = .0016$)], all $ps < .01$. For Psychiatric composite scores, main effects were significant ($ps < .01$) for gender (women $M = .09$ *v.* men $M = .04$) and race (Caucasian $M = .08$ *v.* African American $M = .05$).
Conclusions: Opioid-dependent individuals who were in-treatment reported more medical and psychiatric problems as compared to those not seeking treatment, however overall the severity levels reported were low. Older individuals and women may need specialized services once they enter methadone treatment to address their medical and psychiatric needs.
Financial Support: NIDA Grant # RO1 DA 015842

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IMPULSIVITY + CRAVING = DRUG USE?

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Aims: The primary aim of this study was to determine the relationship between self-reported impulsivity and craving in cocaine versus methamphetamine (METH) using participants.
Methods: Participants included 85 cocaine-dependent users and 73 METH-dependent users. A screening interview included the Barrett Impulsivity Scale (BIS), and a Visual Analog Scale that probed "just before your last use of cocaine/METH, how much craving did you experience?"
Results: Cocaine- and METH-dependent participants were primarily male. Cocaine dependent-participants were primarily African American and METH participants were primarily Caucasian. Significant differences between cocaine and METH users were found for age (44 vs. 35, respectively, $p<0.05$), years of cocaine/METH use (18 vs. 11, $p<0.05$), and years of nicotine use (22 vs 17, $p<0.05$). Participants did not differ with respect to recent use of alcohol, nicotine or marijuana. ANOVA did not reveal significant differences between cocaine and METH users for total craving ($F1, 156=1.45$, $p=0.2310$) or total impulsivity ($F1,156=.489$, $p=0.4856$). Positive correlations were for total impulsivity and total craving in cocaine ($r=0.23$, $p=0.0337$) and METH users ($r=0.31$, $p=0.0083$). Participants were separated into high impulsivity (HIBIS) or low impulsivity (LOBIS) subgroups based on median split. ANOVA revealed a trend toward differences between HIBIS (74.53±23.81; mean ± S.D.) and LOBIS (65.58±24.91) groups for total craving in cocaine users ($F1,83=2.860$, $p=0.0945$), and a significant difference between HIBIS (72.43±25.76) and LOBIS (57.22±29.14) groups for total craving in METH users ($F1,83=5.591$, $p=0.0208$). HIBIS and LOBIS subgroups were used further to explore the relationship between total craving and Attentional, Motor, and Non-Planning subscales of the BIS.
Conclusions: The results indicate a positive relationship between total impulsivity and craving for both cocaine and METH groups, but the magnitude of the relationship was small, indicating that ~90-95% percentage of variance was accounted by undetermined factors.
Financial Support: DA017754

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EFFECTS OF VOUCHER PAYMENT THROUGH CONTINGENCY MANAGEMENT IN TOPIRAMATE TREATMENT FOR COCAINE DEPENDENCE.

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Aims: The benefit of contingency management (CM) to reduce cocaine abuse by a medium to large effect in the context of opioid maintenance treatment is well documented. This study investigated the effect of CM on 3-week continuous abstinence among CM and Non-CM groups in an ongoing RCT of topiramate treatment for cocaine dependence during methadone maintenance.
Methods: Subjects were randomized to CM or a yoked control group (Non-CM) (and double-blind topiramate or placebo). The CM group received vouchers with value based on a pre-determined algorithm. During the 12-week CM period, cocaine was semi-quantitatively tested and the Preston (i.e., new use) rule was applied. Abstinence was defined as 3-weeks or 9 consecutive cocaine negative urine tests (UN9+). This present analysis includes data from 74 completers (CM=35; NCM=39) from the 12-week CM period. The analyses don't account for a possible effect of drug condition as the study is ongoing.
Results: Participants were 43 years old, 50% females, 38% Caucasians, 62% never married, 67% unemployed and had an 11th grade education. In the CM group, 49% were UN9+ compared to 39% in NCM, ($p = 0.48$). Total payment was substantially associated with cocaine-free results in CM patients ($r=0.60$; $p<.01$), and less so in NCM patients ($r=0.19$; $p<.01$). In the CM group, 17 UN9+ subjects earned $886 ± $293 vs $38 ± $22 for 18 UN9- ($p < 0.01$). In the Non-CM group, 15 UN9+ earned $395 ± $479 vs $230 ± $348 for 24 UN9- ($p = 0.21$). Multiple regression analysis among current completers show voucher payment to be associated with UN9+, so that for each $100 received the O.R. of UN9+ is 1.4 (95% CI: 1.2;1.6; $p<0.01$).
Conclusions: Our results show that monetary incentives during cocaine dependence are associated with cocaine abstinence.
Financial Support: Supported by NIDA:R01-DA021808, K24 DA-23186 & T32-DA07209.

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CALIFORNIA'S SUBSTANCE ABUSE AND CRIME PREVENTION ACT, AKA PROPOSITION 36: ARREST OUTCOMES, STATE CRIME TRENDS, AND PRISON POPULATION TRENDS ASSOCIATED WITH IMPLEMENTATION.

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Aims: To examine offender arrests, state crime trends, and state prison population trends associated with SACPA and to discuss the policy implications of the findings.
Methods: Records of eligible offenders were identified in state treatment and criminal justice databases and analyzed to examine re-arrest rates after a SACPA eligible conviction. FBI Uniform Crime Reports and prison records were analyzed to examine the association between SACPA implementation and state crime and prison trends. State trends were compared to national trends for the same period.
Results: Treatment completers were less likely to be arrested for a new offense relative to non-completers. However, the overall percentage of SACPA eligible offenders re-arrested was higher relative to a pre-SACPA comparison group, in part due to lower rates of incarceration for the SACPA group. After SACPA implementation the violent crime rate in California decreased faster than rates did in the rest of the nation, though not as fast as they had prior to SACPA. Property crime rates and drug arrest rates increased slightly after SACPA took effect, but in subsequent years decreased to a greater extent than in the rest of the nation. Over this period, the percentage of the state's prison population used to incarcerate drug offenders declined while the percentage devoted to violent criminals has increased.
Conclusions: SACPA may have influenced crime trends directly by providing treatment while reducing incarceration, and indirectly by producing a shift in the prison population. Although crime trends cannot be definitively causally attributed to the effects of SACPA, the results suggest favorable implications for efforts to divert drug offenders into community treatment nationwide, both for rehabilitation and for increasing the number of prison beds available for more serious offenders. Potential social benefits of diversion must be recognized by policymakers during the current era of budget reductions.
Financial Support: California Department of Alcohol & Drug Programs Contract 07-00152

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CONSTRUCT VALIDITY OF COMPUTERIZED COGNITIVE PERFORMANCE: IMPLICATIONS FOR MEASUREMENT OF ACUTE DRUG EFFECTS.

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Aims: The purpose of this study was to assess the construct validity of three computerized cognitive performance tasks that are commonly used in behavior pharmacology research.
Methods: A sample of forty-three adults (14 female) that included nondrug users (n=23) and weekly marijuana users (n=20) participated in this single day outpatient study. They completed the Digit Symbol Substitution task (DSST), which was administered three times, a Divided Attention task (DAT) and a Repeated Acquisition task (RAT). They also completed a criterion battery of 7 well-established neuropsychological tests, measuring simple attention and concentration, complex attention, motor function, visuospatial construction and executive function.
Results: DSST and DAT performance was correlated with performance on most of the standardized neuropsychological tests, with strong correlations ($r=0.58$ - 0.60; $p<0.05$) between the number of attempts on the DSST and accuracy on the Digit-Symbol Coding test (simple attention),and between DAT reaction time and Trailmaking B completion time (complex attention). No computerized cognitive task was correlated with performance on the Wisconsin Card Sorting Test ($p>0.05$). Although DSST performance improved over three administrations ($p<0.05$), it remained broadly correlated with neuropsychological measures at the third administration.
Conclusions: Performance on the DSST and DAT was correlated with measures of attention and visual-motor functions, indicative of criterion validity, and uncorrelated with a measure of executive function, indicative of discriminant validity. Further, DSST performance retained its degree of construct validity over multiple administrations, suggesting that this test may be suitable for research where repeated assessment within a single session is required (e.g., measuring acute drug effects).
Financial Support: NIDA grants 019933 and 09236

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NON-HUMAN PRIMATE GENETIC MODELS OF SEROTONERGIC DYSFUNCTION IN ADDICTION.

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Aims: The aim of this project is to develop cohorts of animals that model human subpopulations and enhance existing primate models for the preclinical development of personalized therapeutics and as an avenue for the elucidation of gene by environment interactions.
Conclusions: Because of their genetic, physiological and behavioral similarities to humans, non-human primates can be effectively used to model neurological variation in humans. This allows us to isolate specific genetic and environmental components increasing their relative proportion of phenotypic variance and significantly enhancing our power to detect causative factors. Genetic variation in rhesus macaques has been identified that is functionally parallels that seen in humans. This concept can be applied broadly across numerous systems though its applicability and usefulness is perhaps best realized for neurobiology. Our research has focused on variation within the serotonin system, notably the serotonin synthesis enzyme (TPH2), transporter (SERT), and catabolism enzyme (MAOA). These genes have been associated with many neuropsychiatric and drug addiction disorders and include the targets of cocaine, amphetamine, and several of the most commonly prescribed psychiatric medications. Here multiple functional sources of variation have been found in rhesus macaques and humans. Studies of the phenotypic consequences of these genetic variants show a broad similarity to those observed in humans, but also show differential effects based on environmental factors including early childhood development, sociality and generalized stress levels. We have identified significant genotype-phenotype relationships between specific genetic variation and HPA-axis function and cognitive flexibility. We are currently assessing the relationship to alcohol drinking behavior and medication response. Going forward, this work will allow us to elucidate the factors underlying inter-individual differences in propensity towards addiction, progression, treatment and relapse and to enhance existing primate models of addiction.
Financial Support: Supported by DA025697, AA0161494, DA025802, MH077995 and RR000168.

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WITHDRAWN

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SLEEP DYSFUNCTION AND THE EFFECTS OF EXTENDED-RELEASE ZOLPIDEM DURING CANNABIS WITHDRAWAL.

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Aims: There is currently a need to identify medications that can aid the treatment of cannabis use disorders. Zolpidem, an approved hypnotic, was selected for study as a candidate medication because sleep disturbance is a hallmark feature of cannabis withdrawal, and has been identified as a precursor for relapse.
Methods: An initial within-subject crossover study (N=20) characterized the effects of cannabis withdrawal on sleep architecture during 3-day periods in which daily cannabis users received extended-release zolpidem or placebo at bedtime. Baseline assessments were conducted during 2-day periods in which cannabis was used ad-libitum. Sleep EEG recordings were collected each night. A second study (N=2) has been initiated using the same design, but in which the duration of abstinence was increased to 16 days to assess time course.
Results: Study 1 indicated that, compared with when participants were allowed to use cannabis, abrupt abstinence in the absence of active medication resulted in reduced time asleep, sleep efficiency, REM latency, and Stage 1 sleep, and an increase in sleep latency and REM sleep. Administration of zolpidem during abstinence attenuated the reduction in sleep efficiency and alterations in REM sleep. Data from the first 2 participants in Study 2 replicate findings from Study 1 and suggest that sleep disturbance persists for at least 16 days and increase in severity during the first 2 weeks of abstinence.
Conclusions: These data provide objective evidence that sleep function is disrupted in heavy cannabis users when they abruptly quit. The magnitude of sleep disturbance observed was clinically significant. The results also indicate that the sleep disruption associated with cannabis withdrawal can be attenuated by zolpidem, suggesting that hypnotic medications might be useful as an adjunct pharmacotherapy in the treatment of cannabis use disorders. Clinical trials to determine the efficacy of adding hypnotic medications to existing behavioral interventions for cannabis use disorders is warranted.
Financial Support: NIH Grants DA025794, DA12471 and UL1 RR025005

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DISCRIMINATIVE-STIMULUS EFFECTS OF METHAMPHETAMINE IN HUMANS: EFFECTS OF ACUTE D-AMPHETAMINE AND BUPROPION PRETREATMENT.

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Aims: The drug discrimination paradigm has been used to identify effective pharmacotherapies for stimulant dependence based on the notion that the interoceptive effects of drugs contribute to their abuse. Evidence from animal models suggests that, using drug discrimination methods, effective agonist-replacement medications given chronically attenuate the discriminative effects of the abused stimulant. Administered acutely, however, these medications have an additive influence on the discriminative effects of the abused stimulant. These were the first studies to explore this notion using the drug discrimination paradigm in human volunteers.
Methods: Two separate laboratory studies were conducted that examined the effects of sustained-release d-amphetamine and extended-release bupropion, two potential agonist-replacement medications for stimulant dependence, on the discriminative, subject-rated, cardiovascular and performance effects of methamphetamine in recreational stimulant users. Procedures were identical. Participants learned to discriminate methamphetamine (10 mg) from placebo. Following acquisition of the discrimination (i.e., ≥ 80% correct responding on 4 consecutive days) a range of doses of methamphetamine (0, 1.25, 2.5, 5 and 10 mg) was tested alone and in combination with sustained-release d-amphetamine (0 or 15 mg) or extended-release bupropion (0 or 150 mg).
Results: Pretreatment with sustained-release d-amphetamine shifted the methamphetamine dose response curve leftward. Pretreatment with bupropion did not alter the discriminative-stimulus effects of methamphetamine.
Conclusions: The results of these studies translate findings from the animal laboratory to the human laboratory and help establish the predictive-validity of drug discrimination methods in the discovery of agonist-replacement medications for stimulant-use disorders.
Financial Support: NIDA DA025032-01 (Craig R. Rush)

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SMOKING AND DEPRESSION IN POST-PARTUM WOMEN: DOES SEVERITY MATTER?

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Aims: Maternal depression is associated with adverse infant and child outcomes (Maughan et al., 2007); recent studies affirm maternal smoking and depression are correlated (Allen, et al., 2009). The present study examined severity of nicotine dependence and depressive symptomatology and their association in postpartum women.
Methods: Participants (n=216) were mothers of infants receiving care at an urban, university-based pediatric clinic. Mothers completed semi-structured interviews with research staff. Measures included the Fagerstrom Test of Nicotine Dependence (FTND; Heartherton et al., 1991) and the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). Pearson correlation was used to examine relationship between tobacco and depressive symptoms severity. Chisquare and t-tests were used to examine severity indicators.
Results: Participants were predominantly African-American (86.1%), in their mid-twenties (mean=25.3, SD=5.6), and never married (81.5%). Smoking was reported by 62% of the sample (n=134); 74.4% of smokers (n=61) reported smoking ten cigarettes or less per day. The majority of the sample had a CES-D score indicating no depression (68.1%, n=145) and 23% had a score indicating mild depression (n=49). A significant correlation (r =.233, p=.001) was found between CES-D score and nicotine dependence; women with high FTND scores reported more depressive symptoms. Women who reported moderate/high nicotine dependence were more likely to report mild depression (X^2= 6.2, p < .05). The number of cigarettes smoked per day was positively associated with depression severity (X^2 = 10.5, p < .05).
Conclusions: Findings support a link between quantity of cigarettes smoked in postpartum women and severity of depressive symptoms. Screening postpartum women for tobacco use may provide pediatric health care providers with a mechanism to identify women at risk for depression and whose children are subsequently at risk for a host of problems.
Financial Support: Research supported by the Alcoholic Beverage Medical Research Foundation and the Centers for Disease Control and Prevention.

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IMPULSIVITY AND HIV SEXUAL RISK BEHAVIORS IN BULGARIAN HEROIN USERS.

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Aims: The aim of our study was to explore the associations between neurocognitive, personality, and psychiatric indices of impulsivity and HIV sexual risk behaviors in Bulgarian heroin users
Methods: We tested 50 currently abstinent individuals with a history of heroin dependence and no significant history of dependence on other substances. Exclusion criteria included positive urine toxicology screen and currently being on opioid substitution therapy. We administered four measures assessing different neurocognitive indices of impulsivity: (1) Iowa Gambling Task (IGT); (2) Balloon Analogue Risk Task (BART); (3) Delayed Reward Discounting Task (DRDT); and (4) Stop Signal Task (SST). In addition, participants completed self-report measures related to impulsivity, measuring impulsivity as a trait (BIS-11), psychopathy, and ADHD. HIV sexual risk behaviors were assessed by the Social Network Project Questionnaire, previously validated in Bulgarian and comprised of 5 scales: 1) HIV Risk Behavior Knowledge; 2) Safer Sex Intentions; 3) Safer Sex Attitudes; 4) Safer Sex Peer Norms; and 5) Safer Sex Self-Efficacy.
Results: We performed five multiple regression analyses to test our hypothesis that higher impulsivity would be related to more risky HIV sexual behaviors. The models were significant for two of the HIV sexual risk behavior scales: Safer Sex Attitudes (F=2.881, p<.02) and Safer Sex Peer Norms (F=6.981, p<.000). Safer Sex Attitudes was predicted by BART, SST, ADHD, BIS-11, and anxiety. In contrast, Safer Sex Peer Norms was predicted by BART, SST, Psychopathy, and IQ.
Conclusions: Overall, the results support our hypothesis that HIV sexual risk behaviors are related both to neurocognitive and self-report indices of impulsivity. On the other hand, impulsivity was not related to other indices of HIV sexual risk behaviors, such as HIV risk behavior knowledge, intentions, and self-efficacy. The relation between HIV sexual risk behaviors and impulsivity appears to be complex and influenced by additional variables such as IQ and anxiety.
Financial Support: NIDA - Grant 1R21DA025417-01

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A RAPID METHOD TO MEASURE LIMBIC AND STRIATAL BEHAVIOR AND DOPAMINE NEUROCHEMISTRY IN MICE.

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Aims: Dopamine mimetic drugs with different presynaptic mechanisms produce unique patterns of change in dopamine and its metabolites (neurochemical fingerprints) in the brain (Heal et al, this meeting). We have used the dopamine releasing agent, d amphetamine (d-AMP), and determined whether it is possible in a single experiment to study limbic and striatal dopaminergic function using behaviour and striatal neurochemistry.
Methods: Adult, male C57/BL6 mice (n = 6-9) were acclimatised in photobeam activity cages and injected IP with d amphetamine (3 or 10 mg/kg) or saline. Activity was measured for 60 min with stereotypy scored (0-2) at 30 min. Mice were killed 60 min after d amphetamine (10 mg/kg) for the HPLC-ECD quantification of striatal dopamine, DOPAC and HVA (Cheetham et al, 1996) and 3 MT (Heal et al, 1990). Neurochemistry results are expressed as % control and all changes are significantly different ($p < 0.001$). In the 3 component protocol, mice were injected with d AMP (3 mg/kg at 0 min + 7 mg/kg at 30 min) or saline x 2. Activity was monitored for 0 30 min and 35-65 min, stereotypy was measured at 55 min and brains were then taken for neurochemical analysis.
Results: Locomotor counts [0–30 min; 30–60 min; 0–60 min]:
(Saline x 1 = 359±73; 57±36; 451±97; d-AMP (3) = 1727±120a; 2321±156a; 4053±244a; d-AMP (10) = 748±69a; 745±105a; 1510±140a) (Saline x 2 = 279±55; 75±32; ND; d-AMP (3+7)=1458±159a,b; 794±85a,c; ND)
Stereotypy score (Saline x 1 = 0; d-AMP (3) 0; d-AMP (10) = 1.7a) (Saline x 2 = 0; d-AMP (3+7) = 1.9a,c)
aP<0.005 vs appropriate control; bNS from d AMP (3); cNS from d AMP (10). ND Not determined
Neurochemical fingerprints were also identical: d-AMP(3+7) = DOPAC decreased (34%), 3-MT increased (351%), HVA unchanged vs d-AMP(10) = DOPAC decreased (35%), 3-MT increased (381%), HVA unchanged
Conclusions: The results are as robust and precise as data generated when each component was measured using single d-AMP doses. This technique provides a rapid and efficient method to study multiple behavioural and neurochemical endpoints.
Financial Support: Supported by RenaSci

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LONG ACCESS TO SELF-ADMINISTERED COCAINE CAUSES LASTING INCREASES IN IMPULSIVE CHOICE IN A DELAY DISCOUNTING TASK.

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Aims: Cocaine use is associated with high levels of impulsive choice (preference for immediate over delayed rewards), but it is not clear whether cocaine use causes elevated impulsive choice, or whether elevated impulsive choice is solely a predisposing factor for cocaine use. We have shown previously that both experimenter- and self-administered cocaine cause long-lasting increases in impulsive choice. This study extends our previous work to determine how the duration of cocaine access influences impulsive choice.
Methods: Male Long-Evans rats were implanted with i.v. catheters, and allowed to self-administer cocaine HCl (approx. 0.5 mg/kg/infusion) for 6 h/day for 14 consecutive days. A control group of rats was allowed to self-administer a 20% sucrose solution, such that the number of sucrose reinforcers earned was yoked to the number earned by cocaine rats. Following three weeks of withdrawal, all rats were food-restricted and trained on a delay discounting task in standard operant chambers for 20 sessions. On each trial in a session, rats were given a choice between two levers. A press on one lever delivered a small food reward immediately, and a press on the other delivered a large food reward after a variable delay period (0-32 s).
Results: Consistent with our previous findings, rats that self-administered cocaine displayed greater impulsive choice (enhanced preference for the small immediate over the large delayed reward) compared to sucrose controls, although there was no relationship between impulsive choice and amount of cocaine intake.
Conclusions: These data suggest that cocaine use can cause lasting elevations in impulsive choice, and that elevated impulsive choice in human cocaine users may be due in part to long-term effects of cocaine on brain function. Ongoing studies are examining the effects of short access cocaine self-administration sessions on impulsive choice, as well as the effects of cocaine self-administration on other types of decision-making.
Financial Support: DA024671 (BS)

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ALCOHOL DEPENDENCE DOES NOT INFLUENCE DRUG ABSTINENCE OUTCOMES FROM CONTINGENCY MANAGEMENT TREATMENT AMONG COCAINE-DEPENDENT HOMELESS PERSONS.

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Aims: From 57% to 88% of individuals in treatment for cocaine use disorders also have an alcohol use disorder. Despite this comorbidity, cocaine dependent patients with and without alcohol dependence have similar levels of drug abstinence after contingency management treatments. Given that all reports in the literature to date have involved outpatients in relatively stable socioeconomic circumstances, our aim was to determine if similar relations hold for homeless persons.
Methods: In this clinical trial, all participants were homeless, had a diagnosis of cocaine dependence or abuse, and received abstinent-contingent housing and vocational training. Half of the participants also received behavioral day treatment (BT, n = 97), and half did not receive behavioral day treatment (NBT, n = 95). We created a 4-level categorical variable regarding DSM-IV alcohol-related diagnoses at baseline: (1) No Diagnosis (n = 52); (2) Alcohol Dependence in Sustained Remission (n = 28); (3) Alcohol Abuse (n = 28); and (4) Alcohol Dependence (n = 84).
Results: The alcohol-related diagnoses were distributed similarly across the two treatment groups ($p = .385$). The primary dependent variable was the number of consecutive weeks of drug abstinence during the one-year treatment and post-treatment interval. Linear models showed a significant effect for treatment group ($p = .014$), with BT having more drug abstinence, but no effect for alcohol-related diagnosis ($p = .697$), or for the interaction of treatment and alcohol diagnosis ($p = .753$).
Conclusions: These results replicate earlier reports in the literature for outpatients with cocaine use disorders. That is, for both outpatients and homeless persons, individuals with cocaine use disorders benefit equally from contingency management treatments regardless of whether or not they also have an alcohol use disorder.
Financial Support: DA11789

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TREATMENT PROCESSES WITHIN SEVEN BRIEF THERAPIES FOR ADDICTION.

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Aims: The aim of this study was to compare unique and common treatment processes within different psychological therapies for addiction.
Methods: We evaluated 7 evidence-based single treatment sessions conducted by master therapists demonstrating Motivational Interviewing, Cognitive Therapy, Harm Reduction Therapy, Stages of Change Therapy, Reality Therapy, 12-Step Facilitation Therapy, and Solution Focused Therapy. Videos were rated by six coders who had achieved high inter-rater reliability across two passes. Constructs included therapist global empathy, collaboration, autonomy support, evocation, and direction, client change talk, therapist behaviors such as questions, reflections, advice, providing information, etc., therapist traps and strategies, interpersonal dimensions, and psychotherapy process and content. Measures included reliable and valid instruments from the addiction and psychotherapy fields.
Results: Therapist behavior patterns and global ratings varied considerably across the seven therapy approaches. Reflective listening was the predominant communication method in MI, while questioning was the most common method in all other therapies. Therapist affiliation and dominance varied significantly by approach. MI and Solution Focused therapy focused on past and near future events, whereas other therapies focused on the past, with 12-step and cognitive therapies strongly focused on past events.
Conclusions: Expert demonstrations differed across therapeutic approaches. These differences could be explored further as potential mediators of outcome in clinical samples.
Financial Support: Supported by R01 AA015930

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INFLUENCE OF MARIJUANA USE ON THE EFFECTS OF D-AMPHETAMINE.

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Aims: Individual differences influence drug use. The results of controlled non-human animal and human laboratory studies are mixed regarding the interaction between marijuana and d-amphetamine. We hypothesized that recent marijuana use would reduce some behavioral effects of d-amphetamine.
Methods: In order to examine the influence of marijuana use on the effects of d-amphetamine, we performed a retrospective analysis of data from six studies conducted in our laboratory that used identical procedures and measures. Eleven light and nine heavy marijuana using humans (as indicated by the presence or absence of self-reported past month use) learned to discriminate 15 mg oral d-amphetamine. After acquiring the discrimination (i.e., > 80% correct responding on 4 consecutive sessions), the effects of a range of doses of d-amphetamine (0, 2.5, 5, 10, and 15 mg) alone and in combination with other drugs were assessed. Only data from sessions in which d-amphetamine was administered alone were included in this analysis. Data were analyzed using a mixed-model ANOVA.
Results: As expected, d-amphetamine functioned as a discriminative-stimulus and produced prototypical subject-ratings and cardiovascular effects. Heavy marijuana users were less sensitive to the subject-rated, but not discriminative-stimulus, effects of d-amphetamine.
Conclusions: The results of this study indicate that marijuana use influences the subject-rated effects of d-amphetamine. These results also indicate a possible cross-tolerance between marijuana use outside the laboratory and d-amphetamine administered within the human laboratory. Future human laboratory studies should prospectively examine the influence of marijuana use on the behavioral effects of d-amphetamine using sophisticated procedures like drug self-administration.
Financial Support: NIDA Grants R01 DA 010325 and 013567 (CRR).

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CORRELATES OF MEXICO-US DRUG INJECTION RELATIONSHIPS AMONG IDUS IN TIJUANA, MEXICO.

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Aims: The social dynamics of drug users living in border areas are understudied, though reports suggest that drug users cross international borders to purchase and use drugs. Little is known about the extent of social mixing between drug users from the US and Mexico.
Methods: We studied 1056 IDUs residing in Tijuana, Mexico recruited from 2004 to 2006 to identify correlates of having ever injected drugs with someone from the US.
Results: Overall, 97% were born in Mexico; distributive and receptive syringe sharing in the past 6 months were reported by 61% and 59%, respectively. Almost half (47%) reported ever injecting drugs with someone from the US. IDUs who had injected with someone from the US were older (median age 39 vs 34, p<.01), initiated injection drug use at a younger age (median age 19 vs 21, p<.01), were less likely to identify as Latino (79 vs 85%, p=.01), knew more people who travel to the US at least once/yr (median 3.5 vs 3.0, p<.01), were more likely to have ever traveled to the US (96 vs. 61%, p<.01), to socialize with other IDUs in the US (54 vs 20%, p<.01), and to have ever used drugs in the US (95 vs 23%, p<.01). In logistic regression, factors independently associated with having ever injected with someone from the US were older age (Adjusted odds ratio 1.08 per yr, 95% CI 1.06, 1.11), younger age at first injection (AOR 0.90 per yr, 95% CI 0.88, 0.92), identifying as Latino (AOR 0.65, 95% CI 0.44, 0.95), ever traveling to the US (AOR 10.5, 95% CI 6.29, 17.52) and socializing with drug users in the US (AOR 2.87, 95% CI 2.09, 3.94).
Conclusions: These data suggest that there is mixing between drug using networks in Tijuana and the US, and that drug using networks may transcend international borders. These findings have implications for cross-border transmission of blood borne infections via potentially unsafe injection practices. Programs and policies around illicit drug use should consider the structure and geographic distribution of drug using networks.
Financial Support: NIDA R01DA079829 & T32DA023356

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DATA GAPS REGARDING DIVERSION AND ABUSE OF PRESCRIPTION OPIOID ANALGESICS.

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Aims: The increase in the use and misuse of prescription opioid analgesics reflects a complex interaction of access to the medications, public policies to control the use and abuse of the medications, and user characteristics. We are constructing a high-level systems dynamic model that interlinks data on initiation, prevalence, treatment, and outcomes associated with prescription opioid abuse and nonmedical usage.
Methods: The model requires data on use and misuse of prescription opioids. As a result, we identify and describe data gaps that confound efforts to address fundamental questions. We offer suggestions for addressing these gaps and propose a common data set for monitoring use and misuse.
Results: Our review of potential data sets found discrepant data regarding deaths attributed to prescription opioids; limited data regarding factors influencing use, misuse, and cessation; inconsistent definitions for abuse versus nonmedical use; and unclear relationships between overdose events and DAWN mentions. Gaps also relate to the effectiveness of risk evaluation and mitigation strategies (REMS) such as tamper-resistant formulations, prescription monitoring programs, and training programs for prescribers and patients.
Conclusions: Multiple variables influence prescription opioid use and misuse. Closing data gaps will help researchers to predict REMS effectiveness and find ways to reduce negative outcomes without compromising pain treatment. Changes in the wording of questions found in the National Survey on Drug Use and Health and the coding used for the Drug Abuse Warning Network might contribute to improved data and increased precision in modeling.
Financial Support: A contract from Purdue Pharma L.P. supported the model construction.

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METHADONE ENHANCES ANTINOCICEPTIVE BUT NOT DISCRIMINATIVE EFFECTS OF THC.

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Aims: Previous research has shown that cannabinoids and opioids can act synergistically to produce antinociception. The aim of this study was to determine whether cannabinoid-opioid synergism occurs similarly on measures of antinociception, discrimination and locomotion.
Methods: Male Sprague-Dawley rats (N = 9) were trained to discriminate Δ9-tetrahydrocannabinol (THC, 3 mg/kg, i.p.) from vehicle (1:1:18 ethanol:cremaphor:saline) using a two-lever, food-reinforced drug discrimination procedure. Once reliable discrimination was established, the discriminative, antinociceptive, and motoric effects of THC (0.18 - 10.0 mg/kg), methadone (0.32 – 5.6 mg/kg) and THC + methadone combinations were examined. Discriminative effects were measured 30 min post-injection (20-min test); antinociception (paw pressure), horizontal locomotion (# of photobeams broken in 5 min) and catalepsy were measured starting 50 min post-injection.
Results: The ED50 for THC discrimination was 0.70 ± 0.05 mg/kg. Methadone partially generalized to THC, with a maximum of 40% THC-lever responding at 5.6 mg/kg. Both THC and methadone dose-dependently reduced operant response rate and locomotor activity when tested alone. In addition, both drugs produced moderate antinociception (40 - 60% MPE). High doses of both drugs also produced catalepsy. Methadone (0.32 – 3.2 mg/kg) did not alter the THC discrimination curve, but enhanced the antinociceptive effects of THC. Methadone also enhanced THC-induced catalepsy but did not significantly alter THC's effects on locomotor activity.
Conclusions: These results suggest that opioids can enhance the antinociceptive and operant response rate-decreasing effects of cannabinoids without altering their discriminative effects, even when all endpoints are tested in the same subjects.
Financial Support: This research was supported by a grant from the Peter F. McManus Charitable Trust.

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OFFSPRING EARLY SUBSTANCE USE AND RISKS FROM PARENTAL DRUG PROBLEMS AND PARENTAL SEPARATION.

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Aims: We examine early use of alcohol, tobacco, marijuana and other illicit substances as a joint function of parental drug problems and parental separation.
Methods: Data were drawn from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a representative sample of 43,093 non-institutionalized men and women living in the U.S. Survival analyses were conducted using Cox proportional hazards regression models predicting age at first substance use from respondent report of parental "drug problems" (DP) and parental separation during childrearing years.
Results: Compared to female offspring of married DP- parents, female offspring of married DP+ parents are more likely to smoke, smoke regularly, drink alcohol, and use marijuana by age 12 or 14 (HRs = 2.75-5.21), as are female offspring of separated DP- parents (HRs = 2.10-3.96). Female offspring of separated DP+ parents demonstrate even greater risk across substances through ages 12-14 (HRs = 3.19-18.47). For male offspring, similar although somewhat weaker associations are observed (HRs = 1.35-15.01).
Conclusions: Together, results for both female and male offspring confirm that it is very young adolescents (ages 14 and younger) from substance abusing families where parental separation has occurred who are at especially high risk of early substance involvement.
Financial Support: NIDA grant DA023696.

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DRUG ABUSE, POSTTRAUMATIC STRESS, AND IMPULSIVITY IN WOMEN.

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Aims: Drug dependence and trauma exposure are highly comorbid. Cocaine use, sexual trauma, and PTSD symptoms are all associated with increased risk-taking behaviors and impulsivity. Understanding risk-taking propensity and maladaptive decision-making in PTSD/substance use comorbidity will be important to addressing those problems in treatment. Aims: To compare women with and without cocaine dependence and with and without subsyndromal PTSD on laboratory and self-report measures of impulsivity.
Methods: Community-based women were assigned to four groups based on the presence or absence of cocaine dependence (assessed with SCID) and at least subsyndromal PTSD (assessed with CAPS) related to a sexual assault: cocaine group (COC) n = 13, PTSD group (PTSD) n = 26, comorbid group (COC/PTSD) n = 11, control n = 27. Impulsivity was measured with a delay discounting task, the Balloon Analog Risk Task (BART), and the Barratt Impulsiveness Scale (BIS).
Results: The COC group had the steepest discounting curve. The COC/PTSD discounting curve was more similar to the COC than to PTSD or control. Discounting was not significantly associated with frequency or severity of recent cocaine use. BART scores were not significantly associated with PTSD scores or cocaine frequency or severity. However, COC/PTSD had higher BART scores than did PTSD and control. BIS total and subscale scores were higher in all clinical groups compared to the control group, but clinical groups did not differ. Discounting and BART were not correlated, but select BIS subscales were associated with each task.
Conclusions: Although impulsivity is a clinical feature associated with substance use and PTSD, the form that impulsivity takes may vary by diagnosis. Different measures may be needed to capture different aspects of impulsivity across populations. As clinicians increasingly recognize the importance of directly addressing impulsivity and risk-taking in their patients, tools for brief assessment become more important for monitoring change.
Financial Support: NIDA/ORWH, 1-K23-DA018718, PI: Waldrop

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ADOLESCENT RATS ARE MORE SENSITIVE TO BEHAVIORAL ACTIVATION BY GUARANA AND REPEATED ADMINISTRATION DURING ADOLESCENCE RESULTS IN COCAINE CROSS-SENSITIZATION.

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Aims: Guarana is a tropical berry containing caffeine and other methylxanthines (MX) that is used in energy drinks and weight loss supplements. Adolescents are often high guarana consumers and this could be a concern as neural systems are still maturing. We tested the hypothesis that adolescent rats would be more sensitive to the locomotor stimulating effects of guarana.
Methods: Acute locomotor stimulation induced by 25 mg/kg caffeine, 25 mg/kg guarana extract (containing 21% caffeine) and a MX cocktail (MXC) that mimicked the MX content of guarana were compared. Guarana effects were determined by two routes of administration, ip and po (gavage). Finally, rats were given four doses of guarana or vehicle po every other day starting on PN28 or PN70 and after six drug-free days were evaluated in a cocaine-challenge experiment.
Results: A high dose of caffeine, 25 mg/kg ip, induced locomotor stimulation in periadolescent, late adolescent and adult male rats, but the effect was greatest in periadolescent, PN28 rats. Guarana and MXC increased locomotor activity when given ip and po. The time course of effects showed that guarana po caused an onset of behavioral stimulation as rapid as ip but with longer duration. Guarana (25 mg/kg) po induced more locomotor behavior in the youngest rats. The MXC induced levels of locomotion in PN28 rats similar to those elicited by 25 mg/kg guarana. A low challenge dose of cocaine (10 mg/kg) induced equal levels of locomotion in control and guarana-treated adults. Cocaine effects were greater in guarana-treated than control adolescent rats. Cocaine effects were also greater in the guarana-treated adolescents than adults.
Conclusions: Periadolescent rats were more sensitive to acute behavioral effects of oral guarana. Repeated guarana resulted in greater sensitivity to cocaine challenge only when the exposure occurred in adolescence. High caffeine and guarana exposures to children and adolescents are a growing public health concern that could be relevant to future drug use.
Financial Support: Supported by DA019114

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HIGHER ACUTE CARE HOSPITAL UTILIZATION AMONG MEDICAL INPATIENTS DISCHARGED WITH A SUBSTANCE USE DISORDER DIAGNOSIS.

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Aims: To determine whether a substance use disorder diagnosis among general medical inpatients is associated with subsequent emergency department visits and rehospitalization.
Methods: This observational cohort study used data collected among 738 hospitalized general medical patients enrolled in a randomized controlled trial of re-engineered discharge services. The primary independent variable was a substance use disorder diagnosis among the discharge diagnoses at the index hospitalization. The main outcomes were rate and risk of an emergency department visit or rehospitalization within 90 days of discharge.
Results: At discharge, 17% of subjects had a substance use disorder diagnosis. These subjects had higher rates of recurrent acute care utilization compared to subjects without substance use disorder diagnoses (1.30 vs. 0.74 events per subject at 90 days, $p<0.01$) and increased risk of any recurrent acute care utilization (52% vs 38% at 90 days, $p<0.01$). In poisson regression models, adjusted for age, gender, depressive symptoms, having a PCP, insurance, homelessness in the last 3 months, employment, and the Charlson Comorbidity Index score, the incident rate ratio at 90 days was 1.38 (95% confidence interval 1.13 to 1.67) for subjects with substance use disorder diagnoses compared to those without. In subgroup analyses, higher utilization was attributable to those with drug diagnoses or a combination of both drug and alcohol diagnoses, but not to those with exclusively alcohol diagnoses.
Conclusions: Discharged medical patients with substance use disorder diagnoses, specifically drug related diagnoses, have higher rates of recurrent acute care utilization than those without substance use disorder diagnoses. Further research is warranted to determine whether re-engineered discharge programs targeted to substance users can reduce acute care utilization.
Financial Support: Agency for Healthcare Research and Quality and National Heart, Lung, and Blood Institute (Dr. Jack).

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SUBSTANCE USE AMONG URBAN ADOLESCENTS PRESENTING TO INDIGENT PRIMARY CARE CLINICS.

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Aims: The urban primary care setting represents an underutilized venue for addressing drug use among adolescents. This paper describes rates and correlates of substance use among adolescents in indigent primary care clinics. Compared to non users, adolescents reporting poly-substance use were expected to: be older age, male, and working; try substances before age 15; report having sex, poor grades, poor health, depressive symptoms, and marijuana dependence.
Methods: Patients (ages 12-18) self-administered a computerized survey. Latent class analysis (LCA) was used to identify groups of participants based on substance use. Multinomial logistic regression was used to compare groups based on demographic and health variables.
Results: 1412 adolescents (85% participation; 37% male; 63% African-American) were surveyed. Rates of recent substance use were: 17% cigarettes, 26% marijuana, 23% alcohol, 10% binge drinking, 11% illicit drugs and 7% painkillers. LCA identified three risk groups: 64% low, 25% moderate and 11% high. Compared to the low risk group, the moderate risk group was more likely to report cigarette, alcohol, and marijuana use whereas the high risk group was more likely to report binge drinking, prescription and illicit drug use. The moderate and high risk groups reported similar rates of marijuana dependence. Compared to the low risk group, the moderate risk group was more likely to be older age, report poor grades, poor health, depressive symptoms, and having sex; the high risk group was more likely to be male, older age, Caucasian race, report poor grades, currently working, poor health, depressive symptoms, and having sex. Adolescents who tried cigarettes and alcohol before age 15 tended to be in the high risk group.
Conclusions: Rates of marijuana use greatly exceeded national data. Primary care-based interventions for urban adolescents need to address poly-substance use.
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BUPROPION METABOLISM BY HUMAN PLACENTA.

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Aims: The aim of this investigation is to determine biotransformation of bupropion in placentas obtained from nonsmoking and smoking women as well as to identify and characterize the enzyme(s) responsible for its metabolism.
Methods: Metabolites of bupropion formed by different subcellular fractions of human placenta were identified and quantified by HPLC/MS. Identification of the placental enzymes involved in the biotransformation of bupropion was achieved by utilizing monoclonal and polyclonal antibodies raised against CYP450 isoforms and chemical inhibitors selective to carbonyl reductases.
Results: The data obtained revealed that human placental subcellular fractions metabolize bupropion to hydroxybupropion (OH-bupropion), threo-, and erythrohydrobupropion. The rates of threo- and erythrohydrobupropion formation exceeded that of OH-bupropion by several fold and exhibited saturation kinetics with an apparent Km value for bupropion of 40 μM. Placental 11β-hydroxysteroid dehydrogenase was identified as the major carbonyl-reducing enzyme responsible for reduction of bupropion to threo- and erythrohydrobupropion based on subcellular localization (microsomal, mitochondrial, and cytosolic), cofactor dependence (NADH and NADPH), and results of chemical inhibition, the human. On the other hand, CYP2B6 was responsible for bupropion hydroxylation to OH-bupropion. Furthermore, the formation of all three metabolites of bupropion in placentas obtained from women who smoked during pregnancy (≥ 20 cigarettes per day) was significantly higher than in placentas of nonsmokers or occasional smokers (≤ 10 cigarettes per day).
Conclusions: The data obtained in this investigation suggest that different enzyme(s) are involved in placental metabolism of bupropion, which is a substrate of both carbonyl-reducing and oxidative enzymes, and components of cigarette smoke could affect the activity of placental enzyme(s) responsible for its metabolism.
Financial Support: This work was supported by a NIDA grant RO1DA024094 to TN.

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ADDICTION-ASSOCIATED SPONTANEOUS BRAIN ACTIVATION ALTERATIONS IN THE RESTING STATE.

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Aims: Spontaneous brain activity study using resting fMRI, has become a major interest of recent brain function research. Accumulated evidence has shown that the resting state can be altered by various brain disorders. The aim of this work is to test the hypothesis that addicted individuals may have alterations in the spontaneous activity of the resting brain, also known as the default mode network (DMN).
Methods: Resting arterial spin labeling (ASL) perfusion MR images were obtained from 20 cocaine users (COC), and 11 age- and education-matched normal controls (MC). The ASL tagged-untagged patterns were filtered out from the motion-corrected ASL images, which were then normalized to the standard MNI space, using concurrently-acquired structural images. FSL software was used to run an independent component analysis (ICA) for both groups (COC and MC) after temporally concatenating all subjects' data into a large time series for each group. The DMN underlying the spontaneous brain activity was pursued using two criteria: 1) independent component maps (thresholded with $z>2.5$) should match DMN patterns in the literature, and 2) the major frequency of associated time course should be between 0.001-0.1 Hz.
Results: DMN consisting of anterior cingulate cortex (ACC), orbitofrontal cortex (OFC), prefrontal cortex (PFC), posterior cingulate cortex (PCC), and parietal cortex (PA) was revealed in both groups ($z>2.5$; $p<.012$), with a major frequency of 0.025 Hz and 0.0253, respectively. DMN of cocaine users demonstrated more activation in bilateral OFC and insula, but much less in PCC and bilateral PA.
Conclusions: Although a direct statistical comparison between the drug users' DMN and normal controls' DMN is the focus future work, the group level ICA offers the first evidence that cocaine dependence could alter the spontaneous brain activity in the DMN.
Financial Support: NIDA R21/R33-DA026114 (ARC), R03DA023496(ZW), and P60-DA-005186

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ELECTRONIC MONITORING OF CORTISOL DAYTIME PROFILES DURING ALCOHOL WITHDRAWAL IN HUMANS.

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Aims: Alcohol intoxication activates HPA axis. It is suggested, that alcohol withdrawal increases Cortisol as well. We investigated the correlation of Cortisol and the intensity of alcohol withdrawal syndrome in alcohol dependent human individuals.
Methods: Objective compliance was measured by using an electronic monitoring system. 10 male alcohol dependent patients were instructed to collect six samples of saliva throughout the day. The profile was measured on the second, third, and tenth day during an inpatient detoxification phase.
Results: The available evalualtions show a clear increase of the cortisol daytime profile in the first 6 hours after awakening. An equivalent low concentration of cortisol is found between 3 pm and 10 pm. The maximum rise lies between 30 minutes after awakening and 11 am. During alcohol withdrawal a flattening of the daily profile shows up. After 10 days in most cases there is a normalization of cortisol level in the saliva. Only a small subgroup showed persistant HPA activation, possibly connected to intense craving.
Conclusions: This investigation shows the connection between alcohol withdrawal syndrome and an activation of the HPA axis. During a vulnerable phase in the morning the HPA axis activity is affected by alcohol withdrawal. Persisting increased Cortisol level in a subgroup may have clinical implications like intense craving in these individuals.
Financial Support: none

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EFFECTS OF VOUCHER-BASED TREATMENT FOR CIGARETTE SMOKING CESSATION ON MATERNAL WEIGHT GAIN DURING PREGNANCY.

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Aims: Excessive maternal weight gain associated with smoking cessation among pregnant women is a potential medical concern due to associated maternal and neonatal adverse outcomes. The question of whether smoking cessation treatment causes excessive weight gain during pregnancy has been understudied. The success of voucher-based contingency management (CM) in producing significant increases in antepartum cessation rates provides an opportunity to investigate this question.
Methods: Participants (N = 158) were smokers at the start of prenatal care who participated in controlled trials with voucher-based CM for smoking cessation. Across trials women were assigned to either abstinence-contingent vouchers wherein they earned vouchers by abstaining from smoking or to a control condition where they received comparable vouchers independent of smoking status. Information of weight gain (kg) was collected from hospital birth records.
Results: No significant differences in maternal weight gain were observed between the abstinence-contingent and control treatment conditions (15.04 ±0.76 kg vs. 15.00 ±0.85 kg, p = .97). A univariate comparison of weight gain among abstainers vs. smokers independent of treatment condition revealed significantly more weight gain among abstainers (17.17±1.14 kg vs. 14.38 ±0.65 kg, p = .04), but that difference was not significant in multivariate analyses. In multivariate analyses pre-pregnancy body mass index (BMI) and being pregnant the first time were the only significant predictors (p = .0001 and p = .0095).
Conclusions: Overall, we see no evidence that excessive maternal gain should be a major concern in the use of voucher-based CM for smoking cessation during pregnancy.
Financial Support: Training grant T32 DA07242-17 & Research grant RO1DA009378 from the National Institute on Drug Abuse.

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PSYCHOSTIMULANT DRUG EFFECTS ON SPIKE TRAIN CODING OF SENSORY AND DECISION-RELATED SIGNALS IN RODENT THALAMIC AND CORTICAL CIRCUITS DURING QUIET RESTING AND SUSTAINED ATTENTION.

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Aims: While the biochemical action of the psychostimulant methylphenidate (MPH) is well established, i.e blockade of catecholamine transmitter reuptake, the physiological basis for the efficacy of this drug in promoting wakefulness and enhancing cognition is unknown. The present study assessed the effects of low dose MPH on spike train coding of sensory and decision-related signals in thalamic and cortical circuits of rat brain during quiet resting or performance of a sustained attention task.
Methods: Extracellular recordings using fine wires were made in visual and cognitive brain regions while animals were either quietly resting in a behavioral chamber or performing a visually guided sustained attention task (McGaughy and Sarter, 1995). Task naïve animals were presented with a pseudorandom sequence of light flashes of 10, 15, 25, or 40 ms duration.
Results: Lateral geniculate (LGN) unit activity was monitored following systemic injections of either saline or MPH (0.5, 2, or 5 mg/kg). MPH facilitated LGN unit responses to visual stimuli according to an inverted-U dose response function with optimal response augmentation occurring at 2 mg/kg, a dose known to achieve drug plasma levels that are effective in treating ADHD and in facilitating rat performance in the sustained attention task. Evidence of enhanced responding included increased magnitude of both excitatory and inhibitory components of the response and greater temporal fidelity to stimulus presentation. Prefrontal recordings from task-performing animals revealed neurons that respond to light cues, with stronger responses in successful trials. Like LGN cells, their responses were also enhanced by 2 mg/kg MPH.
Conclusions: Acute administration of MPH produces noradrenergic-like modulatory effects in sensory and cognitive circuits of rat brain. These actions may be related to the drug's ability to enhance vigilance and executive functions.
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ASSESSING TEMPTATIONS TO USE HEROIN AND COCAINE DURING DRUG DETOXIFICATION USING ECOLOGICAL MOMENTARY ASSESSMENT.

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Aims: Temptations to use drugs share characteristics with relapse episodes and may identify individuals at risk of relapse. We examined mood and cognition in temptations by administering explicit and implicit cognitive assessments on a handheld computer (PDA) in an EMA setting.
Methods: Heroin abusers (N = 64) attending an inpatient drug detoxification unit carried around a PDA for 1-week. Participants completed up to 4 random assessments (RAs) per day. They also completed an assessment when they experienced a temptation to use drugs (TA). At each assessment, participants reported their mood, craving, and attitudes to drugs. Implicit cognitions were assessed with a drug Stroop task (attentional bias) and an Implicit Association Test (implicit attitudes).
Results: Participants completed 1483 assessments (354 TAs, 1129 RAs). Analyses used linear mixed models. Rates of TAs were maximal during the first two days. Participants reported higher levels of negative affect, anxiety, difficult concentrating, and more positive explicit attitudes to drugs at TAs (vs RAs, ps < .01). Participants exhibited elevated attentional bias to drug cues at TAs (p < .05). Participants who relapsed or dropped out of treatment (n=10) during the week did not report more temptations prior to relapse than non-relapsers. However, relapsers showed significantly elevated explicit and implicit attitudes, and elevated attentional bias, at TAs, but not RAs.
Conclusions: Temptations are problematic: they are associated with negative affect, more positive attitudes to drugs, and elevated attentional bias. In addition, elevated attentional bias and implicit/explicit attitudes during temptations may be a marker of relapse risk. Ecological momentary interventions could be developed that target cognitions during temptations.
Financial Support: Supported by NIDA DA020436-S3 and ZonMw 31180001

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REINFORCEMENT-ENHANCING EFFECTS OF NICOTINE ON RESPONDING FOR AN UNCONDITIONED VISUAL REINFORCER IN ADOLESCENT RATS.

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Aims: Data suggest that adolescents are at heightened risk to begin abusing tobacco. The Dual Reinforcement Model states that nicotine (NIC) promotes smoking by acting as a weak primary reinforce and by enhancing concurrently available non-pharmacological reinforcers. To model factors of adolescent tobacco risk, we tested the reinforcement-enhancing effects of NIC with adolescent male rats.
Methods: Rats were assigned to one of four groups (saline, 0.1, 0.32 and 1.0 mg/kg NIC) and received drug prior to each daily 1-h session from postnatal day 28 to 42. Responding was maintained by an unconditioned visual reinforcer (VS) under a fixed ratio (FR) or a progressive ratio (PR) schedule of reinforcement.
Results: We found dose-dependent increases in break points defined as the highest ratio requirement completed. Similarly, we observed dose-dependent increases in VS presentations under the FR schedule. Interestingly, group differences were observed during the first session of testing, whereas these differences typically take 2-3 sessions to surface with adults. The magnitude of NIC effect on VS responding peaked in late compared to early adolescence.
Conclusions: The results of these studies illustrate that reinforcement-enhancement by NIC occurs in adolescents. Furthermore, the immediacy of the effect suggests that adolescents may be more sensitive to these effects. Future research aimed at determining how these effects change over development and compare to adults is currently underway.
Financial Support: National Institute of Health: DA10464

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PRESCRIPTION DRUG MISUSE IN AN URBAN PRIMARY CARE CLINIC.

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Aims: Many clinicians are concerned about prescribing medications with potential for abuse. The prevalence of abuse of some prescribed controlled substance medications in the U.S. in similar to that of illicit drugs. Most people with substance use disorders—especially prescription drug abuse—go undetected and untreated. Screening patients for aberrant medication-taking behaviors (AMTB) has tremendous potential for identifying and influencing undetected prescription drug abuse. Computer-delivered screening and intervention approaches have shown positive effects on substance use outcomes in specific populations. The current research was designed to develop and test a computer-delivered general health screening questionnaire and substance use assessment in general medical patients.
Methods: A computer-delivered program was developed and piloted in 115 patients attending an urban, academic medical center primary care clinic. Patients completed screening with an interactive computer program administered on a laptop computer in the clinic waiting area. Patient demographic, medical, psychological, and behavioral variables were examined.
Results: Participants were middle-aged (46.4/13.3) women (61%) and men (39%). 15% reported that they had any prescription drug issues. AMTB reported in the previous 30 days: 10% took more pills than prescribed or took more often than prescribed, 6.5% took someone else's prescribed medication, and 2% received concurrent prescriptions from multiple physicians. In comparison, 8% had used illicit drugs in the past 30 days.
Conclusions: A computerized screening program can be used to identify and assess general medical outpatients at risk for prescription drug abuse. Rates of AMTB are comparable to rates of illicit drug use in this population. Patients in this setting may be more willing to provide information about AMTB to a computer program than a prescribing physician. The next phase is a computer-delivered intervention, which may potentially provide a unique opportunity to affect substance use behavior.
Financial Support: NIDA award R01DA026091

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LIFETIME AND PAST-YEAR PREVALENCE OF DRUG USE AND DRUGGED DRIVING AMONG RURAL APPALACHIAN DUI OFFENDERS.

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Aims: Although alcohol is the substance most associated with driving under the influence (DUI), research indicates that drugs other than alcohol are becoming more prevalent in instances of impaired driving. In fact, the NSDUH estimates that more than 10 million Americans reported driving after illicit drug use during the past year (SAMHSA, 2006), including driving after the non-medical use of a prescription drug. The Appalachian region of the US has particularly high rates of prescription drug misuse, but few studies have examined drugged driving in the general or DUI offender population in this region. The current study examines the lifetime and past year prevalence of drug use and drugged driving in rural Appalachian Kentucky.
Methods: As part of a larger project examining impaired driving in rural Appalachian Kentucky, 42 individuals convicted of DUI were recruited and interviewed about their use of 12 illicit drugs, including the non-medical use of a prescription drug, and whether they had ever driven after using each of the drugs. Lifetime and past year prevalence rates were computed for drug use and drugged driving.
Results: Analyses found that more than 95% of DUI offenders had used drugs in their lifetime, including 86% in the past 12 months. The majority of the sample reported lifetime (79%) and past year (69%) driving under the influence of drugs. Participants were most likely to report driving under the influence of sedatives (50%), marijuana (36%), OxyContin (24%) and other non-prescribed opiates (26%) in the past 12 months.
Conclusions: These data suggest that drug use and drugged driving are prevalent among individuals convicted of DUI in rural Appalachia, regardless of whether drugs were involved in their DUI arrest. In fact, for many DUI offenders drug use, rather than alcohol, may be the primary feature of their substance abuse problem, and if left untreated, may put a person at higher risk for continued problems including DUI recidivism.
Financial Support: This research was supported by NIAAA grant #R03AA015964.

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ALTERED SEROTONIN1A RECEPTOR SYSTEM IS RELATED TO THE INCREASED COCAINE INTAKE WITH EXTENDED ACCESS IN RATS.

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Aims: A strong comorbidity between psychiatric disorders and drug dependence has been documented with depression as one of the most prevalent disorders in dependence on various drugs. Cocaine has profound effects on the serotonergic (5-HT) system. Dysfunctional 5-HT1A receptors have been implicated in depression, anxiety and dysphoria. Therefore, the present study tested the hypothesis that extended access to cocaine self-administration in rats, a rodent model of cocaine dependence, produced neuroadaptation in the 5-HT1A receptor system, which may be related to increased cocaine intake and the development of depressive-like states.
Methods: Rats were trained to self-administer cocaine (0.5 mg/kg/infusion) in daily one-hour sessions (baseline). After ten baseline sessions, the rats were divided into two groups balanced by cocaine intake in the last session. The rats then self-administered cocaine with either one-hour (short access, ShA) or six-hour access (long access, LgA) for 15 days. The effect of buspirone, 5-HT1A receptor partial agonist, on cocaine self-administration was examined under fixed-ratio (FR) and progressive-ratio (PR) schedules.
Results: LgA rats showed upward-shifted dose-response functions of cocaine under FR and PR schedules. The acute pretreatment with buspirone shifted dose-response function of cocaine downward in a dose-dependent manner under a FR schedule, but at a lower dose in LgA rats than in ShA rats. Similarly, cocaine self-administration in LgA rats was more sensitive to an acute treatment of buspirone under a PR schedule than that of ShA rats.
Conclusions: Collectively, it is concluded that extended access to cocaine self-administration produced greater neuroadaptation in 5HT1A receptor system compared with short access to cocaine. This neuroadaptation may be related to cocaine withdrawal symptoms and comorbidity of depression in cocaine dependence in humans.
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EVALUATION OF THE REINFORCING EFFECTS OF 1,4-BUTANDIOL IN BABOONS.

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Aims: 1,4-butendiol (1,4-BD) is a prodrug for gamma-hydroxybutyrate (GHB). When ingested, 1,4-BD is metabolized to GHB in the body. Illicit use of 1,4-BD for its euphoric effects by young adults has been reported. The aim of current study was to evaluate the intravenous reinforcing effects of 1,4-BD in baboons (n=4).
Methods: A drug substitution procedure was used; self-injection was first established with 0.32 mg/kg cocaine as the baseline drug, then a dose of a 1,4-BD (10-100 mg/kg/injection) or its vehicle was substituted for cocaine for 15 days. Sessions were continuous (24 h/day, 7 days/week). Each injection was contingent upon completion of 160 lever responses [i.e., a fixed-ratio (FR) 160 schedule of reinforcement]. A 3-hr timeout began with completion of the response requirement, limiting the number of injections to a maximum of 8 per 24 h. Cocaine maintained 6-8 injections per day. The cocaine baseline (6-8 injections/day) was reestablished before each dose of 1,4-BD or vehicle was evaluated. The mean of the last 5 days of each dose or vehicle substitution period was used to characterize self-administration. Food pellets were continuously available 24 h/day under an FR30 schedule of reinforcement on a second lever.
Results: In two of the three baboons that have completed full dose effect evaluations, 1,4-BD maintained self-injection significantly greater than vehicle control and doses of 78-100 mg/kg maintained 5-8 injections per day. Both of these baboons had a history of GHB self-administration. The third baboon, who did not have prior drug self-injection experience, did not self-administer any dose of 1,4-BD greater than vehicle. Evaluation of 1,4-BD self-administration in a fourth baboon are ongoing.
Conclusions: These preliminary data suggest that like, GHB, 1,4-BD may have abuse liability.
Financial Support: NIH/NIDA R01 DA14919

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ESTRADIOL AND PROGESTERONE DIFFERENTIALLY ALTER COCAINE-INDUCED RESPONSES IN DOPAMINE-PKA MEDIATED INTRACELLULAR PATHWAY IN THE NUCLEUS ACCUMBENS.

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Aims: An extensive body of literature provides evidence that ovarian hormones contribute in part to the sexual dimorphism of behavioral activation and reward responses to cocaine. Sex differences and estrous cycle effects of cocaine effects on dopamine (DA)- and protein kinase A (PKA)-mediated intracellular pathway have been shown. We hypothesized that estradiol and progesterone effects on cocaine-induced activation of this pathway—including activation of PKA cascade and phosphorylation of CREB and FosB induction—may contribute to the sex differences in and estrous cycle effects on the PKA pathway and in behavioral responses to cocaine.
Methods: To this end, ovariectomized (OVX) female rats were treated with vehicle (sesame oil; 48 and 4 hours), estradiol (20 μg, s.c; 48 hours), progesterone (500 μg; 4 hours) or estradiol plus progesterone follow by a single i.p. injection of saline or cocaine (20 mg/kg). The nucleus accumbens (NAc) and caudate putamen (CPu) were dissected and analyzed via Western blot for: PKA, phosphorilated- CREB (p-CREB), c-Fos and delta-FosB protein levels.
Results: In the NAc, vehicle treated rats had higher delta-FosB protein levels than estradiol-, progesterone- or estradiol + progesterone- treatments, while they had lower levels of pCREB than progesterone or estradiol + progesterone treatment. Cocaine increased PKA protein levels in vehicle and estradiol +progesterone treated groups. While pCREB and cFos protein levels were increased by cocaine in vehicle-treated groups, pCREB levels decreased after cocaine and estradiol + progesterone treatment.
Conclusions: Taken together, these novel findings suggest that the females endocrinological profile may contribute to the previously reported sex differences and estrous cycle effects in PKA signaling and behavioral responses to cocaine.
Financial Support: This work was supported by SCORE 506-GM60654, MIDARP DA12136, and RCMI RR-03037.

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INTERNET SURVEY TO EXPLORE METHODS FOR COLLECTING STREET PRICE OF PRESCRIPTION OPIOIDS.

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Aims: This survey examines methods for collecting street price data for various prescription opioid products and the knowledge base and perceptions of newly developed abuse deterrent opioid products among a sample population of recreational drug abusers to evaluate trends in nonmedical prescription opioid use. Research within this online recreational drug use community may reveal the first glimpse of new patterns of drug use/abuse among active drug abusers.
Methods: A web-based survey was conducted among individuals who visited a recreational drug use discussion board. Survey respondents self reported 3-digit ZIP Code, drug abuse, source of prescription opioids and street price of prescription opioids purchased. Ten opioid products reported as frequent drugs of abuse were selected as indicator drugs. Based on self-report of past 30 day abuse of these opioids and drug source as either dealers, or family members/friends, one of the following three street price questions were randomly assigned: 1) price for a specific dosage, 2) price per milligram of a certain product, and 3) price per quantity of pills and milligrams of a specific product (the standard).
Results: Street price questions will be compared using the question of price per quantity and milligrams as a standard to determine the most effective method of collecting this information. In conjunction with determining geographic street price the survey explores the current level of interest in and the knowledge base of this community regarding abuse deterrent formulations.
Conclusions: This survey answers the question whether it is possible to collect data, across geography, brand, dosage, and bulk purchasing to determine street price at a local scale for geographic comparisons. Information on interest in new abuse deterrent products, street price data, and relative rates of abuse among a population of recreational drug abusers may provide an early indication of a prescription drug's propensity for diversion from medical sources into the illegal market at a geographic level.
Financial Support: Actavis

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DRUG TREATMENT OUTCOMES AMONG HIV-INFECTED OPIOID-DEPENDENT PATIENTS RECEIVING BUPRENORPHINE/NALOXONE.

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Aims: To determine the impact of integrated buprenorphine/naloxone (BUP) and HIV treatment in HIV-infected opioid dependent patients.
Methods: We conducted a prospective study in 303 patients that initiated BUP treatment at 9 clinical sites across the United States. Seven of the nine sites had limited to no experience providing BUP prior to the study. Uniform assessments using self-report and chart review were conducted at baseline and every 3 months (Quarters 1 through 4) for one year. The primary outcomes were retention in BUP treatment, self-report of illicit drug use, and addiction treatment processes.
Results: Retention in BUP treatment was 74%, 67%, 59% and 49% during quarters 1,2 3, and 4. Self-reported illicit opioid use in the past 30 days decreased from 84% of patients at baseline to between 39% and 43% in retained patients over the 4 quarters of the study. On average, patients were 52% less likely to use opiates, 19% less likely to use stimulants and 17% less likely to use sedatives in the past 30 days for each quarter that they remained in BUP treatment (all $p \leq .01$). The mean dose of BUP ranged between 16.9 mg and 18.2 mg and did not differ by quarter. The median number of BUP-related office-visits per quarter decreased from 5 to 3 over the 4 quarters of the study. The median number of urine toxicologies performed per quarter decreased from 3 to 1 over the 4 quarters of the study.
Conclusions: It is feasible to incorporate BUP into HIV primary care settings. Strategies that target addiction treatment processes may improve treatment retention and produce further declines in illicit drug use.
Financial Support: Health Resources and Services Administration: H97HA03793

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INTEGRATING THEORY TO ADDRESS THE ASSOCIATION BETWEEN SUBSTANCE USE AND SEXUAL RISK BEHAVIOR AMONG MSM.

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Aims: Research shows a consistent association between substance use and sexual risk behavior among men who have sex with men (MSM). Despite evidence for a causal link, MSM engage in sexual risk without substances and vice versa. Two theories have been applied to these associations: Expectancy Theory (expectations of substances' effects drive this association) and Alcohol Myopia Theory (alcohol limits one's cognitive abilities, the effects of which are best seen under conditions of conflict). With evidence for both theories, researchers have called for their integration. The present study examined the synergistic role of conflict (about unsafe sex) and expectancies in sex behavior among 135 MSM in an intervention trial.
Methods: Participants are HIV-, reported > 1 recent incident(s) of sexual risk behavior (unprotected anal sex with a casual partner or serodiscordant main partner), and > 5 substance use days in the previous 3 months. Men completed psychosocial scales on ACASI and reported substance use and sex behavior using Timeline Followback. Two conflicts were examined: (1) The conflict between motivation to improve safer sex practices and temptation for unsafe sex; and (2) The conflict between motivation to improve safer sex practices and perceived benefits of unsafe sex.
Results: Factorial ANOVAS (2 X 2; high vs. low expectancies and conflict vs. no conflict) revealed a significant interaction between each conflict and expectancies such that those with both strong expectancies and strong conflict engaged in a higher percentage of their sexual activity under the influence and a higher percentage of their sexual risk behavior under the influence, when compared to all other groups.
Conclusions: Results demonstrate the synergistic effects of conflict and expectancies and highlight the need to integrate existing theories. This paper suggests ways in which these theories may be integrated to inform prevention and intervention efforts designed to reduce sexual risk behavior, even in the face of substance use.
Financial Support: This research was supported by R01 DA020366

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EFFECTS OF BASOLATERAL AMYGDALA - DORSAL HIPPOCAMPUS DISCONNECTION FOLLOWING COCAINE MEMORY REACTIVATION ON SUBSEQUENT COCAINE-SEEKING BEHAVIOR IN RATS.

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Aims: Microinfusions of the protein-synthesis inhibitor anisomycin (ANI) into the basolateral amygdala (BLA) or sodium-channel blocker tetrodotoxin into the dorsal hippocampus (DH) inhibit the reconsolidation of context-response-cocaine memories and thereby disrupt context-induced cocaine- seeking behavior in rats. Thus, the BLA is likely a site of anisomycin-sensitive memory reconsolidation, whereas the DH modulates this process. To further this line of research, this study examined whether serial information processing by the BLA and DH is necessary for this phenomenon using a disconnection procedure.
Methods: Rats were trained to lever-press for cocaine infusions in a distinct context followed by extinction training in a different context. They were then re-exposed to the previously cocaine-paired context followed immediately by unilateral infusion of ANI (0 or 62.5 μg/0.5 μl) into the BLA and of the GABA agonists baclofen/muscimol (BM; 0 or 0.1/0.01 mM/0.5 μl) into the contralateral DH. Drug-seeking behavior (non-reinforced active lever pressing) was assessed in the cocaine-paired context after additional extinction training (reinstatement test) and after an additional 20-day drug-free period (test of spontaneous recovery).
Results: Re-exposure to the cocaine-paired context elicited robust cocaine seeking behavior in the control rats on both test days. BLA-DH disconnection after memory reactivation impaired reinstatement of cocaine-seeking behavior and produced a trend for a similar effect on spontaneous recovery.
Conclusions: These effects are consistent with the interpretation that the BLA and DH are serially connected in a neural circuit that promotes memory reconsolidation. Alternatively, these brain regions may inhibit the extinction of associative memories that support cocaine-seeking behavior since the effects were not resistant to spontaneous recovery.
Financial Support: NIDA R01 DA17673 and R01 DA17673-S1.

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MIXED EMOTIONS: EVIDENCE SUPPORTING THE SIMULTANEOUS OCCURRENCE OF CONFLICTING MOOD STATES VIA EMA.

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Aims: Either positive or negative emotions may be triggers for drug use (e.g., Epstein et al., 2009), but we know of no studies examining drug use in relation to mixed emotional states. The purpose of this research was to examine the co-occurrence of positive and negative emotions in self-reports collected in real time and its relationship to drug use.
Methods: Ecological momentary assessment (EMA) data were collected on a cohort of 114 outpatient methadone-maintained cocaine and heroin users on handheld electronic devices. Self-reports, elicited at random times throughout participants' waking hours, included ratings of mood and craving and reports of daily activities, current companions, and location. We evaluated the occasions in which participants reported feeling "happy" or "relaxed" while also reporting that they felt "stressed" or "irritated."
Results: Simultaneous reports of positive and negative emotions were common. They occurred in 4,087 (15%) of the 27,240 randomly prompted entries in which mood data were present. Of the 114 participants, 107 (94%) provided at least one report of mixed emotions. The occurrence of mixed emotions in relation to reports of drug use, e.g. the circumstances, activities, companions, and locations in which they were reported, will also be examined.
Conclusions: Our findings support prior contentions that feelings of opposite valence are often experienced simultaneously (Schimmack, 2001), an assertion that has been disputed (Brehm and Miron, 2006). Additional research in this area may have implications for both affective research and addiction research, e.g. exploring the impact of mixed emotions on risk of relapse.
Financial Support: This study was supported by the Intramural Research Program (IRP) of the National Institute on Drug Abuse (NIDA) at the National Institutes of Health

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BALLOON ANALOGUE RISK TASK AND AFFECT.

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Aims: Aim: The Balloon Analogue Risk Task (BART) is a computerized measure of behavioral risk taking. Although the BART contains elements such as monetary earnings and failure feedback which may affect mood and emotion, there are no published data on emotional responses to this task. The present study investigated affective responses to the BART risk task in healthy volunteers.
Methods: Method: The study used a within-subjects, repeated-measures design to assess affective responses to the BART on two separate days in young adults using the Morrone et al. (2000) positive and negative activation scales.
Results: Results: Performance of the BART increased participant ratings of positive activation ($F(1,38)=55.3$, $p<.001$) and, paradoxically, also increased negative activation compared to pre-BART ratings ($F(1,38)=44.7$, $p<.001$) on both test days. The increases in positive and negative activation were related to personality scores. Individuals who scored high on the Social Potency scale (trait dominance/ reward sensitivity) on the Multidimensional Personality Questionnaire Brief Form (MPQ-BF) reported greater increases in positive activational responses to the BART on both test days ($r=+.35$, $p<.05$), and greater negative affective responses to the BART on day 1 ($r=+.34$, $p<.01$).
Conclusions: Conclusion: The findings indicate that the BART risk task has direct effects on subjective mood in healthy young adult volunteers.
Financial Support: Supported by National Institute on Drug Abuse (NIDA) grants DA09133 and DA020725.

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EFFECTS OF REIMBURSEMENT ON RATES OF MISSING, POSITIVE, AND NEGATIVE URINE DRUG AMONG OPIOID-DEPENDENT CLINICAL TRIAL PARTICIPANTS.

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Aims: To determine the effect of monetary incentives on rates of missing data and observed rates of drug use among opioid dependent subjects aged 15-21 during participation in a randomized trial.
Methods: 154 subjects seeking treatment for opioid dependence were randomized to 2 week detoxification with buprenorphine/naloxone (DETOX) or 12 weeks buprenorphine/naloxone (BUP), each with weekly individual and group drug counseling. At week 4, 8, and 12, extensive assessments were done, and participants were reimbursed $75. At all other weeks, assessment was limited to urine drug screen and self report of drug use, and participants were reimbursed $5. We compared rates of drug screens that were missing, positive for opioids, and negative for opioids in the high-reimbursement weeks (4, 8, and 12) vs. the surrounding low-reimbursement weeks (3, 5, 7, 9, and 11).
Results: Rates of missing data were significantly lower for weeks 4, 8, and 12 than for the weeks immediately before and after these weeks (38% vs. 60%). The percentage of opioid-positive urine drug screens was higher in the high reimbursement weeks compared to the low reimbursement weeks (26% vs. 11%). The percentage of opioid-negative drug screens was also higher in the high-reimbursement vs. the low reimbursement weeks, but less markedly so (36% vs. 28%). Ignoring missing data, the percentage of positive drug screens (out of total non-missing cases) was higher in the high-reimbursement weeks (41% vs. 29%). The effect of reimbursement on rates of missing, positive, and negative drug screens was smaller for the BUP treated participants than those in the DETOX group ($p < 0.001$).
Conclusions: This study demonstrated in quantitative terms the effect of participant reimbursement on rates of missing data and rates of documented drug use and abstinence. The results demonstrate the importance of adequate reimbursement to maintain follow-up rates, and suggest that the higher reimbursement rate preferentially enhanced follow-up rates among those who were using opioids.
Financial Support: NIDA Clinical Trials Network

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BRIEF INTERVENTION FOR DRUG-ABUSING ADOLESCENTS.

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Aims: To evaluate the effectiveness and identify mediators and moderators of a brief intervention for adolescents with a drug abuse problem.
Methods: We present evaluation results from a randomized controlled trial to examine the efficacy of a manualized brief intervention for moderate drug abusing adolescents. Student/parents (N = 180) were randomly assigned to receive either a 2-session adolescent only (BI-A), 2-session adolescent and additional parent session (BI-AP), or assessment only control condition. Measures of drug use behaviors, inter- and intra-personal functioning, parenting, and health service utilization were collected at intake, and then at 3- and 6-months post-intervention. Analyses examined relative effectiveness of the three intervention groups and moderating/mediating variables related to outcome.
Results: Follow-up assessments at 3- and 6-months post-intervention showed statistically significant improvement on drug use variables for adolescents in 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 were improved parenting and use of community services after the intervention.
Conclusions: Three major significant findings were observed from the study: (1) both brief intervention conditions were associated with significantly reduced drug use levels and related consequences, and these improvements exceeded the changes in the assessment-only control group; (2) when the two intervention conditions were compared to the control group, the group that included a parent session (BI-AP) exhibited greater and more consistent intervention effects compared to the condition in which only the adolescent client received services (BI-A); and (3) improvements in parenting and use of community-based counseling services post-intervention mediated positive outcomes.
Financial Support: This study was supported by grants K02 DA015347 and R01 DA017492 from the National Institute on Drug Abuse.

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TRAINING HIV+ DRUG-ABSTINENT PEERS IN A CARE LINKAGE INTERVENTION (PEERLINK) FOR HIV+ SUBSTANCE USERS.

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Aims: To develop a 45" MI-based care linkage intervention, train peers to administer it, and test acceptability, feasibility, and promise.
Methods: 4 African-American PLWHA in recovery from drug disorders with basic HIV Peer training, all with GED or HS diploma, trained 3 hours weekly for 6 months. They developed a 7" video based on their lives, and role model stories using CDC guideline. Training included didactics, role-playing, and a National Cancer Institute peer program. An MI trainer provided a one-day intensive training, and MITI-3 ratings on pre- and post-training sessions. Competency required >=4/5 on all MITI-3 global ratings. Peer interview responses about training and intervention effectiveness were coded using Grounded Theory.
Results: MITI ratings for all peers improved over 6 months; 3/4 achieved competency. Pre→post ratings in MI Spirit for each Peer were: 3.3→4.7, 3→4.7, 2.7→4.3, 3.3→4. Of 10 MI skills, peers found open questions and heightening discrepancies hardest to learn; emphasizing personal choice and change planning were easiest. Of note, peers who found MI skills hardest to master got the highest MITI ratings. Themes in MI mastery were: technique being divergent from peer's upbringing; focusing on the other; temptation to give advice. Peers rated all training components as "extremely" or "very" useful, except rating each other's sessions. Themes in training effectiveness were: trainers or video characters as role models; importance of being challenged, and repeated practice. PEERLINK components rated most useful to patients were: details about clinics, discussing referrals, PEERLINK video, role model stories, and motivational rulers.
Conclusions: 3 of 4 peers with no prior clinical training achieved high MITI ratings with moderately intensive training. Should PEERLINK show promise in the current RCT (N=60), it could be a cost-effective and replicable care-linkage intervention for substance users with HIV or other disease.
Financial Support: NIDA R21

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EVALUATION OF MORPHINE AND CHLORDIAZEPOXIDE WITHDRAWAL WITH TELEMETRY.

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Aims: We describe the use of telemetry as a sensitive tool to study withdrawal. This technique allows us to continuously follow body temperature (BT), blood pressure (BP), heart rate (HR) and locomotor activity (LMA), as well as food intake and body weight gain over 20 days of treatment and 8 days of withdrawal.
Methods: Male Wistar rats were implanted with telemetric devices and 1 week later, were placed in individual home cages to record mean arterial BP(mmHg), HR, BT, and LMA. Recordings were taken in 30s blocks every 5 min starting 2 days before the 20-day treatment period with either vehicle, morphine HCl (MOR; 32 or 64 mg/kg, b.id.) or chlordiazepoxide (CDP; 16, 32, or 64 mg/kg, b.i.d., and for 8 days of withdrawal. Daily body weight and food intake were also monitored from days 18-28.
Results: During the treatment phase, MOR reduced food intake and body weight gain, and disrupted the normal circadian patterns of BT, BP, HR and LMA. CDP slightly increased food intake and body weight gain throughout the treatment period, but tolerance to increases in BP and HR and decreases in BT and LMA that occurred after acute treatment developed within 10 days of treatment.
Repeated handling and vehicle injections had little impact on the parameters measured, although the effect of handling was clearly present as transient increases in several parameters, particularly HR.
Following withdrawal, both MOR- and CDP-treated rats showed a marked decrease in food intake and loss of weight which were dose-related and maximal on days 2 and 3 of withdrawal. In MOR groups, there was also marked nocturnal hypothermia (-2°C) and moderate diurnal hypertension (+30 mmHg) on day 1 and 2 of withdrawal, respectively. Small diurnal increases in LMA and HR were observed over the first 3 days of withdrawal. CDP-treated rats showed small increases in BP, HR, BT and LMA which also lasted 1-3 days.
Conclusions: These data show that telemetry broadens the range of parameters measured during withdrawal, enabling the detection of changes that might otherwise be missed.
Financial Support: This work was supported by Porsolt and Partners Pharmacology

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INTRASYNAPTIC DOPAMINE RELEASE MEASURED BY PET IN ALCOHOL-DEPENDENT SUBJECTS.

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Aims: To examine the role of the dopamine (DA) system in alcohol dependency in those at risk vs. healthy controls.
Methods: PET measurements of intrasynaptic dopamine release (DAR) with 11C raclopride displacement via an intravenous amphetamine challenge were carried out in 19 subjects, all with a DSM-IV diagnosis of alcohol dependence (AD). We included both non treatment seekers and treatment seekers (who we recruit immediately after a clinical detoxification program). They were compared to 15 healthy controls as well as offspring of healthy social drinkers (family history negative). Binding potentials (BPND) were obtained by both the simplified tissue method (SRTM) and the Logan Reference Tissue Graphical Method (RTGA).
Results: As compared to age-matched healthy controls, we found significant decreases in amphetamine-induced dopamine release (DAR) in our AD subjects, ranging from 30% (putamen) to 89% (in posterior caudate), and were significant at $p < 0.05$, by t-test. Both BPND at baseline and after amphetamine decreased in all striatal subdivisions in AD vs HC by 14-19%. As tested by linear regression (with BPND as the outcome variable and subject group as the predictor) the reduction was significant in all regions with $p < 0.05$ (using both RTGA and SRTM). We have yet to find significant DAR differences in treatment vs. non-treatment seekers, but this is affected by a small N (4 subjects in the treatment seeking group). We also observed correlations of dopamine release with behavioral and subjective effect data, which will be elaborated upon.
Conclusions: The DA system is highly compromised in AD in both treatment and non-treatment seekers.
Financial Support: NIH-NIAAA AA012839; NIH-NIAAA AA010158

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BACK TO BASICS: UTILIZING TRAINING, PERFORMANCE FEEDBACK, AND COACHING TO DEVELOP A CLINICAL SUPERVISION INFRASTRUCTURE FOR FRONTIER STATES.

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Aims: To examine a Clinical Supervision Coaching Academy utilizing training, performance feedback, and coaching activities usefulness in developing an "expert" clinical supervisor cohort that can assist in building a viable clinical supervision infrastructure. Clinical supervision is considered a critical component in the delivery of quality substance abuse treatment services, serving as a "protective factor" against staff turnover (Knudsen et al., 2007) and facilitating the implementation of EBPs (Carroll & Rounsaville, 2007). However, competent supervision requires observation of practice and performance feedback (Miller et al., 2007) and often is not part of practice as usual. To address this issue, the Mountain West ATTC developed a Clinical Supervision Coaching Academy that builds on existing clinical supervision training practices by adding performance feedback and coaching activities. The goal is to develop an "expert" clinical supervisor cohort that can assist in building a viable clinical supervision infrastructure by training/mentoring other clinical supervisors in its six-state frontier region using a combination of in-person training, telephone coaching, performance feedback, and web-based education.
Conclusions: The lack of effective program-based supervision is one of the largest barriers to the implementation of EBPs in clinical practice and has been shown to be a factor in staff turnover. The Clinical Supervision Coaching Academy goes back to the basics of using training plus performance feedback and coaching activities to develop a quality clinical supervision infrastructure, thereby reducing costs associated with training and staff turnover. Providing competent supervision through observation and performance feedback rather than relying solely on counselors' self-report about what occurs in sessions can make addiction counseling services more accountable and improve delivery of quality substance abuse treatment services.
Financial Support: Funded by the Mountain West ATTC

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DIMENSIONAL MODELING OF SUBSTANCE USE AND CONDUCT DISORDER AND THEIR ASSOCIATION WITH NEUROCOGNITION IN ADOLESCENCE.

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Aims: Substance use disorders (SUDs) and related conduct disorder (CD) problems may be best conceptualized as a continuous latent dimension of externalizing psychopathology (EXT). Adults high in EXT have shown poorer functioning in neurocognitive domains, but it is not known if similar deficits exist in adolescents. We hypothesized that greater EXT would be associated with poorer executive function and verbal short-term memory in a sample of adolescents with SUD and CD symptoms.
Methods: Adolescent probands (N=244, mean age = 16.1) and siblings (N=227, mean age = 18.2) completed a neurocognitive battery, structured interviews, and measures of substance use. Probands had ≥1 symptom of both CD and SUD. Rates of CD and SUD were 78% and 93% for probands, and 34% and 60% for siblings, respectively. Structural equation modeling was used to create latent variables for EXT, executive function, and verbal short-term memory. Age, years of education, lifetime alcohol withdrawal, and recent drinking were included as exogenous predictors, and we tested paths from EXT and these predictors to neurocognitive outcomes.
Results: Based on descriptive fit indices, the final model was an acceptable fit, $\chi 2(92, N=437) = 280.48$, $p < .001$, CFI = .93, RMSEA = .07. Standardized correlation coefficients of all paths were examined for statistical significance. Greater EXT predicted worse performance in verbal short term memory (-.26) but not executive functioning (.08). Younger age and more years of education were related to better performance in both executive functioning verbal short-term memory. Lifetime alcohol withdrawal and recent drinking were not significantly related to neurocognitive outcomes.
Conclusions: The results provided mixed support for our hypothesis, in that greater EXT was related to poorer verbal short-term memory but not executive function. Future studies will identify specific aspects of memory and executive function that are likely to be impaired in adolescents high on externalizing dimensions.
Financial Support: National Institute on Drug Abuse

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SEX, DRUGS, AND ROCK AND ROLL: VISUALIZING BEHAVIORAL MORTALITY FOR THE US POPULATION.

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Aims: Mortality is the undisputed master outcome, gaining epidemiology the honorific of the "dismal science." Individuals crafting risk management plans for opioid pain therapies, addiction treatments, or behavioral interventions need to look at mortality rates, and in doing so require ways to estimate anticipated behavioral mortality rates.
Methods: The age and gender specific death data for 2006 was used to construct by year age and gender specific death rates for the US population in 2006. These were then analyzed by sequential linear regression methods into death rates for children, young adults and adolescents, and finally, mature adults. The resultant parametric models were then checked against the National Center for Health Statistics (NCHS) cause-specific death data.
Results: The primary force of mortality is an exponential (linear in the semi-log plot) effect of aging with the functional form: Death Rate = R0 * e (k*Age). Increasing age is associated with an increase in mortality rate, greater for males than females. The residuals are distributed in a bimodal fashion. The first, (pediatric) distribution (ages 1-12) of the residuals can be fitted with an exponential pediatric mortality rate in early childhood. The second distribution of residuals is a log-normal distribution of excess mortality that is greater for males than females, starts about age 13 and ends about age 40, and is the exact expected age distribution of "behavioral" mortality (suicide, homicide, accident, drugs and alcohol).
Conclusions: These three elements sum into a parametric hazard equation that allows the estimation of mortality risk in risk management plans, knowing age and gender, for US clinical populations in risk management programs.
Financial Support: This work was funded by Rock Creek Pharmaceuticals, Inc., Gloucester, MA.

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METHADONE MAINTENANCE TREATMENT IN CHINA: PERSPECTIVES OF CLIENTS AND SERVICE PROVIDERS.

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Aims: To explore barriers and facilitators for participation in methadone maintenance treatment (MMT) in China.
Methods: Focus groups were conducted in Shanghai and Kunming of China; two in each site and separately for current or former MMT patients and service providers. Each focus group included 8-12 individuals. Focus group discussions were digitally recorded, transcribed, and analyzed (ATLAS.ti).
Results: A major barrier identified by both patients and providers is the requirement of sharing patients' information with the public security system. Both groups also stressed financial burden of fee requirement (10 Yuan for the daily medication) on patients who often do not have stable employment and steady income. Discussions also revealed logistical barriers such as limited hours of operation and availability in different localities (most facilities operate during regular work hours—a problem for patients who try to keep a regular job; MMTs are only available in certain areas of China and transfer between MMTs in different localities is difficult particularly if patients need to travel). Another major theme identified in patient focus groups is the resistance of methadone: some expressed concerns of being on another addictive drug and some attempted to reduce dose or quit methadone on their own. This issue signifies a lack of understanding about maintenance or long-term nature of MMT. Factors that facilitate MMT participation and retention include pressure from family members, social worker supervision, fear of incarceration, and assertive recruitment strategies adopted by MMTs providers.
Conclusions: The study findings highlight the need for reconsidering or adjusting current policies (e.g., police involvement, fee requirement) and operations (e.g., hours, locations, take-home options). Education about the long-term nature of MMT and appropriate dosage may also help to increase the treatment participation and retention among Chinese MMT patients.
Financial Support: NIDA R21DA025385 & K05DA017648 (PI: Hser)

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PHYSIOLOGICAL STRESS PROFILE BY DIFFERENT TYPES OF STRESS EXPOSURES IN YOUNG, LOW-INCOME WOMEN.

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Aims: Current estimates of stress exposure remain partial and inadequate. Further, the relationships between different types of stressors and stress biomarkers are inconclusive. The current study assessed associations of stressors and Physiological stress profile.
Methods: A sample of low-income women (n=696) aged 18 to 30 in southeast Texas participated in the study between December 2006 and July 2009. Different types of stressors included childhood trauma, major life events, chronic stressors and daily hassles. Physiological stress profile included cortisol, cytokines, eg, IL-6, TNF α, TNF α-r1, and DHEA-s.
Results: Our data showed significant correlations of self-reported discrete events such as major life events, childhood trauma, and chronic stressors with physiological markers. Meanwhile, we did not find significant associations between perceived stress and daily hassles. Further, our findings here, particularly cortisol and, are consistent with similar results in populations with chronic stress, drug use, or PTSD, as lower cortisol is related to higher stress.
Conclusions: In conclusion, our results may provide some insight to explain inconsistencies of previous findings on the relationships between physiological stress profile and self-reported stress, perhaps depending upon the choice of stress measures. Further, individuals living in chronically deprived environments may have different biological stress profiles than the general, healthy population.
Financial Support: This research was funded by NIDA grants # R01 DA020053 (PI: HW) and K01 DA021814 (PI: HW).

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SUBREGION-SPECIFIC EFFECTS OF MGLUR1 ANTAGONISM IN THE NUCLEUS ACCUMBENS ON DRUG CONTEXT-INDUCED REINSTATEMENT OF COCAINE-SEEKING BEHAVIOR IN RATS.

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Aims: The functional integrity of the nucleus accumbens (NAC) core and shell is necessary for context-induced reinstatement of cocaine-seeking behavior. Furthermore, metabotropic glutamate receptor subtype 1 (mGluR1) stimulation is necessary for drug context-induced reinstatement of drug-seeking behavior. Therefore, the present study was designed to evaluate the contribution of mGluR1s in the NAC core and shell to context-induced reinstatement of cocaine-seeking behavior.
Methods: Sprague-Dawley rats were trained to press a lever for un-signaled cocaine infusions in a distinct context followed by extinction training in a different context. Using a within-subject testing design, cocaine-seeking behavior (non-reinforced active lever pressing) was then assessed in the cocaine-paired and extinction contexts. Before each test session, rats received bilateral microinfusions of the highly potent mGluR1-selective antagonist, JNJ16259685 (0.5 or 25 nM/0.3 μl/hemisphere) or 0.1% DMSO vehicle (0.3 μl/hemisphere) into the NAC core, NAC shell, or the overlying ventral caudate-putamen (vCPu).
Results: Intra-NAC core microinfusions of 25 nM, but not 0.5 nM, of JNJ16259685 significantly impaired drug context-induced reinstatement of cocaine seeking relative to vehicle, without attenuating instrumental behavior in the extinction context, general motor activity, or food-reinforced instrumental behavior in control experiments. Conversely, intra-NAC shell or intra-vCPu microinfusions of 0.5 nM or 25 nM of JNJ16259685 failed to alter drug context-induced reinstatement of cocaine-seeking behavior relative to vehicle.
Conclusions: Thus, mGluR1 stimulation in the NAC core, but not the NAC shell or vCPu, is necessary for context-induced reinstatement of cocaine seeking. This suggests that different neuropharmacological mechanisms underlie drug context-induced motivation for cocaine in these striatal subregions.
Financial Support: NIDA R01 DA17673, NIDA R01 DA17673-S1

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EFFECTS OF D-CYCLOSERINE ON EXTINCTION OF NICOTINE CUES AMONG COCAINE-DEPENDENT CIGARETTE SMOKERS.

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Aims: Exposure to drug cues can result in craving leading to drug use. We examined the effects of D-cyloserine, which has been shown to enhance extinction-based learning, on cigarette craving elicited by cues. Additionally, we are examining the effects of D-cycloserine plus cognitive behavioral therapy (CBT) on smoking cessation.
Methods: Cocaine-dependent cigarette smokers seeking treatment for their cigarette use visit the research laboratory 3 times/week for 1 month. Cocaine abusers are an important target population as they exhibit smoking rates 3-4-fold greater than the general population. Participants are randomized to receive either 50 mg D-cyloserine or placebo. At each visit, (1) smoking and illicit drug use are assessed, (2) nicotine- and neutral-related virtual reality (VR) cues are presented, and (3) CBT is delivered.
Results: To date, 14 participants have completed the study with 90.5% of sessions attended. Breath carbon monoxide levels during treatment were 10±10 (Mean±SD) ppm, which is a 3-fold reduction from baseline (30±19 ppm). At day 1, relative craving scores were significantly greater following nicotine sessions compared to neutral sessions (p=0.003), indicating that the VR session is effective in eliciting nicotine craving. By study day 9, relative differences were no longer significant, indicating extinction to nicotine cues.
Conclusions: The preliminary results are promising and suggest that our treatment is both acceptable and effective at reducing nicotine use among cocaine-dependent cigarette smokers. Based on these initial findings, we predict reaching our target N=40 by June 2010, and that we will subsequently be able to ascertain the effects of D-cycloserine on VR-elicited nicotine craving and cigarette smoking following VR exposure and CBT.
Financial Support: DA023588

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DISCRIMINATIVE STIMULUS EFFECTS OF VARIOUS CLASSES OF PSYCHOACTIVE COMPOUNDS IN KETAMINE-TRAINED RATS.

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Aims: Ketamine, one of the dissociative anesthetic agents, has been shown to produce psychotomimetic effects, such as nightmares and hallucination. In the present study, we investigated the similarity of the discriminative stimulus effects of ketamine to other types of hallucinogens and to psychostimulants.
Methods: Fischer 344 rats were trained to discriminate between ketamine (5 mg/kg, i.p.) and saline under a fixed-ratio 10 food-reinforced schedule.
Results: Non-competitive antagonists for both NR2A- and NR2B-containing NMDA receptors, such as phencyclidine (PCP; 0.1-1 mg/kg, i.p.) and dizocilpine (0.003-0.03 mg/kg, i.p.), and the NR2A-containing NMDA receptor-preferred antagonist dextromethorphan (3-56 mg/kg, i.p.) fully substituted for the ketamine cue in a dose-dependent manner (>80% of ketamine-lever responding). In contrast, the 5-HT2 receptor agonist DOI (0.1-0.56 mg/kg, s.c.), which is a potent hallucinogen, and the sigma receptor ligand DTG (0.3-3 mg/kg, s.c.) displayed no substitution for the ketamine cue (23% and 33% of ketamine-lever responding, respectively). In addition, the psychostimulant methamphetamine (0.1-1 mg/kg, i.p.) also failed to substitute for the ketamine cue (44% of ketamine-lever responding). Furthermore, an atypical antipsychotic agent clozapine (1 mg/kg, s.c.) that interacts with multiple receptors blocked the discriminative stimulus actions induced by any doses of ketamine, whereas the dopamine D2 receptor antagonist sulpiride (40 mg/kg, i.p.) did not have any effects on the ketamine dose-response curve of discriminative effects.
Conclusions: These findings suggest that NR2A-containing NMDA receptor antagonism may be critical for the expression of the discriminative stimulus effect induced by ketamine. Furthermore, the multiple interactions with multiple receptors as well as NMDA receptor may contribute to the expression of the discriminative stimulus effect induced by ketamine.
Financial Support: Grants from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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GENDER DIFFERENCES IN MDMA-INDUCED CYP2D6 AUTOINHIBITION IN HUMANS.

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Aims: 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) is a synthetic compound structurally related to stimulants and hallucinogens. MDMA is predominantly O-demethylenated in humans by the polymorphic enzyme cytochrome P450 isoform 2D6 (CYP2D6), CYP1A2 and CYP3A4. This drug is also a mechanism-based inhibitor or CYP2D6. Gender differences in MDMA induced CYP2D6 inhibition were studied.
Methods: A controlled clinical trial was conducted in 12 healthy female and 15 healthy male subjects which were extensive metabolizers for CYP2D6 activity. Dextromethorphan (DEX) was used as a CYP2D6 probe drug. On day 1, 30 mg of DEX (1.4 mg/kg) were administered alone, on day 2 a single oral dose MDMA was given and 4 hours later DEX was administered. DEX was repeatedly administered in the following days (about 10 days) until its clearance returned to baseline. The urinary metabolic ratio (MR) DEX/dextrorphan was used to assess the time course of CYP2D6 recovery and to make comparisons between genders.
Results: Urinary MR increased almost 50-fold in women from 0.0220 ± 0.0273 to 0.9881 ± 0.4388 after MDMA administration whereas there was a 100-fold increase in men (from 0.0061 ± 0.0056 to 0.4322 ± 0.2848 after MDMA administration). These differences between genders in MR were statistically significant in day 1 ($p = 0.032$; $F = 5.189$) and in day 2 ($p = 0.048$; $F = 4.309$) but they disappeared once CYP2D6 recovers its activity over the time. DEX urinary levels were higher in women in each time period but were significantly different at 4-12h ($p = 0.008$; $F = 8.453$) and 24-32 h after MDMA intake ($p = 0.039$; $F = 4.767$).
Conclusions: Urinary data shows that, while 48h after MDMA administration CYP2D6 recovery pattern is similar in both genders, MR in women are higher than in men. Taken together, our results indicate that CYP2D6 inhibition by MDMA and also its recovery is more relevant in men than in women.
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EXAMINATION OF THE EFFECTS OF THE 830 BP INDEL OPRK1 PROMOTER POLYMORPHISM AND PDYN MRNA LEVELS ON OPRK1 EXPRESSION IN THE CAUDATE FROM POSTMORTEM HUMAN BRAIN.

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Aims: A number of single nucleotide polymorphisms of the human prodynorphin (PDYN) and the kappa opioid receptor (OPRK1) genes have been associated with vulnerability to develop specific addictions. The 830 bp insertion/deletion (indel) in the OPRK1 promoter was associated with alcohol dependence in Caucasians (Edenberg et al, 2008). In this study, we examined (1) the relationship between this polymorphism and levels of the OPRK1 mRNA in the caudate in post-mortem human brains, and (2) the relationship between PDYN and OPRK1 mRNA levels in this region.
Methods: Tissues from postmortem brains were obtained from the Manhattan HIV Brain Bank (The Mount Sinai Medical Center, New York, NY). Using PCR assay and gel electrophoresis, 40 subjects (African Americans, Caucasians, and Hispanics) were genotyped for the OPRK1 indel. In nine subjects, levels of PDYN and OPRK1 mRNA in the caudate were measured using a quantitative real time RT-PCR assay, normalized with GAPDH. Three subjects were homozygous for the 830 bp insertion, three were homozygous for the deletion, and three were heterozygous, who were selected for expression analysis.
Results: No correlation was found between the OPRK1 indel with OPRK1 mRNA levels. As expected, there was higher expression of PDYN in the caudate compared to OPRK1. Interestingly, we found an apparent negative correlation between PDYN and OPRK1 mRNA levels ($r = -0.42$), although in this small sample it did not reach statistical significance ($p=0.13$).
Conclusions: Further studies with a larger sample size are needed to characterize the role of the OPRK1 indel and PDYN expression in the regulation of OPRK1 expression and their potential contribution to the development of addictions.
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EFFECT OF VARENICLINE ON CUE-INDUCED CIGARETTE CRAVING: A RANDOMIZED PLACEBO-CONTROLLED STUDY.

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Aims: Varenicline, an alpha4beta2 nAchR partial agonist, is the most recently approved drug for smoking cessation. While clinical trials have shown that varenicline can decrease self-reported craving related to withdrawal, studies investigating the effect of varenicline treatment on cue-induced craving for cigarettes have not been done. The aim of this double-blind, randomized, placebo controlled trial was to investigate the effect of a two-week course of varenicline (standard titrated dosing) on tobacco cue-induced craving in daily dependent smokers who are either light, social drinkers (n=24) (<14 drinks/wk for males; <9 drinks/wk for females; Alcohol Dependence Scale (ADS) < 8) or heavy drinkers (n=24) (>20 drinks/wk for males; >14 drinks/wk for females; ADS >13).
Methods: The Questionnaire of Smoking Urges and Visual Analog Scales were used to assess tobacco craving following neutral or tobacco/alcohol cues at baseline and after 2-weeks of treatment.
Results: Twenty-four heavy drinkers (16M:8F), 36.1±11 years old, who smoked 18.6±5.5 cigarettes per day (FTND 5.5±1.8) and drank an average of 24.5±6.0 drinks per week, completed the study. There was an overall decrease in cigarette consumption over the study period, but with no significant differences between treatment conditions. Among the heavy drinkers, VAS cue-induced cigarette craving decreased from baseline to post-treatment in the varenicline-treated group (n=13) (58.9 ± 5.3 to 28.5 ± 7.6; $p=0.002$) but not the placebo-treated group (n=11) (41.1 ± 10.3 to 34.5 ± 10.1; $p>0.4$).
Conclusions: Varenicline significantly reduced cue-induced cigarette craving in heavy drinkers. Comparison data from the social drinker group will also be presented.
Financial Support: This research was supported through the Canadian Institutes of Health Research New Emerging Team Grant (LZ, UB)and Tobacco Use in Special Populations Training Grant (PS, GS).

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DO DOPAMINERGIC DRUGS INDUCE A PLACE PREFERENCE IN NORMAL RAT?

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Aims: Hedonistic homeostatic dysregulation (HHD) is a behavioral disorder that was initially described in association with addiction and substance misuse. It is presented as spiraling cycles of misregulation of the brain reward systems, increasing progressively and resulting in compulsive drug use and loss of control over drug taking. In Parkinson's disease (PD), the equivalent of HHD is called dopamine dysregulation syndrome (DDS). It is defined by severe dopamine addiction to dopaminergic replacement therapy (DRT) and behavioral disorders such as hypersexuality, pathological gambling, compulsive buying, and psychopathological states. The high consumption of DRT could be linked to the motor improvement or could be induced by the powerfull addictive capacity of these molecules.
Our hypothesis is repeated dopaminergic drugs administrations in normal rats induce a place preference.
Objective : The potential rewarding effect of different selective dopaminergic agonists (DA) for D1, D2, D3 receptors and Levodopa will be assess using the conditioned place preference (CPP) test in normal rats.
Methods: To highlight the rewarding effects of DA and Levodopa in the control rat, CPP test will be performed on 8 rats per drug and per dose.
Drugs tested are R(+)-SKF-81 297 (selective D1 receptors agonists ; 1.0, 3.0 and 10.0 mg/kg), Bromocriptine (selective D2 receptors agonists ; 0.1, 1.0 and 10.0 mg/kg), (+)-PD 128 907 (selective D3 receptors agonists ; 0.3, 1.0 and 3.0 mg/kg) and Levodopa (50, 100 and 200 mg/kg).
Results: Only 3mg/kg of SKF-81297, 1.0mg/kg of Bromocriptine and 1.0mg/kg of PD 128 907 produced a significant place preference. Levodopa, as saline in control rats, didn't induced a place preference in normal rats.
Conclusions: Our hypothesis about the addictive power of dopaminergic agonists was confirmed by this pre-clinical study. The next step will be to study the impact of these molecules on a rat model of PD, a neurological disease known to facilitate addictive behaviors and directly concerned by these therapeutic drugs.
Financial Support: APIS

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TETRAHYDROISOQUINOLINES AS OREXIN-1 RECEPTOR ANTAGONISTS: STRUCTURE-ACTIVITY RELATIONSHIPS.

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Aims: Orexins and the orexin receptors have been implicated in a wide range of physiological functions including sleep/wake cycle regulation, energy homeostasis, neuroendocrine function, and feeding and reward. ACT-078573 (almorexant), a tetrahydroisoquinoline derivative, has been shown to be a potent dual OX1/OX2 receptor antagonist in vivo. Interestingly, limited structure-activity relationship results showed that minimal structural modifications could significantly change the selectivity of this class of compounds. This study is to further study the SAR of these tetrahydroisoquinolines, with the aim that selective OX1 and OX2 antagonists will be developed.
Methods: Target compounds were fully characterized and then evaluated in a calcium-dependent functional assay using a FlexStation II 384 and the calcium-4 dye kit in RD-HGA16 (Molecular Devices) cell lines stably expressing the OX1 receptor.
Results: Substitutions at various positions were examined and the results will be presented. For instance, 7-position alkyl ethers on tetrahydroisoquinoline with substituents including butyl or hexyl displayed potency comparable to the tetrahydropapaverine parent compound. Replacement of the 1-benzyl group with groups such as 4-aminophenylmethyl or naphthylmethyl also did not affect the potency. Analogs modified at the amido position with groups such as 3-dimethylaminopropyl were inactive as OX1 antagonist.
Conclusions: We have synthesized a series of tetrahydroisoquinolines that are based on the structure of ACT-078573 and characterized them using a calcium mobilization functional assay. We have identified positions sensitive to substitutions such as the amido position and locations having tolerance for steric bulk such as the 7-position. The SAR results obtained will help develop antagonists selective for the OX1 or OX2 receptors.
Financial Support: NIDA DA026582

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EFFECTS OF COCAINE PLACE CONDITIONING, CHRONIC ESCALATING-DOSE "BINGE" PATTERN COCAINE ADMINISTRATION AND CHRONIC WITHDRAWAL ON POMC GENE EXPRESSION IN RAT HYPOTHALAMUS.

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Aims: Recent studies suggest a role for the pro-opiomelanorcortin (POMC) gene and its derived peptides in the modulation of cocaine reward and addiction-like behaviors in rodents. In this study, we determined whether POMC gene expression levels in the medial hypothalamus (MH, including arcuate nucleus), amygdala and anterior pituitary of Sprague-Dawley rats are altered following: (1) cocaine (10-30 mg/kg, i.p.) conditioned place preference (CPP); (2) chronic (14 days) cocaine exposure using both steady-dose (45 mg/kg/day) and escalating-dose (45 to 90 mg/kg/day) "binge" pattern administration; and (3) acute (1 day) and chronic (14 days) withdrawal from cocaine.
Methods: Exp 1: rats received CPP testing 4 days after the last conditioning session (5 injections of 0, 10 or 30 mg/kg cocaine over 10 days) or after the same pattern of cocaine injections without conditioning; Exp 2: chronic steady-dose (45 mg/kg/day for 14 days) or escalating-dose (45 mg/kg on day 1 up to 90 mg/kg on day 14) "binge" cocaine administration; Exp 3: acute (1 day) or chronic (14 days) withdrawal from steady-dose or escalating-dose "binge" cocaine. POMC mRNA levels were quantitatively measured using solution hybridization/RNase protection assay.
Results: POMC mRNA levels were increased after cocaine place conditioning (10 mg/kg), but not after cocaine in the same pattern without conditioning, in the MH only. Cocaine CPP had no effect on plasma ACTH or corticosterone levels. Decreased MH POMC mRNA levels were observed after chronic escalating-dose, but not steady-dose, cocaine administration. Moreover, acute withdrawal from chronic escalating-dose cocaine led to an increase in POMC mRNA levels in the MH, which persisted into chronic withdrawal.
Conclusions: Alteration of POMC gene expression is region-specific after cocaine place conditioning, and dose-dependent after chronic exposure. Increased POMC gene expression in the MH may contribute to the increased propensity for cocaine seeking behavior during withdrawal.
Financial Support: NIDA-P60-05130 (MJK)

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SEXUALLY DIMORPHIC PATTERN OF STRIATAL PKA SIGNALING RESPONSES MAY MEDIATE COCAINE-INDUCED SENSITIZATION AND TOLERANCE.

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Aims: Studies have shown sexually dimorphic patterns in behavioral responses to cocaine in all phases of cocaine addiction and these sex-specific differences may reside in the disparate regulation of dopamine - PKA signaling. We sought to determine the contribution of this pathway to the known sex differences in cocaine-induced behavioral sensitization and tolerance.
Methods: Ambulatory and rearing responses and protein levels of PKAc, p-CREB, FosB, delta-FosB, Cdk5, and p35 in the nucleus accumbens (NAc) and caudate-putamen (CPu) were measured in male and female rats after 1 to 14 days of administration of saline or cocaine (15 mg/kg; ip).
Results: Female rats exhibited higher cocaine-induced behavioral responses and developed faster sensitization and tolerance than males. Whereas females developed behavioral sensitization to cocaine after 2 days and tolerance after 14 days, male rats developed sensitization after 5 days. Female rats also demonstrated faster changes in protein levels in the NAc and CPu than male rats (NAc: by 2 days p-CREB decreased and FosB increased in females whereas in males all six proteins increased after 5 days; CPu: in females FosB levels were increased after 2 days and PKAc, p-CREB, Cdk5, and p35 increased after 14 days whereas in males FosB and delta-FosB were increased after 5 days of cocaine treatment). In female rats, behavioral activity was positively correlated with FosB levels in the NAc and CPu, and negatively correlated with Cdk5 and p35 in the CPu.
Conclusions: Thus, a sexually dimorphic pattern of cocaine-induced PKA intracellular responses appears to underlie sensitizations and tolerance to cocaine.
Financial Support: This work was supported by SCORE 506-GM60654, MIDARP DA12136, and RCMI RR-03037.

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METHADONE-ASSOCIATED DEATHS BY FORMULATION AS REPORTED BY THE RESEARCHED ABUSE, DIVERSION AND ADDICTION-RELATED SURVEILLANCE SYSTEM.

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Aims: To describe methadone-associated deaths by formulation as reported to RADARS System poison centers (PC).
Methods: PCs use a standard electronic system to record calls from the public. RADARS System PCs cover 44 states (84% of the US population) and perform quality checks to verify coding accuracy. We describe deaths associated with methadone by formulation (2006-2008).
Results: 180 methadone-associated deaths were reported. Mean age was 35.9 years (SD 13.7), and a majority (63.9%) were male. Fifty-five (30.6%) were associated with tablets, 5 (2.8%) with liquids, 3 (1.7%) with diskettes and 117 (65.0%) were not classifiable due to incomplete data. 114/142 (80.3%) deaths were associated with intentional exposures (55 suspected suicides, 2 intentional misuse, 38 intentional abuse and 19 intentional unknown). In 28 of the deaths, patients co-ingested other substances (21.4% opioids, 57.1% benzodiazepines, 25% psychotropics, 10.7% ethanol and 17.9% illicit drugs).
Conclusions: Of available data, most deaths are associated with tablet exposures. However, we cannot create a point estimate for deaths associated with methadone tablets as drug formulation information was not available for many exposures. Our conclusions are limited to cases reported to PCs.
Financial Support: Denver Health is a public non-profit organization providing data to industry, regulatory agencies and researchers through the RADARS System.

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THE USE OF THE ASSIST AMONG HIV-POSITIVE PATIENTS ON REGULAR ANTIRETROVIRAL THERAPY IN SOUTHERN BRAZIL.

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Aims: Few studies have used specific screening tools to detect risky use of psychoactive substances among HIV-positive people in Brazil. The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) was developed by Word Health Organization as a drug use screening tool and later validated in Brazil. Aim: to use the ASSIST as a screening tool in a sample of HIV-positive people attending an infectious disease outpatient clinic in Southern Brazil.
Methods: 41 HIV-positive patients who attended an infectious disease clinic completed the ASSIST during a clinical interview.
Results: 63.4% (n=26) of individuals were male. The mean age was 38.1 years (range=27-62). The majority of participants was from lower socio-economic strata and had incomplete primary school education. The most commonly consumed substances were tobacco (n=27, 65.8%); alcohol (idem); cannabis (n=10, 24.4%); cocaine (n=6, 14.6%); sedatives (n=1, 2.4%) and hallucinogens (ibid). Four participants (9.75%) never used any substance. In addition, 70.3% (n=19) of patients with tobacco use and 26% (n=7) of those who consumed alcohol were at a moderate risk of harm, which would recommend a brief intervention. In addition, 18.5% (n=5) of tobacco users and 3.7% (n=1) of alcohol users were at a high-risk category, which would recommend a brief intervention and referral to further treatment. Eighty percent of cannabis users and 83.3% of those who consumed cocaine/crack were at moderate risk of harm. One participant reported use of sedative/sleeping pills, while another participant reported use of hallucinogens, being both at low risk of problems related to the use of these substances.
Conclusions: These preliminary results attest to the usefulness of the ASSIST as a screening tool for substance use among HIV-positive people in Brazil. The results of this study suggest that substance use is a common and adverse phenomenon among HIV-positive patients who attend infectious diseases outpatient clinics in Southern Brazil.
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DRUG USE AND SEXUALLY TRANSMITTED INFECTIONS IN RURAL NORTH CAROLINA.

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Aims: The rural south is suffering from high rates of HIV and other sexually transmitted infections (STIs).
Methods: Respondent driven sampling (RDS) was used to recruit drug users, men who have sex with men (MSM) and sexual partners of these groups. Between 2005 and 2008, participants were recruited in two rural counties in central North Carolina and tested for HIV, syphilis, gonorrhea and Chlamydia. Bivariate analyses were conducted to identify variables that were associated with a current STI. Variables that were significant at $p < 0.20$ were entered into a multiple logistic regression analysis to identify variables that were independently associated with testing positive for an STI.
Results: The sample was 50% female, 63% African-American and 36% non-Hispanic white. The mean age was 37.9 and the median age was 37 years. Prevalence was 3.1% for syphilis, 4.9% for gonorrhea, 4.1% for Chlamydia and 10.4% for any of these STIs. HIV prevalence was 6.9%. Binge drinking in the previous 30 days was reported by 56%, crack use by 38%, powder cocaine use by 40% and methamphetamine use by 4% of participants. No drug use or demographic variables were associated with STI infection in bivariate analyses. In multivariate analyses being incarcerated within the previous 2 years was the only variable significantly associated with current STI infection (Odds Ratio [OR]=2.35; 95% Confidence Interval [C.I.] = 1.21, 4.56).
Conclusions: STIs were prevalent among rural drug users, MSM and their sexual partners. Although we examined a variety of sexual risk behaviors and drug use variables, none of these were clearly associated with prevalent STI infection in this sample. However a recent history of incarceration was associated with increased risk of STI infection and having at least a high school education was associated with decreased odds of prevalent STI infection. More research is needed to understand the factors driving the STI epidemic in rural North Carolina.
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CHARACTERISTICS OF HIV AND HBV MONO AND CO-INFECTIONS AMONG BLACK SOUTH AFRICAN DRUG USERS.

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Aims: South Africa has high rates of HIV and HBV, and these viruses frequently occur co-morbidly. Co-infection has been associated with adverse health outcomes and a reduced survival rate, and is particularly common among drug using populations. However, few studies have examined the risk factors for co-infection among drug users in this region. Therefore, the present study sought to examine risk factors for HIV and HBV mono and co-infections among black drug users recruited from Pretoria, South Africa.
Methods: This cross-sectional study included 378 black South African drug users from the Pretoria Region aged 18-40 years of age. Descriptive statistics were used to describe the sample. Chi-Square tests were used to examine the association between infection status (HIV mono-infection, HBV mono-infection, HIV/HBV co-infection, or no infection), and various sociodemographic characteristics.
Results: Of the 372 black South African drugs users, 173 had no infection, 65 had HBV mono-infection, 76 had HIV mono-infection, and 60 had HBV/HIV co-infection. Bivariable chi-square analyses indicated significant associations between infection status and living with a parent or grandparent ($\chi 2(df)=17.7$ (3), p=.001), having traded sex for money during the past six months ($\chi 2(df)=51.1(3)$, p<.001) and having traded sex for survival during the past six months ($\chi 2(df)=43.9(3)$, p<.001).
Conclusions: When compared to drug users who lived with a parent or grandparent, drug users who were not in this type of living situation were more likely have HIV or HBV infections, and even more likely to have both infections. Similar trends were observed for individuals who traded sex for money or survival in the past six months, such that those who traded sex were more likely to be co-infected. The study findings demonstrate the importance of interventions that integrate the family in the treatment of drug-using populations in order to minimize the health risks of this group.
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